✓2021 Edition

Yao & Artusio's ANESTHESIOLOGY

Problem-Oriented Patient Management

NINTH EDITION

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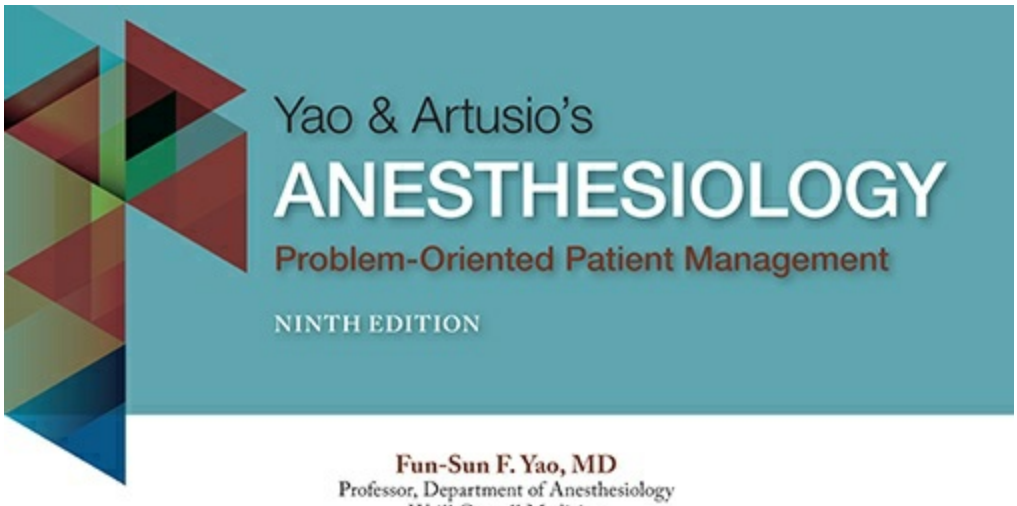

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This book is dedicated to the late
***Joseph F. Artusio Jr., MD**, who taught us not*
only to be good anesthesiologists but also to become
better persons.

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Jaroslav K. Usenko and Fun-Sun F. Yao

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Alessia Pedoto, Paul M. Heerdt, and Fun-Sun F. Yao

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Yasdet Maldonado, Nikolaos J. Skubas, and Fun-Sun F. Yao

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Lisa Q. Rong, Mudit Kaushal, and Adam D. Lichtman
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D.1. When and how is a patient weaned off IABP support?

D.2. How is weaning from ECMO accomplished?

7 Valvular Heart Disease

Meghann M. Fitzgerald and Natalia S. Ivascu

A. Medical Disease and Differential Diagnosis

A.1. What are the major etiologies of AS, AI, mitral stenosis (MS), and MR?

A.2. What are the major changes in the loading conditions of the LV that result from the four different lesions? Why do they occur? What changes result from them?

A.3. What are pressure–volume (P–V) loops? What do the different inflection points represent?

A.4. What are representative P–V loops for the four valvular lesions?

A.5. Draw the pressure/time curves for the LV, left atrium, pulmonary artery, and aorta for a normal patient and for patients with each of the four valvular lesions.

Aortic Stenosis

Aortic Insufficiency

Mitral Stenosis

Mitral Regurgitation

A.6. What are the basic principles of echocardiography? What are M-mode, B-mode, and Doppler color modalities? How do TTE and transesophageal echocardiography (TEE) differ?

A.7. What are the three TEE vantage points for the comprehensive imaging of the LV? How are pressure gradients measured by echocardiography? How do the pressure gradients derived from Doppler echocardiography differ from those obtained in the catheterization laboratory by direct pressure measurement?

A.8. What is the role for three-dimensional (3D) echocardiography in the operating room?

A.9. *What are the echocardiographic and cardiac catheterization criteria for the four valvular lesions?*

Aortic Stenosis
Aortic Insufficiency
Mitral Stenosis
Mitral Regurgitation

B. Preoperative Evaluation and Preparation

B.1. *What are the presenting signs and symptoms of the four valvular lesions listed previously?*

Aortic Stenosis
Aortic Insufficiency
Mitral Stenosis
Mitral Regurgitation

B.2. *What is the New York Heart Association classification of heart failure?*

B.3. *Discuss the role of premedication for patients with the four different valvular lesions.*

B.4. *How would you premedicate the patient with severe AS and MR?*

C. Intraoperative Management

C.1. *Outline the hemodynamic management goals for each of the four valvular lesions. What are the anesthetic goals with respect to heart rate and rhythm, preload, afterload, and contractility?*

Aortic Stenosis
Aortic Insufficiency
Mitral Stenosis
Mitral Regurgitation

C.2. *What are the hemodynamic goals for this patient with the combination of severe AS and MR?*

C.3. *How would you monitor this patient with severe AS and MR?*

C.4. *Should the patient have a pulmonary artery catheter placed*

before induction?

C.5. *Is a pulmonary artery catheter with pacing capabilities indicated?*

C.6. *What anesthetic technique would you employ? Why?*

C.7. *What muscle relaxant would you use for this patient?*

C.8. *What are the usual TEE findings in a patient with AS or MR? How do you grade the severity of AS by TEE? How do you quantify the severity of MR? What is the impact of AS on the severity of MR?*

C.9. *What special considerations particular to cardiopulmonary bypass (CPB) operations do you have for each of the four lesions? Focus on these concerns with respect to the induction and prebypass, bypass, and postbypass periods.*

Aortic Stenosis
Aortic Insufficiency
Mitral Stenosis
Mitral Regurgitation

C.10. *The patient cannot be weaned from CPB following an AV replacement and MV replacement. What are the possible causes?*

C.11. *How would you diagnose right-sided heart failure and pulmonary hypertension? How would you treat it?*

C.12. *How does an intra-aortic balloon pump (IABP) work to benefit the failing heart?*

C.13. *What role does the IABP have in this setting?*

C.14. *What role does TEE play in the placement, timing, and demonstration of efficacy of an IABP?*

C.15. *How would you properly time the IABP cycle?*

C.16. *What are the contraindications to the use of an IABP?*

C.17. *What is the role for ventricular assist devices?*

D. Postoperative Management

D.1. *In the intensive care unit (ICU) 4 hours later, the patient became hypotensive with a low cardiac output. How could*

you distinguish between cardiac tamponade and pump failure? How would the TEE images differ?
D.2. *Would you extubate this patient early in the ICU? Why?*
D.3. *What are the advantages and disadvantages of early extubation?*
E. Alternative Treatments
E.1. *What are the percutaneous options for MV repair?*
E.2. *How is percutaneous MV repair performed?*
E.3. *What are the percutaneous options for AV repair and replacement?*
E.4. *How is percutaneous AV replacement performed?*
E.5. *What anesthetic techniques and monitors are used?*
E.6. *What is minimally invasive cardiac valve surgery?*

8 Pacemakers, Implantable Cardioverter-Defibrillators, and Cardiac Resynchronization Therapy Devices
Alan Cheng and Fun-Sun F. Yao
A. Medical Disease and Differential Diagnosis
A.1. *What are the indications for PPMs?*
A.2. *What is sick sinus syndrome? What is chronotropic incompetence?*
A.3. *How would you diagnose first-, second-, and third-degree AV block; bifascicular block (right bundle branch block [RBBB] with left anterior fascicular hemiblock or left posterior fascicular hemiblock); and trifascicular block?*
A.4. *Is it necessary to insert a temporary pacemaker before general anesthesia for an asymptomatic patient with bifascicular or trifascicular block?*
A.5. *What are the three-letter and five-letter identification codes of the North American Society of Pacing and Electrophysiology (NASPE) and British Pacing and Electrophysiology Group (BPEG) generic (NBG) code for pacemaker classification?*
A.6. *How many modes of pacing are available in modern PPMs?*

How do they work? What is the difference between DDD pacing and DDI pacing?

A.7. *The patient was mechanically hyperventilated during surgery, and her pacemaker gradually increased her heart rate. What feature of the PPM is accounting for this?*

A.8. *What are the advantages and disadvantages of atrial pacing only? What are the disadvantages of right ventricular pacing only?*

A.9. *What are the indications for and complications associated with AV sequential PPMs?*

A.10. *How would you know if the patient's PPM was atrially, ventricularly, or atrioventricularly sequentially pacing?*

A.11. *What is a biventricular PPM or CRT device? What are the indications for such a device?*

A.12. *What are the usual lifespans of PPMs and implantable cardioverter-defibrillators (ICDs)?*

A.13. *What is an ICD? How does it work? What is a subcutaneous ICD?*

A.14. *What are the indications for ICDs?*

A.15. *What is the NASPE and BPEG generic defibrillator (NBD) code?*

B. Preoperative Evaluation and Preparation

B.1. *How would you preoperatively evaluate the patient described earlier?*

B.2. *How do you determine whether the patient has a cardiac implantable electronic device (CIED) and define what type of CIED?*

B.3. *How do you determine whether the patient is dependent on the pacing from the CIED?*

B.4. *How do you know if the implanted PPM or ICD is working?*

B.5. *What information would you like to obtain from interrogating this device?*

B.6. *How do you preoperatively prepare the patient for surgery*

and anesthesia?

B.7. *Would you recommend reprogramming this device to asynchronously pace before surgery? What would you recommend regarding the ICD functions of the device?*

B.8. *The patient requires an abdominal magnetic resonance imaging (MRI) prior to the surgery. What considerations should you make regarding her CIED?*

C. Intraoperative Management

C.1. *How would you monitor this patient?*

C.2. *What drugs and equipment would you like to have on hand in the operating room?*

C.3. *How would you set up the transcutaneous external pacer and defibrillator?*

C.4. *Had this patient's ICD been implanted the day before surgery, would you consider avoiding certain inhalational gases for anesthesia?*

C.5. *Electromagnetic interference (EMI) from electrocautery results in significant noise on your cardiac monitor. You recall that EMI also can inhibit pacing function from the PPM. In this pacemaker-dependent patient, how can you determine whether inappropriate inhibition of the PPM is occurring?*

C.6. *What are the potential responses of pacemakers and ICDs to electrocautery?*

C.7. *How would you prevent the effects of EMI on the pacemaker or ICD from the electrocautery?*

C.8. *What are the effects of a magnet on pacemakers and ICDs?*

C.9. *In the middle of surgery, the patient developed ventricular tachycardia. What would you do?*

C.10. *What precautions should be taken when a patient with a CIED is undergoing extracorporeal shock wave lithotripsy (ESWL)?*

C.11. *Is electroconvulsive therapy (ECT) contraindicated in*

patients with pacemakers or ICDs?

C.12. What precautions should be taken during radiofrequency ablation for a patient with a CIED?

C.13. During surgery, the patient developed frequent premature ventricular complexes and some of these resulted in rapid ventricular pacing (see Fig. 8.8). What is accounting for the pacemaker's behavior?

D. Postoperative Management

D.1. How would you monitor this patient in the postanesthesia care unit?

D.2. How would you confirm that the CIED is functioning properly after surgery?

9 Thoracic and Thoracoabdominal Aortic Aneurysms

Yong Zhan, Frederick C. Cobey, Sharon L. McCartney, Madhav Swaminathan, and Jamel Ortoleva

A. Pathophysiology and Differential Diagnosis

A.1. What is a thoracic aortic aneurysm (TAA) and TAAA, and how do they typically present?

A.2. How are TAAs and TAAAs classified?

A.3. What is the pathogenesis of aortic aneurysms and what genetic conditions predispose to their formation?

A.4. What are the risk factors for TAA rupture?

A.5. What is the natural history and medical management of thoracic aneurysms?

A.6. What is a thoracic aortic dissection, and how does it typically present?

A.7. How are thoracic aortic dissections classified?

DeBakey Classification

Stanford Classification

Penn Classification

B. Preoperative Evaluation and Preparation

B.1. What are the indications and timing of surgical intervention for TAAs?

- *B.2. Which patients are candidates for endovascular aortic repair, and what are the advantages to this approach?*
- *B.3. What are the preoperative considerations for the anesthesiologist before TAA repair?*
  - Cardiovascular
  - Respiratory
  - Renal
  - Neurologic
- *B.4. What is the preoperative management of a patient presenting with an acute aortic dissection (AAD)?*
- *B.5. What is the spinal cord blood supply?*

C. Intraoperative Management

- *C.1. What are the surgical approaches to thoracic aneurysm repair?*
  - Ascending and Arch Aortic Aneurysms
  - Thoracoabdominal Aneurysms
- *C.2. How is the open repair performed?*
  - Ascending and Arch Aortic Aneurysms
  - Thoracoabdominal Aneurysms
- *C.3. How are endovascular repairs of TAAAs performed?*
- *C.4. What are the surgical approaches to aortic dissections?*
  - Type A Aortic Dissection
  - Type B Aortic Dissection
- *C.5. What are the specific considerations for anesthetic management of the patient presenting for open TAAA repair?*
- *C.6. What are the specific considerations for anesthetic management of the patient presenting for endovascular TAAA repair?*
- *C.7. What hemodynamic monitors should be used for the patient undergoing thoracic aneurysm repair?*
- *C.8. What strategies are used for spinal cord protection during a TAAA repair?*

Left-Heart Bypass
Intraoperative Neuromonitoring
Cerebrospinal Drainage
Hypothermia
C.9. *What strategies are used for mesenteric and renal preservation?*
C.10. *What is the pathophysiology of aortic clamping and unclamping?*
Aortic Clamping
Aortic Unclamping
C.11. *Why does a coagulopathy ensue and how is it prevented/treated?*
D. Postoperative Anesthetic Management
D.1. *What are the postoperative complications after open TAAA repair?*
Respiratory Failure
Renal Failure
Spinal Cord Injury
D.2. *What are the postoperative complications after endovascular TAAA repair?*
Left Upper Extremity Ischemia
Stroke
Spinal Cord Ischemia
Renal Failure
Postimplantation Syndrome
Endograft Collapse
Endoleaks
10 Abdominal Aortic Aneurysm Repair
Fun-Sun F. Yao and Anup Pamnani
A. Medical Disease and Differential Diagnosis
A.1. *What risk factors are associated with an abdominal aortic aneurysm (AAA)?*
A.2. *What other diseases are commonly found in patients with*

aortic aneurysms?

A.3. *What is the incidence of morbidity and mortality in these patients if they undergo elective open surgical repair? What is the natural history of the disease without surgical repair?*

A.4. *What should be done for smaller aortic aneurysms that are found in patients?*

A.5. *What is the risk of perioperative myocardial infarction (MI) in patients with ischemic heart disease? What can be done to reduce the risk of ischemic events in these patients?*

A.6. *Does the morbidity and mortality of elective repair of an aortic aneurysm differ significantly from that of an emergency repair?*

B. Preoperative Evaluation and Preparation

B.1. *Which preoperative laboratory tests would you require for this patient?*

B.2. *What is the significance of the preoperative ECG? Would you wish to pursue a preoperative cardiac workup? What tests would you request, and what would they tell you?*

B.3. *Is it necessary to evaluate this patient's pulmonary status?*

B.4. *Preoperative arterial blood gas (ABG) measurement shows pH, 7.35; $Paco_2$, 47 mmHg; and Pao_2, 68 mmHg on room air. What is the significance of this result?*

B.5. *How would you measure creatinine clearance in this patient, and what is its value in this case?*

B.6. *Describe the blood flow to the spinal cord. What is its relevance to surgery involving the abdominal aorta?*

B.7. *How do you detect spinal cord ischemia?*

B.8. *What are the various surgical approaches to repair an AAA?*

B.9. *How does the choice of surgical technique affect the anesthetic management?*

B.10. *How would you premedicate this patient?*

C. Intraoperative Management

C.1. *Would you use an arterial line? What are the complications of arterial line placement?*

C.2. *What various monitors are available for myocardial ischemia? Is a pulmonary artery catheter (PAC) helpful in determining the occurrence of ischemia?*

C.3. *What additional monitors would you employ?*

C.4. *Is there a role for somatosensory evoked potential (SSEP) monitoring during aortic clamping?*

C.5. *How would you anesthetize this patient for an open repair of the aorta? What techniques could be used for an endovascular aortic aneurysm repair? Discuss the various anesthetic techniques that can be employed for this surgery.*

C.6. *This patient is to be heparinized intraoperatively, and anticoagulation may be continued postoperatively. Is this a contraindication to the preoperative placement of either an epidural or intraspinal catheter? What if the patient is receiving anticoagulants in the preoperative period?*

C.7. *What are your plans for fluid and blood replacement during surgery?*

C.8. *What are the hemodynamic changes of aortic cross-clamp placement? What efforts can be made to minimize these changes both before and during cross-clamping? If the patient develops ST-segment depressions with a rising pulmonary capillary wedge pressure (PCWP) during cross-clamp, what maneuvers should be taken?*

C.9. *Because this case involves an infrarenal aneurysm, is renal blood flow affected with the placement of the cross-clamp? If an endovascular repair is chosen, what are the risks to the kidneys? Are there any treatment maneuvers that can be taken to minimize these risks in either repair?*

C.10. *What are the hemodynamic consequences of aortic cross-clamp removal? What can be done to minimize the effects of removing the aortic cross-clamp? If the systemic blood*

pressure remains depressed after removal of the cross-clamp, what is the differential diagnosis? How would you diagnose and correct the problem?

D. Postoperative Management

D.1. What are the parameters used to extubate this patient?

D.2. What are the anticipated changes in postoperative pulmonary function in these patients? How does the surgical technique affect postoperative pulmonary function? Are there any postoperative maneuvers that can improve respiratory parameters?

D.3. How would you control postoperative pain? What are the alternatives in the management of this patient's postoperative pain?

11 Hypertension

Christopher W. Tam and Fun-Sun F. Yao

A. Medical Disease and Differential Diagnosis

A.1. Define hypertension and categorize its severity.

A.2. What is the prevalence of hypertension?

A.3. What is the general classification of hypertension? Enumerate the causes of each type of hypertension.

Etiology of Hypertension

A.4. What are the clinical patterns of hypertension encountered?

A.5. What is the pathophysiology of essential hypertension?

A.6. What is the pathophysiology of isolated systolic hypertension (ISH) and of pulse pressure hypertension (PPH)?

A.7. What are the end-organ damages caused by long-standing hypertension?

Cardiac Involvement

Eye Involvement

Renal Involvement

Cerebral Involvement

A.8. Are hypertensive patients at an increased risk for

perioperative cardiac morbidity?

A.9. Perioperative cerebral and renal complications are mostly associated with which subtype of hypertension?

A.10. Would you employ a controlled hypotensive technique for hypertensive patients? How much would you safely lower the BP?

A.11. What are the BP goals for patients with hypertension and when should antihypertensive drugs be initiated?

A.12. What is the mechanism of action of antihypertensive drugs?

Diuretics
Antiadrenergic Agents
Direct Vasodilators
Dopaminergic Agonists
Calcium Channel Blockers
Angiotensin-Converting Enzyme Inhibitors
Angiotensin II Receptor Blockers
Other Vasodilators

A.13. Does the choice of antihypertensive therapy influence hemodynamic responses to induction, laryngoscopy, and intubation?

A.14. Does chronic angiotensin-converting enzyme (ACE) inhibition influence anesthetic induction?

B. Preoperative Evaluation and Preparation

B.1. How would you evaluate this patient preoperatively?

B.2. Would you postpone the surgery? Why? What BP would you like the patient to achieve before surgery?

B.3. Should all or any of the chronic medications be discontinued before the operation?

B.4. Should hypokalemia be treated before anesthesia? Why?

B.5. Should hypomagnesemia be treated before anesthesia? Why?

B.6. Does an asymptomatic carotid bruit increase the risk in these patients?

B.7. *The surgery was postponed for 6 weeks. The patient was on metoprolol, aspirin, atorvastatin, captopril, hydrochlorothiazide, and potassium chloride. His BP was 160/60 mmHg and potassium 4.0 mEq per L. How would you premedicate this patient?*

B.8. *If the patient is an untreated hypertensive patient with BP 170/70 mmHg, would you treat the patient preoperatively with an antihypertensive agent?*

C. Intraoperative Management

C.1. *How would you monitor this patient?*

C.2. *What are the anesthetic goals for hypertensive patients?*

C.3. *How would you induce anesthesia for the hypertensive patient?*

C.4. *How does tracheal intubation produce hypertension?*

C.5. *What happens to the left ventricular ejection fraction during and immediately following intubation?*

C.6. *What other measures can prevent hypertension and tachycardia at the time of intubation?*

C.7. *After induction and intubation, the BP decreased to 70/40 mmHg. What would you do?*

C.8. *What is your choice of agents for maintenance of anesthesia? Why?*

C.9. *How would you manage fluid therapy for hypertensive patients?*

C.10. *During the surgery, BP increased to 220/120 mmHg. How would you treat the hypertension?*

C.11. *What could you do to prevent hypertension during extubation and emergence?*

C.12. *Would you consider regional anesthesia for this patient?*

D. Postoperative Management

D.1. *The patient developed hypertension, BP 210/110 mmHg, in the postanesthesia care unit. What would you do?*

12 Cardiac Tamponade

June M. Chan

A. Medical Disease and Differential Diagnosis

A.1. What is the differential diagnosis of low CO following cardiac surgery?

A.2. Describe the pathophysiology of cardiac tamponade.

A.3. What are the common etiologies of cardiac tamponade?

A.4. What is the difference between acute and delayed cardiac tamponade?

A.5. What is regional cardiac tamponade?

A.6. Describe the ventricular interaction in cardiac tamponade.

A.7. How is coronary blood flow affected in cardiac tamponade?

A.8. What is the Beck triad? Describe the typical signs and symptoms of cardiac tamponade.

A.9. Define pulsus paradoxus and describe its pathophysiology.

A.10. What is Kussmaul sign? Is this finding consistent with tamponade physiology?

A.11. Which medical conditions mimic cardiac tamponade?

B. Preoperative Evaluation and Preparation

B.1. Interpret and explain the pathophysiologic basis for this patient's hemodynamic findings.

B.2. How would you optimize this patient's cardiovascular status prior to definitive diagnosis and treatment?

B.3. What are the radiographic findings in tamponade?

B.4. A limited bedside transthoracic echocardiogram is performed, demonstrating a layer of clotted blood anterior to the right atrium (RA) and ventricle. What echocardiographic findings support the diagnosis of tamponade?

B.5. What additional information should be obtained from a limited echocardiographic study?

B.6. Describe the procedures for treating cardiac tamponade. What are the clinical indications for each approach?

B.7. *Having made the diagnosis of tamponade, what additional investigations are required prior to surgery?*

B.8. *Explain the technical and physiologic principles behind rotational thromboelastometry.*

B.9. *A rotational thromboelastometry was performed, and a 10-minute analysis reveals the following results (see Fig. 12.9 and Table 12.8). How do you interpret this information?*

B.10. *Given the ROTEM® findings and high clinical suspicion for occult postsurgical bleeding, what hemostatic products would you arrange to have in the operating room?*

B.11. *How would you organize and conduct the transport of this patient to the operating room?*

C. Intraoperative Management

C.1. *What are the cardiovascular effects of commonly used intravenous anesthetic and coinduction agents?*

Propofol
Etomidate
Ketamine
Thiopental
Fentanyl
Midazolam

C.2. *What is the effect of supine positioning and positive pressure ventilation on the hemodynamics of a patient with tamponade?*

C.3. *Describe the induction process for cardiac tamponade.*

C.4. *Following induction and intubation, the systemic blood pressure decreases to 55/30 mmHg. Describe your management.*

C.5. *What hemodynamic changes are frequently associated with opening the pericardial space?*

C.6. *Following the removal of approximately 500 mL of dark blood and clots from the mediastinum, the patient's CO remains low. What are your differential diagnoses?*

C.7. *What is pericardial decompression syndrome (PDS)?*

D. Postoperative Management

D.1. *A pericardial drain is placed following mediastinal decompression. How should this drainage tube be managed?*

D.2. *How would you manage hypertension in the intensive care unit?*

13 Heart Transplantation and Subsequent Noncardiac Surgery

Jeff T. Granton, Ranjana Bairagi, and Davy Cheng

A. Medical Disease and Differential Diagnosis

A.1. *What are the common diagnoses requiring adult heart transplantation?*

A.2. *What are the indications and relative contraindications for recipient selection?*

A.3. *What are the criteria for donor heart selection?*

A.4. *What is the role of donation after cardiac death (DCD) for heart transplantation?*

A.5. *What are the principles of perioperative donor management?*

A.6. *What are the risk factors associated with posttransplant mortality?*

A.7. *What is the difference between the biatrial and bicaval surgical techniques of heart transplant?*

A.8. *When is a combined heart/lung transplant indicated? What are the important differences?*

A.9. *What are the medical and surgical alternatives to cardiac transplantation?*

A.10. *What is the role of ventricular assist devices (VADs) in this type of patient?*

A.11. *What are the considerations in anesthetizing patients for LVAD insertion?*

B. Preoperative Management

B.1. *How would you assess this patient preoperatively?*

B.2. *How would you premedicate this patient? Why?*

C. Intraoperative Management
   - C.1. *What anesthetic equipment and monitors would you set up? Why?*
   - C.2. *What is the role of transesophageal echocardiography (TEE)?*
   - C.3. *Describe the induction and maintenance of anesthesia.*
   - C.4. *How would you manage this patient during cardiopulmonary bypass (CPB)?*

D. Postoperative Management
   - D.1. *What are the early postoperative complications?*
   - D.2. *What are the mechanisms of early right ventricular (RV) failure?*
   - D.3. *How would you treat RV failure following heart transplantation?*
   - D.4. *How does inhaled nitric oxide (NO) work as a selective pulmonary vasodilator?*
   - D.5. *What is the pathophysiology of the denervated heart?*
   - D.6. *What are the common cardiac dysrhythmias following heart transplant?*
   - D.7. *What are the causes of posttransplant bleeding?*
   - D.8. *How would you treat posttransplant bleeding?*
   - D.9. *What are the causes of early graft failure?*
   - D.10. *How would you manage this patient in the intensive care unit?*

E. Subsequent Noncardiac Surgery
   - E.1. *How would you monitor this patient?*
   - E.2. *What type of anesthetic is best for the heart-transplanted patient?*
   - E.3. *What anesthetic technique would you choose for this patient?*
   - E.4. *Do you need to use a muscarinic antagonist with cholinesterase inhibitors to reverse the muscle relaxant in*

heart-transplanted patients?

E.5. *What are the anesthetic implications for heart-transplanted patients?*

E.6. *What is the significant implication of the denervated heart?*

E.7. *What is the significance of allograft rejection?*

E.8. *What is the significance of infection in these patients?*

E.9. *What are the significant implications of drug interactions?*

E.10. *What is cardiac allograft vasculopathy (CAV)? Why is this important?*

E.11. *What is the significant implication of posttransplant hypertension?*

E.12. *What is the significant implication of renal dysfunction?*

E.13. *What types of malignancy are found in recipients?*

E.14. *Is ambulatory surgery appropriate for heart transplant recipients?*

14 Ischemic Heart Disease and Noncardiac Surgery

Christopher Szabo and Manuel Fontes

A. Medical Disease and Differential Diagnosis

A.1. *What are the preoperative predictors for major adverse cardiac events (MACE) perioperatively?*

A.2. *What are the determinants of myocardial oxygen demand? How are they measured clinically?*

A.3. *What factors determine myocardial oxygen supply?*

A.4. *What is the mechanism of perioperative myocardial ischemia and MI?*

A.5. *What is the incidence of perioperative reinfarction for noncardiac surgery?*

A.6. *State the perioperative medical therapy you would employ to reduce the incidence of myocardial ischemia.*

β-Adrenergic Antagonists (Esmolol, Atenolol, Metoprolol, Bisoprolol)

α_2-Adrenergic Agonist (Clonidine)

Nitrovasodilators (Nitroglycerin, Isosorbide Dinitrate)

Calcium Channel Blockers (Verapamil, Diltiazem, Nifedipine, Nicardipine)
Aspirin
Statins

A.7. Based on his MI, would you recommend that the surgery be postponed for a certain period of time? If so, why?

A.8. Would you recommend that this elective colectomy be postponed if the patient underwent placement of a right coronary artery, second-generation DES, and is taking aspirin and clopidogrel (Plavix)?

B. Preoperative Evaluation and Preparation

B.1. How would you evaluate the patient's cardiac condition? What laboratory tests would you like to order?

B.2. Would you recommend further cardiac testing or coronary revascularization before surgery?

B.3. How would you classify the cardiac risk according to the type of surgery?

B.4. What is the role of exercise or pharmacologic stress test for this patient?

B.5. Would you discontinue any medication before surgery?

B.6. How would you premedicate this patient?

B.7. Is there a role for α_2-agonist in premedication?

C. Intraoperative Management

C.1. What are the intraoperative predictors for perioperative MACE?

Intraoperative Predictors

C.2. How would you monitor the patient in the operating room?

C.3. What electrocardiogram (ECG) leads would you monitor? Why lead V_5?

C.4. Would you use a pulmonary artery catheter (PAC)?

C.5. Would you use transesophageal echocardiography (TEE) as a monitor?

C.6. Is regional anesthesia better than general anesthesia for

patients with cardiac disease?
C.7. *How will you induce general anesthesia?*
C.8. *Would you induce anesthesia with etomidate? Why?*
C.9. *What is the best choice of anesthetic agents for maintenance of anesthesia? Why?*
C.10. *You notice a new 3-mm ST-segment depression in lead V_5. How would you treat it?*
C.11. *Would you give prophylactic intravenous NTG to prevent myocardial ischemia?*
C.12. *What is the significance of tight control of the heart rate intraoperatively?*
C.13. *When would you extubate the trachea in this patient? What could you do to prevent hypertension and tachycardia during extubation and emergence?*

D. Postoperative Management
D.1. *What are the postoperative predictors of perioperative MACE?*
D.2. *How would you control postoperative pain?*
D.3. *Is postoperative anemia associated with adverse cardiac outcome?*
D.4. *Is postoperative hypothermia associated with postoperative myocardial ischemia?*
D.5. *How would you make a diagnosis of perioperative MI (PMI)?*
D.6. *How would you manage the patient with a suspected PMI?*

SECTION 3 The Gastrointestinal System

15 Intestinal Obstruction and Enhanced Recovery after Surgery
Leif Ericksen and Tong J Gan

A. Medical Disease and Differential Diagnosis
A.1. *What is the differential diagnosis of the acute abdomen?*
A.2. *What are the causes of intestinal obstruction of the small*

bowel and of the large bowel?

A.3. Differentiate between simple and strangulated bowel obstruction.

A.4. Is it important to differentiate whether the bowel obstruction is located in the small bowel or large bowel? Why? How might the distinction be made?

A.5. What are the causes and effects of bowel distention?

A.6. Describe the fluid shifts during small bowel intestinal obstruction.

A.7. Discuss the systemic derangements that occur with intestinal obstruction.

A.8. What is an ileus? Discuss its causes and pathophysiology.

B. Preoperative Evaluation and Preparation

B.1. What is Enhanced Recovery after Surgery (ERAS)? What are the core tenants of these programs?

B.2. Can ERAS be used in this case?

B.3. What components of ERAS are applied in the preoperative phase of the care of colorectal surgery (CRS) patients?

B.4. Is it important to decompress the abdomen before induction of anesthesia? Why?

B.5. Describe the respiratory implications.

B.6. What are the implications of the tense abdominal wall?

B.7. Outline the methods of abdominal decompression.

B.8. Discuss the goals of fluid management.

B.9. What would you use as a guide to fluid volume replacement?

C. Intraoperative Management

C.1. What dangers are present during induction? How are they planned for?

C.2. Does the administration of antacids and/or histamine-2 (H_2) blockers before the induction of anesthesia have a significant value in patients with small bowel obstruction?

C.3. In what position would you intubate this patient?

C.4. What is the best muscle relaxant to use for the rapid

sequence induction?

C.5. Would you remove or leave the nasogastric tube (NGT) in place before inducing anesthesia?

C.6. Would you use nitrous oxide in this patient?

C.7. Are there any benefits to using a high concentration of inspired oxygen (FIO_2)?

C.8. What components of ERAS are applied in the intraoperative phase of the care of CRS patients?

C.9. What are the strengths, weaknesses, benefits, and challenges of ERAS?

Strengths

Weakness

Benefits

Challenges

C.10. What are the indications for ERAS?

D. Postoperative Management

D.1. What are the principles of postoperative care in this patient?

D.2. Are there any postoperative respiratory problems associated with factors other than aspiration?

D.3. If the patient did aspirate gastric contents, what are the possible sequelae of this event? What is the treatment?

D.4. What is gram-negative sepsis? Describe the clinical picture and treatment.

D.5. What components of ERAS are applied in the postoperative phase of the care of CRS patients?

16 Liver Transplantation

Christopher H. Choi and Vivek K. Moitra

A. Medical Disease and Differential Diagnosis

A.1. What are the potential graft options for liver transplantation?

A.2. What are the indications and contraindications for liver transplantation?

A.3. *What is acute liver failure (ALF)?*
A.4. *What is the MELD score, and how is it used in liver transplantation evaluation?*
A.5. *What is portal hypertension? What are the sequelae of portal hypertension?*
A.6. *Describe the cardiovascular system of patients with end-stage liver disease (ESLD).*
A.7. *What causes acute kidney injury (AKI) in patients with cirrhosis?*
A.8. *What causes hyponatremia in patients with cirrhosis?*
A.9. *Discuss the neurologic manifestations of acute and chronic liver disease.*
A.10. *Why do patients with ESLD have abnormalities of hemostasis?*
A.11. *What is the differential diagnosis for hypoxemia in patients with cirrhosis?*
A.12. *What are the risk factors and treatment guidelines for spontaneous bacterial peritonitis (SBP)?*

B. Preoperative Evaluation and Preparation
B.1. *What preoperative workup is desirable?*
B.2. *How is ascites managed preoperatively?*
B.3. *How is hyponatremia managed preoperatively?*
B.4. *What is a transjugular intrahepatic portosystemic shunt (TIPS) procedure? What is the role of TIPS in the management of patients with ESLD?*
B.5. *How are hepatic encephalopathy and elevated intracranial pressure (ICP) treated?*
B.6. *Should this patient be transfused with fresh frozen plasma prior to surgery?*

C. Intraoperative Management
C.1. *What monitors would you use? Why?*
C.2. *What are the considerations for the induction of anesthesia?*
C.3. *How does liver disease affect intraoperative medication*

management?

C.4. *What happens during the first stage (preanhepatic phase) of the liver transplant operation?*

C.5. *What happens during the second stage (anhepatic phase) of the liver transplant operation?*

C.6. *What physiologic disturbances should be anticipated during the second stage (anhepatic phase) of the liver transplant operation?*

C.7. *What is venovenous bypass? What are the potential advantages and disadvantages of this procedure?*

C.8. *What surgical techniques anastomose the donor and recipient inferior vena cava (IVC)?*

C.9. *What are the potential advantages of the "piggyback" (vena cava preservation) technique?*

C.10. *What hemodynamic changes are expected after removal of vascular clamps? What is postreperfusion syndrome (PRS)?*

C.11. *How would you treat hyperkalemia?*

C.12. *Why should you anticipate hypocalcemia?*

C.13. *What happens during the third stage of the liver transplant operation?*

C.14. *What causes intraoperative bleeding during each phase of liver transplantation? How is coagulopathy monitored and treated? What are thromboelastography (TEG) and rotational thromboelastography (ROTEM)?*

C.15. *What are the complications of massive transfusion?*

C.16. *How are the complications of massive transfusion prevented?*

C.17. *How is hyperfibrinolysis managed?*

C.18. *When is intraoperative renal replacement therapy indicated?*

C.19. *What intraoperative signs suggest that the hepatic graft is working?*

D. Postoperative Management

D.1. *What are the goals of immediate postoperative care of the liver transplant patient?*
D.2. *What postoperative findings suggest that the hepatic graft is functioning?*
D.3. *What coagulation disturbances should be anticipated in the postoperative period?*
D.4. *Can renal function change after liver transplantation?*
D.5. *What vascular and biliary complications occur after liver transplantation?*
D.6. *What immunosuppressive agents will be given after liver transplantation? What are the major side effects?*
Acknowledgment

SECTION 4 The Nervous System

17 Brain Tumor and Craniotomy
June M. Chan, Elena V. Christ, and Kane O. Pryor
A. Medical Disease and Differential Diagnosis
A.1. *What is the pathology of intracranial tumors?*
A.2. *What is intracranial pressure (ICP), and what are its determinants?*
A.3. *How does the presence of a mass alter the ICP in this patient, and what are the clinical manifestations of these alterations?*
A.4. *What is cerebral blood flow (CBF), and what are its determinants?*
A.5. *What are the cerebral steal syndromes?*
A.6. *Are there any issues specific to posterior cranial fossa pathology?*
A.7. *What is the role of preoperative embolization therapy?*
B. Preoperative Evaluation and Preparation
B.1. *What are the special considerations in preoperative evaluation of the patient scheduled for posterior fossa*

craniotomy?

- *B.2. In a patient who presents with intracranial hypertension, what management might have already been initiated preoperatively, and what are the implications for anesthetic management?*
- *B.3. What are the types of intraoperative neurophysiologic monitoring (IOM) that would likely be used for this procedure, and how will they affect the anesthetic management plan?*
- *B.4. What are the options for patient positioning during posterior fossa surgery?*
- *B.5. What are the principal disadvantages associated with the common posterior fossa craniotomy positions?*
- *B.6. How does the sitting position affect your preoperative assessment and planning?*
- *B.7. How should the patient position ultimately be determined?*
- *B.8. Should this patient receive premedication?*

C. Intraoperative Management

- *C.1. What are the anesthetic goals for craniotomy?*
- *C.2. What monitors should be used during craniotomy?*
- *C.3. Would you monitor for venous air embolism (VAE)? What are the monitoring options?*
- *C.4. What specific risks are associated with induction of anesthesia?*
- *C.5. How would you induce anesthesia?*
- *C.6. What are the effects of anesthetics on cerebral metabolic rate of oxygen ($CMRO_2$), CBF, and ICP? With this in mind, how would you maintain anesthesia?*
  - Volatile Anesthetics
  - Nitrous Oxide
  - Intravenous Anesthetics
  - Opioids
- *C.7. How would you manage ventilation and maintain arterial*

carbon dioxide (CO_2)?

C.8. How would you approach diuretic therapy?

C.9. How would you manage serum glucose?

C.10. How would you approach fluid management?

C.11. Once the bone plate is removed and the dura retracted, the surgeon reports that the brain is still "tight." What would be your response?

C.12. If deliberate hypotension is indicated, how will you achieve it?

C.13. While the surgeon is resecting tumor from near the brainstem, the patient's heart rate suddenly drops to 20 beats per minute. What is your assessment and management?

C.14. Are there any measures you can take to prevent VAE?

C.15. During the procedure, the precordial Doppler becomes loud and turbulent. The end-tidal CO_2 ($EtCO_2$) drops from 31 to 13 mmHg, and the systemic pressure from 121/63 to 64/32 mmHg. What is your assessment and management plan?

C.16. What is your approach to emergence? What if the patient does not regain consciousness?

D. Postoperative Management

D.1. What postoperative complications are of greatest concern? What level of monitoring is required?

D.2. What is your approach to postoperative pain control?

D.3. In the ICU, the patient's neurologic status deteriorates and ICP monitoring is instituted. What are the different methods of monitoring ICP, and what are their limitations?

18 Carotid Artery Disease

Priscilla Nelson and Hugh C. Hemmings Jr.

A. Medical Disease and Differential Diagnosis

A.1. What are the presenting symptoms of carotid stenosis?

A.2. What is the prevalence of carotid artery disease?

A.3. *What is the natural course of carotid artery disease as it relates to stroke?*

A.4. *What in the patient's history puts them at higher risk for having carotid atherosclerosis?*

A.5. *Do we screen patients for asymptomatic carotid stenosis?*

A.6. *What is the risk of stroke and cardiovascular events in asymptomatic carotid atherosclerosis?*

A.7. *What are the current medical options that the patient has for treating carotid atherosclerosis?*

A.8. *What are the indications for CEA and carotid artery stenting (CAS) in asymptomatic carotid atherosclerotic disease?*

A.9. *What are the indications for performing a CEA in symptomatic carotid stenosis?*

A.10. *Is there any role for CAS in symptomatic patients?*

A.11. *Discuss the anatomy of the cerebral vasculature, including the carotid artery and the circle of Willis.*

A.12. *Discuss cerebral blood flow (CBF) in the presence of carotid artery disease.*

A.13. *Discuss the different surgical approaches to carotid revascularization.*

A.14. *Discuss the endovascular approaches to carotid stenting.*

A.15. *What is normal CBF?*

A.16. *What is critically low CBF as measured by the electroencephalogram (EEG)?*

A.17. *What is cerebral autoregulation?*

A.18. *How does $PaCO_2$ affect CBF?*

A.19. *What are the principal determinants of CBF?*

A.20. *What is meant by the term luxury perfusion?*

A.21. *What is meant by the term intracerebral steal?*

B. Preoperative Evaluation and Preparation

B.1. *What will you look for in your preoperative evaluation of this patient?*

B.2. *Is this patient's blood pressure too high for elective surgery?*
B.3. *What laboratory data are required preoperatively?*
B.4. *Will you treat this patients' blood glucose?*
B.5. *Will you premedicate this patient?*

C. Intraoperative Management
C.1. *How will you monitor this patient?*
C.2. *How will you know that the patient's cerebral perfusion is adequate during surgery?*
C.3. *Discuss the differences and relative advantages and disadvantages of unprocessed EEG and processed EEG monitoring.*
C.4. *How will you measure CBF intraoperatively? What are the relative advantages and disadvantages of each technique?*
C.5. *Describe the use of stump pressure and its limitations.*
C.6. *Describe the use of transcranial Doppler (TCD) and its limitations.*
C.7. *Describe the use of jugular venous oxygen saturation ($SjvO_2$) and its limitations.*
C.8. *Describe the use of cerebral oximetry and its limitations.*
C.9. *Discuss somatosensory evoked potentials (SSEPs) as a monitor of CBF during CEA.*
C.10. *What type of anesthesia will you choose for this patient if she chose to have an endarterectomy?*
C.11. *What type of anesthesia will you choose for this patient if she chose to have a carotid stent?*
C.12. *How will you induce and maintain general anesthesia in this patient for CEA?*
C.13. *How would you proceed if the patient were to receive regional anesthesia?*
C.14. *Discuss the effects of anesthetics on CBF.*
C.15. *Discuss the protective effects of anesthetic agents on cerebral function.*

C.16. *How will you manage this patient's ventilation under general anesthesia?*

C.17. *How will you manage this patient's blood pressure intraoperatively?*

C.18. *Discuss reperfusion injury following CEA and CAS.*

C.19. *What intravenous fluids will you give this patient intraoperatively?*

D. Postoperative Management

D.1. *The patient does not "wake up" from general anesthesia. Why?*

D.2. *Postoperatively, the patient's blood pressure is 170/96 mmHg. Will you treat this?*

D.3. *What immediate postoperative complications might you expect after a CEA?*

D.4. *What postoperative complications might you expect after a CAS?*

D.5. *Discuss postoperative neurocognitive dysfunction following uncomplicated carotid intervention.*

19 Awake Craniotomy for Mapping and Surgery in the Eloquent Cortex

Thomas A. Moore II and Kenneth G. Smithson

A. Medical Disease and Differential Diagnosis

A.1. *What is the eloquent cortex?*

A.2. *What is the underlying pathology?*

A.3. *What determines intracranial pressure (ICP)?*

A.4. *How does a space-occupying mass alter ICP?*

A.5. *What is autoregulation, and why is it important?*

A.6. *How is cerebral blood flow (CBF) regulated?*

A.7. *What drug therapies may be associated with this pathology?*

B. Preoperative Evaluation and Preparation

B.1. *Why is the craniotomy performed awake?*

B.2. *What neurologic symptoms of the patient are important?*

B.3. *What is the status of their other comorbid conditions?*

B.4. Are there anesthetic implications from current treatment drugs?
B.5. What laboratory data are required?
B.6. What radiology data should be reviewed?
B.7. How do you prepare the patient for an awake craniotomy?
B.8. Should this patient receive premedications?
B.9. What precautions should be made for airway management?
C. Intraoperative Management
C.1. How should this patient be monitored?
C.2. Does this patient require invasive monitoring?
C.3. Can current drug therapy alter eloquent cortex mapping?
C.4. Why use hypertonic fluids during a craniotomy?
C.5. What intravenous fluids (IVFs) are recommended?
C.6. Would a lumbar drain for cerebrospinal fluid (CSF) removal benefit this patient?
C.7. Venous air embolism (VAE): Is it a concern in this case?
C.8. How is the eloquent cortex mapped?
C.9. How are intraoperative seizures treated?
C.10. How will you conduct this anesthetic?
D. Postoperative Management
D.1. What are the major concerns following craniotomy?
Acknowledgments
20 Head Injury
Chris C. Lee, Susan A. Ironstone, and M. Angele Theard
A. Pathophysiology and Differential Diagnosis
A.1. What types of intracranial injuries are most likely to have occurred in this patient?
A.2. What is the difference between primary and secondary injury? What factors contribute to secondary injury?
A.3. What are the benefits and risks of administering mannitol?
Benefits
Risks
A.4. What is the effect of hyperglycemia on neurologic outcome

following head trauma?

A.5. *What alterations in sodium and potassium balance can occur in patients with head injury?*

A.6. *In addition to sodium and potassium, what other electrolyte abnormalities can be present after head trauma?*

A.7. *What are the neuroprotective effects of administering magnesium (Mg)?*

A.8. *What role do gender and female sex hormones have in the pathophysiology of traumatic brain injury (TBI)?*

A.9. *What is the role of decompressive craniectomy (DC) as a treatment option for ICP control after head injury?*

A.10. *Do genetic factors play a role in the outcome after head injury?*

B. Preoperative Evaluation and Preparation

B.1. *What is the GCS? What is the significance of a GCS of 7T in this patient?*

B.2. *In addition to the GCS, what other assessments can be done to evaluate neurologic function?*

B.3. *What is the role of CT scanning in the initial evaluation of the patient with head injury? What are the management options in patients whose neurologic condition is deteriorating before obtaining a CT scan?*

B.4. *What is the role of ICP monitoring in the management of head injury?*

B.5. *How can you clear this patient's cervical spine?*

B.6. *What are the advantages of early endotracheal intubation in this patient?*

B.7. *What is your plan for airway management in this patient? How would it change if the patient were combative? How would it change if the patient had facial fractures with significant swelling of the head and neck?*

B.8. *What are the effects of succinylcholine on ICP? What is the significance of the effect, if any?*

B.9. What coagulation abnormalities are present after TBI? What modalities can be used to provide hemostasis and reduce intracranial hematoma expansion?

C. Intraoperative Management

C.1. What is appropriate hemodynamic monitoring during CT scanning and during craniotomy for evacuation of a subdural hematoma?

C.2. Should hyperventilation be used in this patient?

C.3. What are the implications of arterial hypertension in patients with head injury? How should BP be managed?

C.4. What should be done about intravenous (IV) fluid replacement? Should corticosteroids be given empirically?

C.5. Should hypertonic saline (HTS) be administered to this patient? How is HTS administered?

C.6. The patient underwent a craniectomy for evacuation of a frontal intracerebral hematoma. Should some anesthetic agents be avoided in this situation? Which ones? What agents might be preferred in this situation?

C.7. Should hypothermia be employed in this patient?

D. Postoperative Neurointensive Care Management

D.1. What are the postoperative ventilation concerns in this patient?

D.2. What specific measure should be used to control the patient's ICP? What type of monitoring devices can be used to measure ICP?

D.3. What is neurogenic pulmonary edema? Would you avoid positive end-expiratory pressure (PEEP) in a patient with increased ICP?

D.4. What is the role of antiseizure prophylaxis in the perioperative management of head trauma?

D.5. How can cerebral oxygenation monitoring be used in the clinical management of TBI?

D.6. What methods can be used in the neurointensive care unit to

prevent hyperthermia?

21 Cerebral Aneurysm

Patricia Fogarty Mack

A. Medical Disease and Differential Diagnosis

- *A.1. What are the incidence, prevalence, and causes of subarachnoid hemorrhage (SAH), and what are the risk factors associated with rupture of intracranial aneurysms?*
- *A.2. What are common sizes and locations of intracranial aneurysms?*
- *A.3. What is the pathophysiology of aneurysmal rupture and SAH?*
- *A.4. What are symptoms and signs of SAH?*
- *A.5. How does one assess the severity of SAH?*
- *A.6. What are the cardiovascular effects of SAH?*
- *A.7. How is the diagnosis of SAH made?*
- *A.8. What is the risk for rebleeding for a patient with SAH?*

B. Preoperative Evaluation and Preparation

- *B.1. What are some concerns in going to the interventional neuroradiology suite in the midst of an angiogram to be followed immediately with coiling of an aneurysm?*
- *B.2. What type of anesthesia is required for coiling of an aneurysm?*
- *B.3. Should one proceed with induction of general anesthesia under these circumstances?*
- *B.4. What types of emergencies can occur during coiling of an aneurysm, and how should they be managed?*
- *B.5. What other modalities of endovascular therapy are available?*
- *B.6. A craniotomy is planned for the following day to clip the middle cerebral artery aneurysm. Should surgery be postponed because of the patient's elevated troponin and CPK-MB fractions?*
- *B.7. Would you premedicate this patient before craniotomy?*

C. Intraoperative Management

- *C.1. What are the goals of the induction and maintenance of anesthesia for this patient?*
- *C.2. Is placement of an arterial catheter necessary for induction of anesthesia in this patient in the interventional neuroradiology suite?*
- *C.3. How would you assess fluid status in this patient?*
- *C.4. Would monitoring central venous pressure (CVP) be useful for craniotomy and aneurysm clipping in this patient?*
- *C.5. What other forms of monitoring would you consider?*
- *C.6. What are your specific concerns during induction of anesthesia in this patient?*
- *C.7. How would you accomplish a smooth and safe induction and intubation in this patient?*
- *C.8. Would you perform a rapid sequence induction and tracheal intubation for this patient?*
- *C.9. What are the effects of hypoxemia and hypercapnia, such as would be seen with loss of the airway on induction, on cerebral blood flow (CBF)?*
- *C.10. What is optimal fluid management for aneurysm clipping? Would you use a dextrose-containing solution?*
- *C.11. After the bone plate was removed and as the dura was being opened, the surgeon complained that the brain was "tight." What could you do to achieve better brain relaxation and facilitate surgical exposure?*
- *C.12. How might transmural pressure be decreased to allow for aneurysm clip placement?*
- *C.13. What is the purpose of controlled hypotension, and how is it achieved?*
- *C.14. What are some of the drawbacks of controlled hypotension?*
- *C.15. What methods of cerebral protection might you use during this operation?*
- *C.16. Would you induce mild hypothermia as a means of cerebral*

protection?
C.17. What are the indications for deep hypothermic circulatory arrest?
C.18. What steps should be taken in the case of intraoperative rupture of an intracranial aneurysm?
C.19. How would you plan the emergence from an anesthetic for aneurysm clipping?
D. Postoperative Management
D.1. Would you extubate the patient postoperatively?
D.2. What would be the differential diagnosis if the patient did not return to her preoperative neurologic condition?
D.3. On postoperative day 2, the patient became disoriented and developed hemiplegia. A CT scan was obtained, which shows no new intracranial bleeding. What other diagnostic studies should be performed?
D.4. What is cerebral vasospasm, and what causes it?
D.5. What are pathophysiologic changes seen in cerebral vasospasm?
D.6. How is the diagnosis of cerebral vasospasm made?
D.7. What steps can be taken to prevent cerebral vasospasm?
D.8. What treatments can be undertaken once a diagnosis of cerebral vasospasm is made?
D.9. What are other neurologic complications following SAH and aneurysm clipping?
D.10. What other organ systems may manifest problems postoperatively in aneurysm clipping patients?

SECTION 5 The Endocrine System

22 Pheochromocytoma
Anup Pamnani and Vinod Malhotra
A. Medical Disease and Differential Diagnosis
A.1. What are some common differential diagnoses for arterial

hypertension?

- *A.2. What is a pheochromocytoma?*
- *A.3. Describe the anatomy of the adrenal gland.*
- *A.4. What substances does the adrenal medulla secrete?*
- *A.5. What are the mechanisms of action of epinephrine and norepinephrine?*
- *A.6. What is the pathway for synthesis and breakdown of catecholamines?*
- *A.7. What does the adrenal cortex secrete?*
- *A.8. What are the metabolic actions of the glucocorticoids and the mineralocorticoids?*
- *A.9. What are the clinical features associated with a pheochromocytoma?*
- *A.10. What is the prevalence of pheochromocytomas and paragangliomas?*

B. Preoperative Evaluation and Preparation

- *B.1. How can you diagnose and localize the tumor preoperatively?*
- *B.2. How do you pharmacologically prepare the patient with a pheochromocytoma for surgery?*
- *B.3. What other aspects of preoperative management are important?*

C. Intraoperative Management

- *C.1. What drugs should be avoided during the operation?*
- *C.2. How would you monitor this patient?*
- *C.3. Describe the anesthetic management of the patient with pheochromocytoma.*
- *C.4. What drugs are used to control the effects of catecholamine stimulation during surgery?*
- *C.5. What are some management concerns after the tumor is removed?*
- *C.6. What are some of the concerns with laparoscopic adrenalectomy?*

D. Postoperative Management

D.1. What is the significance of postoperative hypotension? How is it treated?

D.2. What other problems can arise in the postoperative period?

23 Diabetes Mellitus

Mark E. Nunnally and Vinod Malhotra

A. Medical Disease and Differential Diagnosis

A.1. What is the epidemiology of DM in the general population?

A.2. What are the factors in the etiology of the disease?

A.3. How is DM classified?

A.4. What are the complications of DM?

A.5. How are the different forms of this illness treated?

A.6. How is control of the disease adequately monitored?

A.7. What are some of the factors that alter insulin requirements?

A.8. What are the principles of management of diabetic ketoacidosis (DKA)?

A.9. What is a hyperglycemic hyperosmolar state?

B. Preoperative Evaluation and Preparation

B.1. How should this patient be evaluated?

B.2. How would the stiff joint syndrome affect her airway management?

B.3. What are the signs and implications of autonomic neuropathy in the diabetic patient?

B.4. How should this patient be prepared for anesthesia and surgery?

B.5. For elective surgery, how are insulin and glucose requirements managed on the day of surgery?

B.6. How should this patient be premedicated?

C. Intraoperative Management

C.1. What are the effects of anesthesia and surgery on insulin and glucose metabolism?

C.2. What anesthetic techniques should be considered?

C.3. *How should this patient be monitored?*
C.4. *How is hyperglycemia treated intraoperatively?*
C.5. *How is hypoglycemic shock recognized and treated intraoperatively?*

D. Postoperative Management
D.1. *How is diabetes controlled in this patient postoperatively?*
D.2. *Does diabetes increase perioperative risk?*
D.3. *What are the common postoperative complications to be expected in a diabetic patient?*
D.4. *Is it necessary to achieve tight perioperative control of glucose?*

SECTION 6 The Genitourinary System

24 Transurethral Resection of the Prostate and Geriatric Anesthesia
Anuj Malhotra, Vinod Malhotra, and Fun-Sun F. Yao

A. Medical Disease and Differential Diagnosis
A.1. *What comorbidities are common in patients undergoing TURP?*
A.2. *What are the normal physiologic consequences of aging for the various organ systems?*
A.3. *How should drug dosages be adjusted for elderly patients? Should any particular medications be avoided?*
A.4. *Does a history of prior MI increase the patient's risk of perioperative reinfarction or stent thrombosis?*
A.5. *In patients with a history of recent MI, would you recommend that the surgery be postponed for a certain period?*

B. Preoperative Evaluation and Preparation
B.1. *How would you evaluate the patient's cardiac condition? Does he need additional testing?*
B.2. *Would you discontinue any antihypertensives or any*

medications for angina?

B.3. For a patient with a cardiac implantable electronic device (CIED), what information should you know? What precautions should be taken?

B.4. What types of coronary stents are available? What is their perioperative relevance?

B.5. What is the conventional recommendation for dual antiplatelet therapy (DAPT) in a patient with previous percutaneous coronary intervention (PCI) undergoing elective noncardiac surgery?

B.6. What risk is associated with continuing perioperative antiplatelet therapy? What risk is there with stopping it?

B.7. How should patients with coronary stents undergoing noncardiac surgery be managed?

C. Intraoperative Management

C.1. What monitors would you use for this patient?

C.2. Is there a preferred anesthetic technique for patients undergoing TURP, and why?

C.3. Does regional anesthesia result in a lower incidence of perioperative mortality than general anesthesia?

C.4. What intravenous fluid would you use during TURP?

C.5. Forty minutes after a sensory level of T10 was established with intrathecal anesthesia, and monopolar TURP (M-TURP) resection was initiated with the use of glycine as the bladder irrigating solution, the patient becomes agitated and complains of nausea. Further sedation along with an antiemetic is administered. However, shortly thereafter, the patient becomes very restless, blood pressure rises, and heart rate decreases. The patient becomes cyanotic and obtunded, blood pressure precipitously falls, and pupils are dilated and unresponsive to light. What is the most likely cause of these signs and symptoms, and would these occur during bipolar (B-TURP) or laser TURP (L-TURP)

resection?

C.6. *What are the important characteristics of irrigation solutions used during TURP?*

C.7. *What is the effect on body temperature of continuous bladder irrigation during TURP?*

C.8. *What is the definition of TURP syndrome? What are the signs and symptoms of the syndrome?*

Cardiopulmonary

Hematologic and Renal

Central Nervous System

C.9. *How does the patient absorb irrigation solution during TURP?*

C.10. *What factors increase the incidence of TURP syndrome?*

C.11. *What is the effect on cardiopulmonary, renal, and central nervous system (CNS) functions of excessive absorption of irrigation solution during TURP?*

C.12. *What causes CNS dysfunction in patients who have undergone M-TURP?*

C.13. *How does acute hyponatremia affect the cardiovascular system?*

C.14. *What prophylactic measures may reduce the incidence of TURP syndrome?*

C.15. *What therapeutic measures are recommended for patients with TURP syndrome?*

C.16. *Is hypertonic saline administration necessary to correct hyponatremia? Explain. What are the risks of rapidly correcting hyponatremia?*

C.17. *What are the toxic effects of glycine? Is there an antidote to glycine toxicity? What are the metabolic by-products of glycine?*

C.18. *What are the symptoms and clinical course of TURP-induced hyperammonemia?*

C.19. *What are the clinical characteristics, causes, and prognosis*

of TURP-related blindness?
C.20. What are the causes of excessive bleeding during TURP?
C.21. What are the causes, signs, symptoms, and treatment of bladder perforation during TURP?
C.22. What are the causes of hypotension during TURP?
D. Postoperative Management
D.1. What is the source of postoperative bacteremia in patients who have undergone TURP? What factors increase the incidence of bacteremia?
D.2. What are the signs of post-TURP septicemia? What preventive measures are generally recommended?
D.3. Is postoperative hypothermia a risk factor for myocardial ischemia?
D.4. What is postoperative cognitive dysfunction (POCD)? How does this differ from delirium, and what is the time course to resolution?
D.5. What are the mechanisms and risk factors for POCD? How would you mitigate the risk of POCD? Does anesthesia type influence development of POCD?
E. Comparing M-TURP, B-TURP, and L-TURP
E.1. What differentiates M-TURP from B-TURP?
E.2. Are decreased morbidity and mortality associated more closely with M-TURP or with B-TURP?
E.3. What differentiates the technologies for L-TURP?

25 Kidney Transplant
Christine Lennon and Fun-Sun F. Yao
A. Medical Disease and Differential Diagnosis
A.1. What are the causes of chronic renal disease that can progress to renal failure?
A.2. How is chronic kidney disease (CKD) diagnosed?
A.3. What are the indications for dialysis?
A.4. What are the common clinical manifestations of ESRD?
A.5. What electrolyte imbalances occur in patients with impaired

renal function, and how are they treated?

A.6. *How is metabolic acidosis managed in chronic renal failure?*

A.7. *Are patients with renal disease at increased risk of cardiovascular disease?*

A.8. *When is the best time to receive a kidney transplant?*

A.9. *How are immunosuppressive drugs managed in kidney transplant recipients?*

A.10. *How are kidneys allocated to recipients on the waiting list in the United States?*

A.11. *What is donation after cardiac death (DCD)?*

A.12. *What is a living donor transplant program?*

A.13. *What is a paired donor exchange transplant program?*

A.14. *What are some barriers to receiving a kidney transplant?*

A.15. *What surgical techniques are available for donor nephrectomy (DN)?*

A.16. *How is a donor kidney preserved?*

A.17. *Describe the operative procedure of kidney transplantation.*

B. Preoperative Evaluation and Preparation

B.1. *What preoperative workup would you order for a recipient?*

B.2. *How does the presence of obesity affect the outcome of a transplanted kidney?*

B.3. *How are routine medications and immunosuppressive medications managed in the perioperative period?*

C. Intraoperative Management

C.1. *Are a central venous pressure (CVP) monitoring line, an arterial line, and a pulmonary artery catheter required for the transplant procedure?*

C.2. *What type of intravenous fluid should be used during surgery?*

C.3. *How would you conduct the anesthesia induction?*

C.4. *Is succinylcholine contraindicated in renal failure patients?*

C.5. *How are the nondepolarizing muscle relaxants affected by*

renal failure?

C.6. How would you maintain anesthesia during the case?

C.7. What are the effects of inhalation anesthetics on renal blood flow (RBF), glomerular filtration (GFR), and urine output?

C.8. What are the potential nephrotoxic effects of inhalation anesthetics? What are the nephrotoxic metabolites of inhalation anesthetics?

C.9. How does renal failure affect the pharmacology of opioids?

D. Postoperative Management

D.1. How is the diagnosis of transplant rejection made?

D.2. What are immunosuppressive agents, and how do they affect anesthetic care?

26 Robotic-Assisted Laparoscopic Surgery

Judith Weingram

A. Medical Disease and Differential Diagnosis

A.1. What is the incidence of carcinoma of the prostate?

A.2. How is prostate cancer diagnosed?

A.3. How is prostate cancer treated?

A.4. Define laparoscopy.

A.5. Describe the development of robotic-assisted laparoscopy.

A.6. What are the advantages and disadvantages of minimally invasive surgery over open surgery?

A.7. What are the contraindications to laparoscopic or robotic-assisted laparoscopic surgery? Is pregnancy a contraindication to robotic surgery?

A.8. What other specialties commonly perform robotic surgery?

A.9. Why is carbon dioxide (CO_2) the gas of choice for robotic laparoscopy? What are its disadvantages?

A.10. How much endogenous CO_2 is produced at basal level and at maximal exercise?

A.11. How much CO_2 is stored in the body? Where is it stored? Of what significance is this to laparoscopy?

A.12. *Describe the diffusion and solubility properties of CO_2 and their significance in laparoscopy.*

A.13. *Is CO_2 soluble in water or plasma? Is it soluble in blood? Why?*

B. Preoperative Evaluation and Preparation

B.1. *What do you want to know about this patient's history and physical condition that may affect whether or not you clear him for robotic surgery?*

B.2. *What factors increase this patient's risk of pulmonary complications?*

B.3. *What laboratory tests should be performed preoperatively?*

B.4. *What specific information should the patient be given about robotic surgery before obtaining informed consent?*

B.5. *What additional procedures should be done before surgery?*

B.6. *What are the three major forces that uniquely alter the patient's physiology during robotic laparoscopy?*

C. Intraoperative Management

C.1. *What is the anesthetic technique of choice for robotic-assisted laparoscopy? Why?*

C.2. *Can a laryngeal mask airway (LMA) be used?*

C.3. *What anesthetic agents or adjuvant drugs are recommended for laparoscopy? Are any anesthetic agents contraindicated?*

C.4. *Should nitrous oxide (N_2O) be used during laparoscopy? What are the pros and cons? Does N_2O cause bowel distention during laparoscopy? Does N_2O cause nausea and vomiting after laparoscopy?*

C.5. *Can laparoscopy be performed under local or regional anesthesia?*

C.6. *What monitors and devices would you apply to the patient? Why?*

C.7. *How is the patient to be positioned? What special*

precautions are required for robotic laparoscopy?

C.8. *How will you ventilate the patient? What are the respiratory and circulatory effects of the Trendelenburg position during laparoscopy?*

Respiratory

Circulatory

C.9. *What techniques are available for initial access to the peritoneal cavity? What anesthetic problems can arise during insufflation?*

C.10. *What intravenous (IV) solution and how much fluid volume do you plan to infuse?*

C.11. *Under what circumstances should laparoscopy be converted to laparotomy?*

C.12. *What is the arterial to end-tidal CO_2 gradient ($PaCO_2$–$EtCO_2$) in the normal awake patient? What is the cause of the gradient? Does the gradient change during laparoscopy? Why?*

C.13. *Is an arterial line necessary? Why? Does end-tidal CO_2 tension accurately reflect arterial CO_2 tension? Under what circumstances may the $EtCO_2$ exceed the $PaCO_2$? Why?*

C.14. *What are the possible causes of hypercarbia?*

C.15. *What factors play a role in the unusually rapid and marked elevation of CO_2 that is sometimes seen in laparoscopy?*

C.16. *How rapidly does the $PaCO_2$ rise in the apneic patient (endogenous CO_2)? How rapidly does the $PaCO_2$ rise if 5% CO_2 gas is inhaled (exogenous)? How rapidly can the CO_2 rise during laparoscopy? What factors explain the differences?*

C.17. *What is the net effect of pneumoperitoneum, hypercarbia, and steep Trendelenburg on the cardiovascular system?*

C.18. *What is the net effect of pneumoperitoneum, hypercarbia, and steep Trendelenburg on the respiratory system?*

C.19. What is the net effect of pneumoperitoneum, hypercarbia, and steep Trendelenburg on the central nervous system?

C.20. What are the neuroendocrine changes that occur during laparoscopy?

C.21. What is the net effect of pneumoperitoneum, hypercarbia, and steep Trendelenburg on the renal system?

C.22. What is the net effect of pneumoperitoneum, hypercarbia, and steep Trendelenburg on the bowel and gastrointestinal system?

C.23. How would you recognize a CO_2 embolism during laparoscopy? How does this differ from an air embolism? Why should N_2O be discontinued during suspected embolization? Will N_2O increase the size of CO_2 emboli?

C.24. What is the mechanism of increase in shunting resulting from embolization?

C.25. How is a gas embolism (CO_2 or air) treated?

C.26. What are the causes of pneumothorax or pneumomediastinum during laparoscopy? How would you diagnose it? How would you treat it?

C.27. How would you decide when to extubate?

D. Postoperative Management

D.1. What are some of the unique complications of laparoscopy?

Injuries from Instruments
Complications of Pneumoperitoneum
Systemic Effects of CO_2 Absorption
Trendelenburg Position
Late Complications

D.2. In the postanesthesia care unit (PACU), our patient complains of numbness and weakness of the lower extremities after 6 hours of anesthesia for robotic prostatectomy. What tests will you order? When would you remove the Foley catheter and arterial line? Under what

circumstances would you order a chest x-ray film?

D.3. *What is the incidence of postoperative nausea and vomiting?*

SECTION 7 The Reproductive System

27 Placenta Previa/Placenta Accreta Spectrum

Jill Fong

A. Medical Disease and Differential Diagnosis

A.1. *What are the leading causes of maternal mortality, and what role does anesthesia play in this mortality?*

A.2. *What is the differential diagnosis for an antepartum hemorrhage?*

A.3. *How would you diagnose the etiology of antepartum bleeding after midpregnancy?*

A.4. *What is the incidence of placenta previa, and what are the associated conditions?*

A.5. *What are the different types of placenta previa?*

A.6. *What is the usual obstetric management for placenta previa?*

A.7. *What is vasa previa? How is it diagnosed and managed?*

A.8. *What are the risk factors for the development of a placental abruption?*

A.9. *How is placental abruption diagnosed and managed?*

A.10. *What complications are associated with placental abruption?*

A.11. *Who is at risk for uterine rupture, and how is uterine rupture diagnosed?*

A.12. *What is the treatment for uterine rupture?*

A.13. *Is this patient at risk for postpartum bleeding?*

A.14. *What is the placenta accreta spectrum (PAS)?*

A.15. *How is the PAS diagnosed?*

A.16. *How is the PAS managed obstetrically?*

A.17. *What tests and/or interventions can improve neonatal outcome of a preterm birth?*

B. Preoperative Evaluation and Preparation

B.1. *How does pregnancy change respiratory function, and what impact does this have on anesthetic care?*

B.2. *What are the maternal cardiovascular changes of pregnancy?*

B.3. *What are the maternal gastrointestinal changes of pregnancy?*

B.4. *What hematologic changes occur during pregnancy?*

B.5. *What laboratory data do you need before taking this patient to the operating room?*

B.6. *What preoperative medications would you administer to this patient?*

C. Intraoperative Management

C.1. *What monitors would you use for this patient?*

C.2. *What anesthetic could be used in this patient?*

C.3. *What are the absolute and relative contraindications for neuraxial anesthesia?*

C.4. *How is postpartum hemorrhage (PPH) defined, and what are the etiologies of this bleeding?*

C.5. *After delivery of the fetus, the placenta is removed with some difficulty in one small area and generalized oozing from the placental implantation site is noted. What is the most likely cause of this patient's bleeding?*

C.6. *After delivery of the placenta in a cesarean section, what maneuvers and drugs can enhance myometrial contractility and therefore decrease blood loss?*

C.7. *When should this patient receive tranexamic acid (TXA)?*

C.8. *If this patient had ongoing bleeding intraoperatively, what guidelines help determine when red blood cell (RBC) transfusions should be given?*

C.9. *What laboratory tests should be ordered during the*

resuscitation of this patient?

C.10. If this patient had a massive blood loss, what blood replacement therapy would be indicated?

C.11. What is the role of recombinant activated factor VII (rFVIIa) in the hemorrhaging obstetric patient?

C.12. What is the role of type O Rh-negative (universal donor) uncrossmatched blood in emergency transfusions, and how does this change your future management?

C.13. What complications can occur from the transfusion of blood products?

C.14. What is the role of autologous transfusion in obstetric patients?

C.15. Significant intraoperative blood loss required the transfusion of 8 units of type-specific, crossmatched packed RBCs (pRBCs). This patient had generalized oozing in the surgical field and hematuria. What is your differential diagnosis?

C.16. What is disseminated intravascular coagulation (DIC)?

C.17. Define amniotic fluid embolism (AFE) syndrome and discuss treatment.

D. Postoperative Management

D.1. If the patient received epidural anesthesia and subsequently developed DIC, when should the epidural catheter be removed?

D.2. You have successfully treated the patient's massive hemorrhage. Her laboratory values have returned to normal. The patient, however, is still hypotensive despite appropriate intravascular volume replacement and support with vasopressors. What is your concern in this case?

28 Hypertensive Disorders of Pregnancy

Sharon Abramovitz and Jennifer Wagner

A. Medical Disease and Differential Diagnosis

A.1. What is the classification of hypertension disorders in

pregnancy as defined by the American College of Obstetricians and Gynecologists?

A.2. What is preeclampsia?

A.3. What is preeclampsia with severe features?

A.4. What is eclampsia?

A.5. What is HELLP syndrome?

A.6. What are the risk factors for developing preeclampsia?

A.7. What is the mortality associated with preeclampsia?

A.8. Discuss the pathogenesis of preeclampsia.

- Immunologic Factors
- Genetic Factors
- Endothelial Factors
- Platelet Factors
- Calcium
- Coagulation Factors
- Fatty Acid Metabolism
- Markers of Angiogenesis

A.9. Discuss the pathologic alterations of preeclampsia.

- Cardiovascular Changes
- Hemodynamic Changes
- Hematologic Changes
- Renal Changes
- Endocrine Changes
- Respiratory Changes
- Hepatic Changes
- Neurologic Changes
- Uteroplacental Perfusion

A.10. What are some of the complications associated with preeclampsia?

B. Preoperative Evaluation and Preparation

B.1. What initial laboratory studies are recommended for patients with preeclampsia?

B.2. Discuss bleeding time and platelet count evaluation during

preoperative assessment of a patient with preeclampsia requesting epidural analgesia/anesthesia for labor and delivery.

- *B.3. What types of monitoring are important for patients with preeclampsia? When is a central venous pressure (CVP) monitor indicated?*
- *B.4. Discuss the obstetric management of preeclampsia with severe features.*
- *B.5. What are the antihypertensive agents of choice for preeclampsia?*
- *B.6. What drug therapy is the treatment of choice for seizure prophylaxis?*
- *B.7. Discuss the mechanism of action of magnesium sulfate.*
- *B.8. What are the fetal effects of magnesium sulfate therapy?*
- *B.9. Discuss the treatment of magnesium sulfate toxicity.*
- *B.10. What conditions mandate immediate delivery, regardless of the gestational age?*
- *B.11. Discuss the management of eclampsia.*

C. Intraoperative Management

- *C.1. What is your choice of labor analgesia for patients with preeclampsia?*
- *C.2. What is the advantage of prehydration prior to initiation of neuraxial analgesia?*
- *C.3. What sensory level of analgesia is required for labor and delivery?*
- *C.4. Discuss the commonly used local anesthetics for labor analgesia.*
- *C.5. Is the addition of epinephrine to local anesthetics advisable in preeclamptic patients?*
- *C.6. What is the treatment for the abnormal fetal heart rate pattern seen with maternal hypotension after neuraxial analgesia is instituted?*
- *C.7. What would you do after an accidental dural puncture?*

How do you treat postdural puncture headache?
C.8. *How would you manage total spinal anesthesia?*
C.9. *Should methylergonovine be given to preeclamptic patients?*
C.10. *When and how would you give spinal anesthesia?*
C.11. *Discuss a general anesthesia technique for the patient with preeclampsia presenting for cesarean delivery.*
C.12. *What agents can you use to prevent hypertension during the induction of general anesthesia for cesarean delivery?*

D. Postoperative Management
D.1. *Discuss the postpartum management of preeclamptic patients.*
D.2. *Can nonsteroidal anti-inflammatory drugs (NSAIDs) be used to treat postpartum pain in preeclamptic patients?*

29 Breech Presentation, Fetal Distress, and Mitral Stenosis
Jill Fong and Jaime Aaronson

A. Medical Disease and Differential Diagnosis
A.1. *How are fetal lie, presentation, and position defined and determined?*
A.2. *What is the approximate frequency of the various lies and presentations at or near term?*
A.3. *What are the different types of breech presentation, and what is their incidence?*
A.4. *What is the cause of breech presentation?*
A.5. *What are the delivery problems associated with breech presentation?*
A.6. *What is the usual obstetrical management for patients with breech presentation?*
A.7. *What is the incidence of heart disease in pregnancy and the mortality rate associated with maternal cardiac disease?*
A.8. *How is peripartum cardiomyopathy defined?*
A.9. *What classifications help predict an individual pregnant woman's cardiac risk?*
A.10. *What are the cardiovascular changes of pregnancy?*

A.11. *What changes normally occur in heart sounds during pregnancy?*
A.12. *What are the normal electrocardiographic and echocardiographic changes seen during pregnancy?*
A.13. *What causes rheumatic heart disease?*
A.14. *What are the physiologic consequences of mitral stenosis?*
A.15. *What are the auscultatory findings associated with mitral stenosis?*
A.16. *What may be seen on the electrocardiogram (ECG) in patients with mitral stenosis?*
A.17. *What are the echocardiographic findings associated with mitral stenosis?*
A.18. *What is the effect of the physiologic changes of pregnancy on patients with mitral stenosis?*
A.19. *If mitral stenosis is first recognized during pregnancy and symptoms develop, how would you treat the patient?*
A.20. *What are the determinants of fetal oxygenation?*
A.21. *What are the determinants of uterine blood flow?*

B. Preoperative Evaluation and Preparation

B.1. *How is fetal well-being assessed during labor?*
B.2. *How are FHR and maternal contractions monitored?*
B.3. *What is the normal FHR with beat-to-beat variability?*
B.4. *What are FHR decelerations?*
B.5. *How accurate is FHR monitoring in predicting fetal well-being?*
B.6. *In a fetus with minimal FHR variability, what other modalities can be used to assess fetal well-being?*
B.7. *What is the significance of meconium-stained amniotic fluid?*
B.8. *What is meconium aspiration syndrome?*
B.9. *What are the usual noninvasive tests used to evaluate the pregnant cardiac patient?*
B.10. *What preoperative medications, if any, would you give this*

patient?

C. Intraoperative Management

- *C.1. What monitors would you use in this functional New York Heart Association (NYHA) class II patient during her cesarean section?*
- *C.2. When would you use invasive monitoring in a pregnant patient with cardiac disease?*
- *C.3. What are the hemodynamic goals of intraoperative management of the pregnant patient with mitral stenosis?*
- *C.4. What anesthetic technique would you use for this emergency cesarean section?*
- *C.5. How would you manage local anesthetic systemic toxicity (LAST) in this patient?*
- *C.6. If cardiac arrest were to occur prior to delivery, how would you proceed?*
- *C.7. What technique could you use for general anesthesia in this patient?*
- *C.8. If you are unexpectedly unable to intubate this patient, how would you manage the airway?*
- *C.9. Would this patient benefit from the use of β-blockers?*
- *C.10. What is the effect of the inhalation agents on uterine contractility?*
- *C.11. What is the Apgar scoring system?*
- *C.12. What is the significance of Apgar scores?*
- *C.13. At birth, what should be done to minimize an infant's risk of meconium aspiration syndrome?*
- *C.14. If the Apgar score of the newborn is 3 at 1 minute, how would you treat the newborn?*
- *C.15. Blood gases are sent immediately after delivery. What are the normal values for umbilical vein and artery blood gases?*

D. Postoperative Management

- *D.1. Immediately after the baby is delivered, the mother's oxygen*

saturation decreases. What is the differential diagnosis?

D.2. *Additional bleeding occurs in the postanesthesia care unit, and the obstetrician diagnoses retained placenta. What, if any, antibiotics are indicated to prevent endometritis after manual extraction of retained placenta?*

30 Appendectomy for a Pregnant Patient 648

Robert S. White and Farida Gadalla

A. Medical Disease and Differential Diagnosis

A.1. *What is the differential diagnosis for acute abdomen in the pregnant patient?*

Medical Conditions

Obstetric Conditions

Gynecologic Conditions

Surgical Conditions

A.2. *How would you make the clinical diagnosis of acute appendicitis?*

A.3. *What is the incidence of surgery during pregnancy? What is the incidence of appendicitis during pregnancy?*

A.4. *What is the incidence of gangrenous appendix/peritonitis during pregnancy, and is this incidence higher in pregnant than in nonpregnant women?*

A.5. *What are the main concerns associated with nonobstetric surgery in the pregnant patient?*

A.6. *What are the factors influencing teratogenicity from anesthetic agents in humans?*

A.7. *Are there any specific concerns regarding neurotoxicity and cognitive development in the developing fetus?*

A.8. *What factors influence fetal oxygenation, and how would you prevent intrauterine fetal asphyxia?*

A.9. *What is the incidence of trauma during pregnancy, and what are the risks to the mother and the fetus secondary to trauma?*

A.10. *What are other common surgeries performed during*

pregnancy?

B. Preoperative Evaluation and Preparation

B.1. Preoperatively, what would you discuss with this patient? Are any additional medical consultations warranted?

B.2. Is there a difference in the goal of anesthesia for delivery and for nonobstetric surgery in a pregnant patient?

B.3. How would you premedicate this patient?

C. Intraoperative Management

C.1. What factors would alter your anesthetic technique from that used for a nonpregnant patient?

Cardiovascular System
Respiratory System
Gastrointestinal System
Central Nervous System
Airway, Skin, and Mucous Membranes

C.2. If you choose epidural anesthesia, describe your technique and dosage.

C.3. If the patient needs supplemental analgesia, what would be your choice?

C.4. What vasopressor would you choose to improve uteroplacental perfusion?

C.5. When this patient arrived in the operating room, she desired a general anesthetic. Describe your technique.

C.6. Does any controversy exist surrounding the use of nitrous oxide?

C.7. Does any controversy exist surrounding operating room personnel, anesthetic exposure, and pregnancy outcomes?

C.8. What is the impact of nonobstetric surgery on maternal mortality, birth defects, and fetal loss? What factors influence it?

C.9. Should intraoperative fetal heart rate (FHR) monitoring be used? What would you expect to see on the electronic fetal monitor during anesthesia?

C.10. *How would your anesthetic management differ if the patient were having upper extremity surgery?*

C.11. *The surgeon schedules the procedure to be performed laparoscopically. Does this pose any additional problems?*

D. Postoperative Management

D.1. *When would you extubate this patient?*

D.2. *Postoperatively, what monitors would you use?*

D.3. *What other postoperative precautions would you take? What is the incidence of preterm delivery following nonobstetric surgery during pregnancy?*

D.4. *The next day, the patient went into premature labor and now needs a cesarean section for prematurity and breech presentation. She requires another general anesthetic. In what way would your technique differ from your previous anesthetic technique?*

SECTION 8 The Hematologic System

31 Hemophilia and Disorders of Coagulation

Elizabeth M. Staley

A. Medical Disease and Differential Diagnosis

A.1. *Describe the various laboratory tests that evaluate the coagulation cascade and the specific components measured by each.*

A.2. *What is the difference between platelet adhesion, activation, and aggregation at sites of vascular injury?*

A.3. *Describe the physiologic events that occur following endothelial interruption in the blood vessel.*

A.4. *What factors prevent the extension of a clot beyond the site of injury?*

A.5. *Describe the factors involved in the extrinsic, intrinsic, and common coagulation cascade.*

A.6. *Describe the typical presentation history and*

pathophysiology associated with von Willebrand disease (vWD).

A.7. Explain the pathophysiology, frequency, and treatment of significant rare disorders of coagulation (factor VII [FVII], factor XII [FXII], and fibrinogen).

A.8. Differentiate between hemophilia A, B, and C.

A.9. What are the differences in factor replacement therapy between patients with hemophilia A and hemophilia B?

A.10. What is acquired hemophilia?

A.11. Which plasma protein is important in maintaining normal levels of factor VIII (FVIII)?

A.12. How are patients with severe hemophilia managed in the outpatient setting?

A.13. Describe the levels of FVIII necessary to maintain hemostasis in patients with spontaneous or surgical bleeding.

B. Preoperative Evaluation and Preparation

B.1. What steps would you take to normalize this patient's coagulation status before surgery?

B.2. What is meant by 1 unit of FVIII clotting activity, and how much does 1 unit of FVIII clotting activity per kilogram of body weight increase FVIII concentrations?

Approach 1

Approach 2

Plasma Volume Calculation

B.3. Would you administer FVIII using a bolus or infusion technique?

B.4. Can hemophiliac patients fail to mount an appropriate coagulation response following FVIII infusion?

B.5. If a patient with hemophilia does not respond to a bolus injection of FVIII, can an infusion technique be effective?

B.6. How much FVIII activity is present in plasma? What are the risks associated with plasma administration?

B.7. *What are the indications for the administration of plasma?*

B.8. *What is cryoprecipitate, and how is it prepared? How much FVIII activity is present in cryoprecipitate? When is cryoprecipitate indicated?*

B.9. *Describe the advantages and disadvantages of the products that are available for repletion of FVIII activity.*

B.10. *What is the role of desmopressin (D-amino D-arginine vasopressin [DDAVP]) for hemostatic management in this patient?*

B.11. *What is the role of antifibrinolytic therapy in the perioperative period for the patient with hemophilia? What are examples of antifibrinolytics used in the treatment of hemophilia?*

B.12. *What are the options for operative treatment of patients with acquired hemophilia? Describe the mechanism of action and dosing considerations for each of these therapies.*

C. Intraoperative Management

C.1. *Is it safe to administer an intramuscular injection to this patient before surgery?*

C.2. *Would an axillary block be appropriate for this patient?*

C.3. *If general anesthesia is used, would it be safe to intubate the patient's trachea?*

C.4. *Would you use any special precautions for this patient who is positive for HIV?*

C.5. *What special considerations should be taken in choosing anesthetic drugs for this patient?*

C.6. *During an operative procedure, if the surgeon indicates that significant blood loss is occurring, would you transfuse this patient with packed red blood cells (RBCs) or whole blood?*

C.7. *During the transfusion of the first unit of whole blood, the patient's temperature rose from 36.8°C to 37.9°C (98.2°F to 100.2°F). What immediate steps should be taken by the anesthesiologist at this time?*

C.8. *Does giving blood intraoperatively increase the potential for the development of FVIII inhibitors?*
C.9. *Can FVIII be safely administered to patients who have developed circulating inhibitors?*
C.10. *The surgeon has requested the use of a tourniquet to minimize surgical bleeding. What are the physiologic and hemodynamic responses to tourniquet use?*
C.11. *Is it appropriate to suction the endotracheal tube and oropharynx of this patient before extubation?*
D. Postoperative Management
D.1. *What special consideration should be given to postoperative pain management for this patient?*
D.2. *What steps should be taken to enhance the coagulation status of this patient in the postoperative period while at home?*
D.3. *Can this patient be treated with FVIII supplements using home infusion?*
Acknowledgment
32 Sickle Cell Disease
Chris R. Edmonds and Vinod Malhotra
A. Medical Disease and Differential Diagnosis
A.1. *What was the most likely underlying medical condition in this patient? How would you confirm the diagnosis of sickle cell anemia (SCA)?*
A.2. *What is sickle cell disease (SCD)?*
A.3. *What is sickle cell trait (SCT)?*
A.4. *What are some of the other common hemoglobinopathies and what are their clinical features?*
A.5. *What are the clinical features of SCD?*
A.6. *Describe the different types of sickle cell crises.*
A.7. *Discuss the pathophysiologic effects of SCD.*
A.8. *What is acute chest syndrome?*
B. Preoperative Evaluation and Preparation

B.1. What preoperative evaluation and testing would you perform on this patient prior to anesthesia? Would you ask for a hematology consult, and what question(s) would you ask?

B.2. What preoperative instructions would you give this patient prior to being admitted to the hospital? How would you prepare this patient for general anesthesia and regional anesthesia?

B.3. Discuss the indications for perioperative exchange transfusion in this patient.

B.4. What are the indications for blood transfusion in SCD?

Acute conditions

Chronic conditions

C. Intraoperative Management

C.1. Discuss the anesthetic management for this patient. Discuss both regional and general anesthesia considerations.

C.2. Discuss how the comorbidities associated with SCD can affect your anesthetic management.

C.3. What precautions should one take to prevent sickling in this patient?

C.4. Discuss what issues or concerns should be brought up by the team during the debrief at the conclusion of the case. What would you sign-out to the postanesthesia care unit (PACU) staff?

D. Postoperative Management

D.1. Discuss the postoperative management of this patient. What opioid sparing techniques can you use and discuss a multimodal analgesic plan?

D.2. What complications might occur in this patient in the immediate postoperative period?

D.3. What is the treatment of sickle cell crisis?

D.4. What is the role of hyperbaric oxygen therapy in treatment of sickle cell crisis?

SECTION 9 Eye, Ear, Nose, and Throat

33 Airway Trauma

Richard P. Dutton and LaRita Yvette Fouchè-Weber

A. Medical Disease and Differential Diagnosis

A.1. What variables mitigate injury from motorcycle collisions?

A.2. What other significant trauma may be present?

A.3. How is the initial assessment of a trauma patient organized?

A.4. How would you evaluate airway and breathing?

A.5. How would you evaluate the circulation?

A.6. How would you evaluate mental status and neurologic condition?

A.7. What diagnostic tests are indicated for this patient based on the mechanism of injury?

A.8. What are the zones of the neck, and what is their clinical significance?

A.9. What immediate treatment is necessary before diagnostic studies?

A.10. When and where should the impaling object be removed?

B. Preoperative Evaluation and Preparation

B.1. What laboratory tests would you want?

B.2. What x-ray studies are most important to the anesthesiologist?

B.3. Is an electrocardiogram (ECG) necessary?

B.4. Should this patient be intubated before going for computed tomography (CT) scanning?

B.5. When and where should this patient's airway be managed?

B.6. Are any prophylactic medications indicated?

C. Intraoperative Management

C.1. What monitors would you use? Is invasive monitoring necessary before definitive airway control?

C.2. What is the surgical approach to a zone I neck injury?

C.3. Is the patient likely to require tube thoracostomy? Should

this be placed before managing the airway?
C.4. *What are the options for managing this patient's airway?*
C.5. *What are the risks of rapid sequence induction in this patient?*
C.6. *What anesthetic agents would you use for a rapid sequence induction?*
C.7. *How can you minimize the risk of exacerbating cervical spine trauma?*
C.8. *How can you minimize the risks of aspiration?*
C.9. *How would you anesthetize the airway for an awake intubation?*
C.10. *What are the risks of awake fiberoptic intubation?*
C.11. *If the patient cannot be ventilated, what options are available?*
C.12. *Would a laryngeal mask airway (LMA) or other pharyngeal airway be of assistance?*
C.13. *What surgical airway options are available in this case?*
C.14. *What maintenance anesthetics are indicated or contraindicated in this patient?*
C.15. *What complications will the surgical plan introduce?*

D. Postoperative Management
D.1. *What are the criteria for extubation?*
D.2. *What techniques may be used during extubation?*
D.3. *How does alcohol abuse affect postoperative management?*
D.4. *What pain medication should be used?*

34 Open-Eye Injury and Cataract Surgery
Alaeldin A. Darwich

A. Medical Disease and Differential Diagnosis
A.1. *Why is this patient a particular challenge to the anesthesiologist?*
A.2. *What are the determinants of intraocular pressure (IOP) under normal circumstances? What is the normal range? What was the expected IOP in this patient's injured eye?*

A.3. *How is aqueous humor formed and eliminated?*

A.4. *How is IOP affected by arterial P_{CO_2}, systemic blood pressure, coughing and vomiting, deep inspiration, and hypoxemia?*

A.5. *What is the role of the central nervous system (CNS) on IOP?*

A.6. *What is glaucoma?*

A.7. *Is atropine contraindicated in patients with glaucoma?*

A.8. *How do carbonic anhydrase inhibitors work to decrease IOP? By what mechanism may osmotic agents decrease IOP?*

A.9. *Are carbonic anhydrase inhibitors or osmotic diuretics indicated in open-globe injuries?*

A.10. *Are topically applied ophthalmic medications absorbed systemically? How can this absorption be reduced? Which eyedrops may have effects that are of concern to the anesthesiologist?*

- Atropine
- Scopolamine
- Cyclopentolate (Cyclogyl)
- Tropicamide (Mydriacyl)
- Phenylephrine Hydrochloride (Neo-Synephrine)
- Epinephrine
- Timolol Maleate (Timoptic)
- Betaxolol Hydrochloride (Betoptic)
- Acetylcholine
- Echothiophate Iodide (Phospholine Iodide)
- Cocaine

B. Preoperative Evaluation and Preparation

B.1. *Is an open-globe injury always a surgical emergency?*

B.2. *What preoperative evaluation would you require?*

B.3. *The patient ate shortly before the accident. Would you attempt to pass a nasogastric tube or to administer emetics*

to empty the stomach?

B.4. Could this case be done with topical anesthesia or a retrobulbar block?

B.5. How would you premedicate this patient?

C. Intraoperative Management

C.1. What are some factors that may increase the risk of vitreous herniation during induction and maintenance of anesthesia?

C.2. Will you intubate this patient? Would you consider a laryngeal mask airway? How does intubation affect IOP? How can this effect be minimized?

C.3. Would you consider an awake intubation?

C.4. Is succinylcholine contraindicated in open-globe injuries? How does succinylcholine affect IOP?

C.5. Does pretreatment with nondepolarizing muscle relaxants prevent the succinylcholine-induced elevation in IOP?

C.6. How do nondepolarizing muscle relaxants affect IOP?

C.7. How will you perform a rapid sequence induction and intubation without using succinylcholine?

C.8. What are the effects of ketamine on the eye?

C.9. Would you consider the use of etomidate as an induction agent? What about propofol?

C.10. How do inhalation agents affect IOP and by what mechanism?

C.11. During the procedure, the patient's pulse suddenly dropped to 40 beats per minute. What do you think was happening? What is the oculocardiac reflex (OCR)?

C.12. What are the afferent and efferent pathways of the OCR?

C.13. What factors contribute to the incidence of the OCR?

C.14. How do you diagnose and treat the OCR?

C.15. Is atropine useful for the OCR?

C.16. Can a retrobulbar block prevent the OCR? Is it appropriate in this patient?

D. Postoperative Management

D.1. *Would you reverse the neuromuscular blockade in this patient?*
D.2. *Do reversal doses of atropine affect IOP?*
D.3. *What would you do before extubating this patient?*
D.4. *When would you extubate this patient?*
D.5. *The patient awakened in the recovery room and complained of pain and tearing in the opposite eye. The conjunctiva was inflamed. What was the likely cause?*
D.6. *Will taping the eyes shut or applying ointment prevent corneal abrasions? Are there any contributing factors?*
D.7. *What should you do when you suspect your patient might have a corneal abrasion?*
D.7. *A month after the surgical repair, the patient complained of impaired vision in the operative eye. He was examined and found to have a detached retina. As part of the surgical treatment, the ophthalmologist injected a gas bubble into the patient's posterior chamber. Why is this important to an anesthesiologist?*

E. Anesthesia for Cataract Surgery
E.1. *What is a cataract?*
E.2. *What are the causes and risk factors of cataract formation?*
E.3. *How would you conduct the preoperative medical evaluation for a patient having cataract surgery?*
E.4. *What is the cardiac risk for this patient? If this patient is on anticoagulation and/or antiplatelet medications, should he stop or continue these medications?*
E.5. *What are the anesthetic options for cataract surgery?*
E.6. *What is the postoperative course after cataract surgery?*

35 Laser Treatment for Laryngeal Lesions
Stephanie Marie Vecino and Hugh C. Hemmings Jr.

A. Medical Disease and Differential Diagnosis
A.1. *What is the cause of RRP?*
A.2. *What is the usual presentation of RRP?*

A.3. *How do you diagnose RRP?*
A.4. *What are the available treatment options for RRP?*
A.5. *What are common adverse effects of α-interferon therapy?*
A.6. *What is the differential diagnosis of hoarseness in this child?*

B. Preoperative Evaluation and Preparation

B.1. *What are the key points of the preanesthetic history and physical examination in this patient?*
B.2. *What preoperative laboratory tests are necessary?*
B.3. *How should this child be premedicated before coming to the operating room?*
B.4. *What are the special anesthetic considerations prior to inducing anesthesia in this patient?*

C. Intraoperative Management

C.1. *What is a laser, and how does it work?*
C.2. *What are the characteristics of laser radiation?*
C.3. *Discuss some advantages associated with the use of lasers for laryngeal surgery.*
C.4. *What are some disadvantages of lasers compared with microdebriders?*
C.5. *How would you protect the external surface of a conventional endotracheal tube (ETT) for use during laser microlaryngoscopy?*
C.6. *What special ETTs are available for laser surgery?*
C.7. *How would you manage an airway fire?*
C.8. *What is the Venturi effect?*
C.9. *What is Venturi jet ventilation?*
C.10. *How would you institute and maintain manual jet ventilation?*
C.11. *How is anesthesia maintained during jet ventilation?*
C.12. *What are the complications of jet ventilation?*
C.13. *Are there contraindications for the use of jet ventilation?*
C.14. *Discuss airway management options during laryngeal*

papilloma resection.
C.15. How would you plan to monitor this patient?
C.16. How would you induce anesthesia for an intermittent apnea technique?
D. Postoperative Management
D.1. What are the common postoperative complications?

SECTION 10 Pediatrics

36 Tracheoesophageal Fistula
Jacques H. Scharoun
A. Pathophysiology and Differential Diagnosis
A.1. What is the diagnosis? What are the clinical features of this disease?
A.2. What is the pathophysiology of this disease?
A.3. Describe the normal development of the trachea and esophagus.
A.4. How are tracheoesophageal fistula (TEF) and esophageal atresia (EA) inherited?
A.5. How are the different types of TEF/EA classified?
A.6. What other problems may this child have, and when should these be investigated?
A.7. What should the parents be told regarding perioperative risk? Risk of recurrence?
B. Preoperative Evaluation and Preparation
B.1. What laboratory workup should be obtained before surgery?
B.2. Describe management in the NICU before surgery.
B.3. How is severe lung disease managed before repair?
B.4. Should this patient be intubated preoperatively for airway protection?
C. Intraoperative Management
C.1. What invasive lines and monitoring are appropriate before induction? After induction?

C.2. *Discuss fluid and temperature management for this baby.*

C.3. *What are the options regarding induction and intubation?*

C.4. *What is the role of rigid and fiberoptic bronchoscopy in this patient prior to incision?*

C.5. *Describe the steps of an open repair of EA/TEF.*

C.6. *What are common intraoperative problems, and how can they be managed?*

C.7. *If the surgeon decides to proceed thoracoscopically, how will you perform your anesthetic? Is one-lung ventilation required? What are some complications unique to thoracoscopy in the newborn?*

D. Postoperative Management

D.1. *When should the baby be extubated?*

D.2. *What options are available for postoperative analgesia?*

D.3. *What are early and late complications of TEF repair?*

37 Congenital Diaphragmatic Hernia

Dana L. Gurvitch and Fun-Sun F. Yao

A. Medical Disease and Differential Diagnosis

A.1. *What differential diagnoses are compatible with these signs and symptoms?*

A.2. *Describe the incidence and classification of congenital diaphragmatic hernia (CDH).*

A.3. *What are the causes of hypoxemia in patients with CDH?*

A.4. *How do you assess the severity of pulmonary hypoplasia?*

A.5. *How do you make a diagnosis of right-to-left shunting through the patent ductus arteriosus?*

A.6. *What other congenital anomalies are usually associated with CDH?*

B. Preoperative Evaluation and Preparation

B.1. *How would you interpret the following arterial blood gas analyses: pH, 7.20; $PaCO_2$, 55 mmHg; PaO_2, 35 mmHg; and CO_2 content, 19 mEq per L? How would you correct them?*

B.2. *What immediate treatment should be given to improve the newborn's respiratory status preoperatively?*

B.3. *Should CDH be repaired urgently once the diagnosis is made and confirmed?*

B.4. *What are the effects of nitric oxide (NO) on pulmonary and systemic circulation?*

B.5. *What is the current role of extracorporeal membrane oxygenation (ECMO) in the management of CDH?*

C. Intraoperative Management

C.1. *What monitors would you use for this neonate during surgery?*

- Respiratory
- Cardiovascular
- Thermoregulatory

C.2. *How would you induce and maintain anesthesia?*

C.3. *Would you use nitrous oxide for anesthesia? Why?*

C.4. *How would you ventilate the patient?*

C.5. *Is the infant with CDH more at risk from hypothermia?*

C.6. *The surgeon returned the intrathoracic stomach and intestine to the peritoneal cavity and the ipsilateral lung was found to be hypoplastic and collapsed. The resident anesthesiologist tried to expand the collapsed lung manually with positive airway pressure. Five minutes after the abdomen was closed, the blood pressure suddenly dropped from 70/40 to 30/20 mmHg, the heart rate from 150 to 80 beats per minute, and the pulse oximeter from 95% down to 60% saturation. What would you immediately do?*

C.7. *Discuss fluid therapy in this patient.*

C.8. *At the conclusion of surgery, would you extubate the patient in the operating room?*

D. Postoperative Management

D.1. *What is the mortality rate in patients with CDH? What postoperative problems would you expect in this patient?*

38 Tetralogy of Fallot

David Whiting and James A. DiNardo

A. Medical Disease and Differential Diagnosis

A.1. What is TOF?

Tetralogy of Fallot with Pulmonary Stenosis

Tetralogy of Fallot with Pulmonary Atresia

Tetralogy of Fallot with Absent Pulmonary Valve

A.2. What is the pathophysiology of TOF/PS?

A.3. What is shunting, and how is Q_P:Q_S calculated?

A.4. What is the pathophysiology of TOF with pulmonary atresia?

A.5. How is SaO_2 determined in single ventricle physiology?

A.6. What is a "pink Tet"?

A.7. What are hypercyanotic spells? How are they treated?

A.8. What palliative surgical procedures are available for treating patients with TOF/PS?

A.9. What palliative catheter-based procedures are available for patients with TOF?

A.10. What definitive surgical procedures are available for treating patients with TOF/PS?

A.11. What palliative and definitive surgical procedures are available for patients with TOF with pulmonary atresia?

A.12. What are the long-term outcomes of patients with TOF?

B. Preoperative Evaluation and Preparation

B.1. What preoperative history and physical examination information do you want?

B.2. Which other abnormalities need to be considered in this patient?

B.3. What premedication will you give to a child with congenital heart disease?

C. Intraoperative Management

C.1. How will you induce anesthesia in this patient if intravenous (IV) access cannot be obtained?

C.2. *Why would end-tidal carbon dioxide ($EtCO_2$) monitoring be of particular use in a patient with TOF/PS?*

C.3. *What is near-infrared spectroscopy (NIRS) and what does it measure?*

C.4. *What are the important management issues during creation of a palliative shunt?*

C.5. *What is the effect of inhalation anesthetics on airway reflexes, myocardial contractility, systemic vascular resistance (SVR), and pulmonary vascular resistance (PVR) in children?*

C.6. *What are the pre-cardiopulmonary bypass (pre-CPB) anesthetic goals for a patient undergoing definitive surgical correction of TOF/PS?*

C.7. *What interventions will reliably reduce PVR?*

C.8. *How does heparin administration and activated coagulation time (ACT) monitoring for CPB differ in children as compared with adults?*

C.9. *How is heparin reversed?*

C.10. *What is the incidence of protamine reactions in children?*

C.11. *What is the role of transesophageal echocardiography (TEE) in this patient?*

C.12. *What effect would a residual ventricular septal defect (VSD) have in this patient following separation from CPB?*

D. Postoperative Management

D.1. *How should postoperative ventilation be managed in this patient following placement of a transannular patch for TOF/PS?*

D.2. *Following complete repair of TOF/PS in an infant, what SaO_2 is acceptable?*

D.3. *Following placement of a modified Blalock-Taussig shunt (MBTS) for TOF/PS in an infant, what SaO_2 is acceptable?*

D.4. *What is junctional ectopic tachycardia (JET)?*

39 Transposition of the Great Arteries

David Whiting and James A. DiNardo

A. Medical Disease and Differential Diagnosis

A.1. What defines the cardiac situs?

A.2. What is transposition of the great arteries (D-TGA)?

A.3. What additional cardiac lesions are associated with D-TGA?

A.4. What is the natural history of D-TGA?

A.5. What is the pathophysiology of D-TGA?

A.6. What determines the oxygen saturation in patients with D-TGA?

A.7. Why did this infant have reverse differential cyanosis?

A.8. What are the preoperative issues pertaining to the coronary arteries in D-TGA?

A.9. What are the clinical subsets of D-TGA?

A.10. What is the differential diagnosis of D-TGA and how is the diagnosis made?

A.11. What preoperative interventions can help stabilize a patient with D-TGA?

Intact Ventricular Septum

Ventricular Septal Defect

Ventricular Septal Defect and Left Ventricular Outflow Tract Obstruction

Pulmonary Artery Hypertension

A.12. What are the surgical options for repair? Why is one chosen over the others?

Arterial Anatomic Repair: Arterial Switch (Jatene) Operation

Intra-atrial Physiologic Repairs: Mustard and Senning Procedures

Rastelli, LeCompte, and Nikaidoh Procedures

B. Preoperative Evaluation and Preparation

B.1. What information is important to prepare for this case?

- *B.2. What are the anesthetic goals before cardiopulmonary bypass (CPB)?*
- *B.3. What is the plan for glucose management in this patient?*

C. Intraoperative Management
- *C.1. How would you monitor this infant?*
- *C.2. What would be the best method of induction for this patient?*
- *C.3. Is CPB in infants and children different from adults?*
- *C.4. What is modified ultrafiltration (MUF)?*
- *C.5. Briefly describe the surgical techniques of the Mustard/Senning, ASO, and Rastelli procedures.*
  - Intra-atrial Physiologic Repairs: Mustard and Senning Procedures
  - Arterial Anatomic Repair: Arterial Switch (Jatene) Operation
  - Rastelli Procedure
- *C.6. What is hypothermia, and how is it classified? What is low-flow cardiopulmonary bypass (LFCPB)? What is deep hypothermic circulatory arrest (DHCA)?*
- *C.7. Why is hypothermia beneficial to the brain during LFCPB and DHCA?*
- *C.8. Explain the difference between α-stat and pH-stat blood gas management.*
- *C.9. What are the immediate post-CPB issues following ASO?*

D. Postoperative Management
- *D.1. How is myocardial ischemia addressed in the intensive care unit (ICU) following the ASO?*
- *D.2. What immediate postoperative problems would be anticipated following the Rastelli procedure?*
- *D.3. What intermediate and long-term surgical problems are seen after ASO?*
- *D.4. What are the long-term outcomes after ASO?*
- *D.5. What are the long-term outcomes after Rastelli repair for patients with D-TGA with left ventricular outflow tract*

(LVOT) obstruction?
D.6. What is long-term neurologic outcome like after ASO?

40 Pyloric Stenosis
Aarti Sharma and Vinod Malhotra

A. Medical Disease and Differential Diagnosis
A.1. What is the diagnosis in this patient?
A.2. What is the differential diagnosis of pyloric stenosis?
A.3. What are the metabolic problems in this newborn secondary to his disease?
A.4. What are the adverse effects of metabolic alkalosis?
A.5. How would you treat this infant?
Supportive Therapy
Fluids
Electrolytes
Prevention of Aspiration
Diagnostic Tests
Surgery
A.6. How would you determine fluid replacement in a newborn, and what fluids would you use?
Maintenance Fluids
Electrolytes
Correction of Deficits
Replacement of Losses
A.7. How would you correct the metabolic alkalosis in this patient?
A.8. What causes a cardiac murmur?
B. Preoperative Evaluation and Preparation
B.1. How would you evaluate this patient preoperatively?
History
Physical Examination
Laboratory Findings
B.2. How would you evaluate a heart murmur?
B.3. How would you differentiate between functional versus

organic murmur?
B.4. What are the types of VSD? What type of shunt do they cause?
B.5. What are the risks of surgery and anesthesia in a patient with VSD?
B.6. How would you prepare this patient rapidly for emergency surgery? Is surgical intervention an acute emergency in this case?
B.7. How would you prepare this patient for anesthesia?
C. Intraoperative Management
C.1. What induction–intubation sequence would you use?
C.2. What are the anatomic characteristics of the airway in the newborn and how do they differ from those in the adult?
C.3. How do you determine the size of an endotracheal tube in a pediatric patient?
C.4. What anesthesia system would you use and why?
C.5. What are the advantages and the disadvantages of commonly employed nonrebreathing systems?
C.6. How would you monitor this patient intraoperatively?
C.7. How does the pulse oximeter function?
C.8. What factors affect the measurement of oxygen saturation by the pulse oximeter?
D. Postoperative Management
D.1. What are the complications that can occur in the postanesthesia recovery period?
D.2. How would you treat postextubation "croup" in this infant?

41 Inflammatory Airway Disease in Childhood: Laryngotracheobronchitis
Miles Dinner and Anthony Longhini

A. Medical Disease and Differential Diagnosis
A.1. What portion of the airway is affected in the croup syndrome and why?
A.2. What is stridor?

A.3. *How does stridor correlate with anatomic location?*
A.4. *Define croup. What is the clinical presentation of laryngotracheitis?*
A.5. *What is the differential diagnosis of acute upper airway obstruction in children?*
A.6. *What is bacterial tracheitis?*
A.7. *What congenital problems can mimic features of croup?*
A.8. *How is the severity of croup assessed?*
A.9. *What is the medical management of croup? Does this have implications for the anesthesiologist?*
A.10. *What is epiglottitis? What are its common causes? What is the incidence?*
A.11. *What are the clinical manifestations of epiglottitis?*
A.12. *How is the diagnosis of epiglottitis made?*
A.13. *What is postextubation croup? How is it managed?*
A.14. *What are the nonacute causes of partial airway obstruction in children?*

Extrinsic Pathologies
Intrinsic Pathologies

B. Preoperative Evaluation and Preparation
B.1. *Is intubation always required in children with epiglottitis?*
B.2. *Why is general anesthesia administered to a child with epiglottitis?*
B.3. *How would you prepare the patient for anesthesia?*

C. Intraoperative Management
C.1. *How is the airway of the child with epiglottitis best secured?*
C.2. *How would you induce anesthesia?*
C.3. *Should a child with epiglottitis undergo a rapid sequence induction?*
C.4. *Is awake intubation a practical alternative to secure the patient's airway?*
C.5. *What would you do if the airway cannot be secured with intubation?*

C.6. *Should this patient have a nasotracheal or orotracheal tube placed?*

C.7. *Shortly after intubation, frothy secretions were obtained on suctioning the endotracheal tube. What is the reason for this? How can this be treated?*

D. Postoperative Management

D.1. *How long should this patient remain intubated? What criteria determine extubation time?*

D.2. *How would you make this patient comfortable during the course of intubation?*

D.3. *What outcome can one expect for the child with acute epiglottitis?*

42 Cleft Palate

Aarti Sharma

A. Medical Disease and Differential Diagnosis

A.1. *Describe the anatomic concept of a cleft palate and a cleft lip.*

A.2. *What is the cause of a cleft lip or a cleft palate?*

A.3. *What is the incidence of a cleft lip and a cleft palate?*

A.4. *Discuss the pathophysiology of a cleft lip and palate in the neonate and the older child (e.g., age >5 years).*

A.5. *What other conditions are associated with a cleft lip and a cleft palate?*

A.6. *What is Pierre Robin syndrome?*

A.7. *What is Treacher Collins syndrome?*

A.8. *What kind of specialized team care would these patients need?*

A.9. *Discuss indications and timing of closure of cleft lip and palate.*

A.10. *What is velopharyngeal incompetence, and how can it be diagnosed?*

A.11. *What is the relation of tonsillectomy and adenoidectomy to velopharyngeal incompetence?*

B. Preoperative Evaluation and Preparation
B.1. What information do you need before closure of a cleft lip and palate?
B.2. What preoperative orders are needed?
C. Intraoperative Management
C.1. What monitors will you need for cheiloplasty and palatoplasty?
C.2. Discuss the induction and the anesthetic management for cleft lip and palate.
C.3. What positioning is recommended for cleft palate repair surgery?
C.4. What are the reported complications of this type of surgery and anesthesia?
C.5. Briefly describe the surgical techniques used to repair cleft defects.
C.6. How does a pharyngeal flap affect anesthetic management or any subsequent anesthetic administered to this patient?
C.7. What is an Abbe flap? What are its anesthetic implications?
C.8. What is the crucial problem of anesthesia for cleft palate? What are the unique considerations of this surgical repair?
C.9. What is laryngospasm? How would you make a diagnosis of laryngospasm?
C.10. How would you manage the patient with laryngospasm?
D. Postoperative Management
D.1. What complications of cleft lip and cleft palate surgery may be seen in the recovery room?
D.2. How do you protect the airway postoperatively?
D.3. How would you control postoperative pain in patients following a cleft lip and cleft palate repair?

43 Congenital Heart Disease with a Cervical Mass in Infancy
Miles Dinner and Elizabeth Q. Starker

A. Medical Disease and Differential Diagnosis
A.1. What is 22q11 deletion syndrome?

A.2. *What are the associated cardiovascular defects in 22q11 deletion syndrome?*
A.3. *What are the metabolic and endocrine abnormalities in patients with 22q11 deletion syndrome and the attendant manifestations?*
A.4. *What are the immunologic findings in 22q11 deletion syndrome?*
A.5. *What is the differential diagnosis of cervical masses in infancy?*
A.6. *What is a cystic hygroma? What are the complications? What is the treatment?*
A.7. *What is the IAA anomaly?*
A.8. *What is the pathophysiology of the IAA syndrome?*
A.9. *How is ductal patency maintained?*
A.10. *What are the side effects of prostaglandin infusion?*
A.11. *What is the hyperoxia test?*

B. Preoperative Evaluation and Preparation

B.1. *What preoperative studies should be obtained to evaluate the neck mass?*
B.2. *How would you categorize the difficult airway in children?*
B.3. *What features of the difficult airway can be noted on physical examination?*
B.4. *How would you preoperatively optimize the ability to secure the airway in the operating room?*
B.5. *What laboratory studies are necessary before surgery?*
B.6. *What are the causes of heart failure (HF) in the infant? How would you assess this infant in your preoperative evaluation for signs of HF?*
B.7. *How would you optimize the preoperative treatment of HF?*
B.8. *How would you premedicate this infant?*
B.9. *When is premedication useful in infants and children?*
B.10. *Before the planned surgery, the infant is scheduled for a magnetic resonance imaging (MRI) scan. You are asked to*

ensure that the baby remains immobile for 20 minutes to perform the scan adequately. How would you accomplish this?

C. Intraoperative Management

C.1. What anesthesia equipment, circuit, and monitors would you use?

C.2. Describe techniques other than direct laryngoscopy that would be useful for securing the airway in this baby.

Infant Video Laryngoscope
Intubation through a Laryngeal Mask Airway
Retrograde Cricothyroid Wire
Blind Nasal Intubation
Nasal Intubation with Laryngoscope and Magill Forceps
Fiberoptic Intubation

C.3. How would you monitor blood loss in this patient?

C.4. What anesthetic technique should be used in a patient who may experience severe loss of blood intraoperatively?

C.5. How would you induce and maintain anesthesia in this neonate?

C.6. Intraoperatively, the surgeon must dissect the tumor in the anterior mediastinum and needs to have a quiet surgical field. How would you accomplish this in the infant?

D. Postoperative Management

D.1. How would you manage this patient postoperatively?

44 Patent Ductus Arteriosus and Prematurity

Albert C. Yeung and Fun-Sun F. Yao

A. Medical Disease and Differential Diagnosis

A.1. How would you classify prematurity? What are the common problems associated with prematurity?

A.2. What are the survival rates of preterm infants?

A.3. What are the incidence and survival rates of respiratory distress syndrome (RDS)? Discuss its pathophysiology.

A.4. What is bronchopulmonary dysplasia (BPD)? How would

you treat it?

A.5. *What are apnea spells? What are the possible causes of apneic spells?*

A.6. *Discuss the incidence and pathophysiology of PDA in preterm infants.*

A.7. *How would you make a diagnosis of PDA? Describe its treatment.*

A.8. *Would you give digitalis to treat congestive heart failure in preterm infants? Why?*

A.9. *How does indomethacin close the ductus? What are the adverse effects of indomethacin?*

A.10. *When is surgical closure indicated? What are the complications associated with surgical ligation?*

A.11. *What is retinopathy of prematurity (ROP) (retrolental fibroplasia [RLF])? Discuss its etiology, pathophysiology, prognosis, prevention, and treatment.*

A.12. *Define neutral and critical temperatures. What are these values in the preterm neonate, in the term neonate, and in the adult? Discuss temperature regulation in the neonate.*

B. Preoperative Evaluation and Preparation

B.1. *How would you evaluate this patient preoperatively?*

B.2. *What are the normal values of arterial blood gases and pH in neonates and infants?*

B.3. *Interpret the arterial blood gases: pH, 7.30; $Paco_2$, 60 mmHg; Pao_2, 49 mmHg; HCO_3^-, 20 mEq per L on 50% oxygen; and 6 cm H_2O of positive end-expiratory pressure (PEEP). How would you improve them?*

B.4. *What are the normal values of arterial blood pressure, heart rate, and respiratory rate for preterm infants?*

B.5. *What are the normal values of WBC, red blood cells (RBCs), hemoglobin, glucose, electrolytes, calcium, blood urea nitrogen, and creatinine for preterm infants?*

B.6. *Would you transfuse blood to this patient preoperatively?*

B.7. *How would you interpret the urinalysis: specific gravity, 1.005; sugar, 1+; and protein, 1+?*

B.8. *Would you correct a serum calcium level of 6.0 mg per dL? What other information would you like to have? Which contains more calcium, 10 mL of 10% calcium chloride or 10 mL of 10% calcium gluconate? Could you hyperventilate this child safely?*

B.9. *How would you premedicate this patient?*

C. Intraoperative Management

C.1. *Where should the procedure take place? In the neonatal intensive care unit (NICU) or the operating room?*

C.2. *What monitors would you use for this child during surgery?*

C.3. *How does the oxygen analyzer work?*

C.4. *What is the Doppler effect? How does the Doppler transducer measure blood pressure?*

C.5. *What is the mechanism of pulse oximetry? Why is it important to monitor arterial oxygen saturation? What levels of arterial oxygen saturation would you like to keep during surgery?*

C.6. *How would you maintain the patient's body temperature?*

C.7. *How do the anesthetic requirements of the preterm infant differ from those of the adult?*

C.8. *What size endotracheal tube would you have used if the patient had not been intubated?*

C.9. *How would you have induced anesthesia if the patient had not been intubated?*

C.10. *How would you maintain anesthesia?*

C.11. *How would you ventilate the patient? What tidal volume, respiratory rates, and F_{IO_2} would you set for the infant?*

C.12. *Discuss blood and fluid therapy in this preterm infant.*

C.13. *During dissection of the ductus arteriosus, the arterial oxygen saturation dropped from 92% to 80% and the heart*

rate decreased from 140 beats per minute to 80 beats per minute. What were the causes? How would you correct this situation?

D. Postoperative Management

D.1. Would you reverse the muscle relaxants and extubate the patient at the end of surgery?

D.2. How can one minimize the risk of transporting the patient to the NICU after surgery?

D.3. The patient's condition deteriorated postoperatively in the intensive care unit (ICU). Physical examination revealed persistent cardiac murmur. What was the possible diagnosis?

45 Post-tonsillectomy Hemorrhage

Dana L. Gurvitch, Jessica A. Latzman, and Hugh C. Hemmings Jr.

A. Medical Disease and Differential Diagnosis

A.1. Approximately how many pediatric tonsillectomies are performed in the United States each year? What are the indications for tonsillectomy?

A.2. What is the differential diagnosis for this patient?

A.3. What is the treatment for a patient with von Willebrand disease?

A.4. Describe the vascular anatomy of the tonsils. What is the incidence of post-tonsillectomy hemorrhage?

A.5. What are the risk factors for post-tonsillectomy hemorrhage? Does age matter?

A.6. Describe the morbidity and mortality of post-tonsillectomy hemorrhage.

B. Preoperative Evaluation and Preparation

B.1. What is your approach to assessing this patient?

B.2. What will you set up in the operating room for this patient? How will your preparation be different from a routine general anesthetic set up?

B.3. Should you plan to use vasopressors?

B.4. *The patient seems anxious. Will you administer a sedative to calm the patient down?*

B.5. *How do you plan on interpreting this patient's laboratory results?*

B.6. *What are your expectations of the surgeon, specifically as it relates to induction of anesthesia?*

C. Intraoperative Management

C.1. *What is your plan for induction of anesthesia? During the initial procedure, this patient underwent an uneventful inhalational induction, with postinduction intravenous (IV) placement. Would you perform an inhalational induction again? Why or why not?*

C.2. *What is your plan for management of blood in the oropharynx?*

C.3. *What is your plan for airway management?*

C.4. *Laryngoscopy and intubation prove challenging due to blood in the airway. What options do you have now?*

C.5. *What is your plan for maintenance of the anesthetic? What other medications might you want to give?*

C.6. *Assuming the surgical intervention is successful, what is your plan for emergence and extubation?*

D. Postoperative Management

D.1. *Is postoperative management in the pediatric intensive care unit (PICU) indicated?*

D.2. *What would you require for safe transport from the operating room to the PICU?*

D.3. *Discuss potential postoperative complications for this patient.*

D.4. *What discharge instructions should be given post-tonsillectomy?*

SECTION 11 Pain Management and Neuraxial

Blocks

46 Brachial Plexus Block

Tiffany Tedore and William Urmey

A. Medical Disease and Differential Diagnosis

A.1. What are the presenting problems in this patient?

A.2. What additional medical history would you want to obtain?

A.3. What implications does the use of atenolol have on the patient's coexisting medical condition?

A.4. Why is immobilization of the arm important following humeral fracture?

A.5. What nerve is at particular risk for injury from humeral fracture?

B. Preoperative Evaluation and Preparation

B.1. What testing would be helpful to elucidate the cause of this patient's fainting spells?

B.2. What premedication would you order?

B.3. What are the respiratory effects of benzodiazepines?

C. Intraoperative Management

C.1. What anesthetic technique would you use?

C.2. Describe the relevant anatomy of the brachial plexus.

C.3. What relevant anatomic structures in the neck and below the neck can be injured or injected accidentally during brachial plexus block?

C.4. What regional technique would you choose to block the brachial plexus in this patient?

C.5. What are the advantages and disadvantages of the following blocks?

Interscalene Block

Supraclavicular Block

Infraclavicular Block

Axillary Block

C.6. Describe the landmarks and procedures for nerve stimulator

and ultrasound-guided interscalene block.

C.7. *Describe the landmarks and procedures for supraclavicular block.*

C.8. *Describe the landmarks and procedures for infraclavicular block.*

C.9. *Describe the landmarks and procedures for axillary block.*

C.10. *The patient requests to have the brachial plexus block performed after you administer general anesthesia. Would you agree to this request?*

C.11. *What relevant respiratory complications or side effects are you concerned about in this patient?*

C.12. *What is the incidence of hemidiaphragmatic paresis following interscalene brachial plexus block? Can this complication be avoided by decreasing the volume or concentration of local anesthetic injected or by using ultrasound-guided supraclavicular block?*

C.13. *Describe the pulmonary function changes that occur after interscalene brachial plexus block.*

C.14. *What would you do if the patient complained of dyspnea after you performed an interscalene or supraclavicular block?*

C.15. *The surgeon prefers to perform the surgical procedure in the sitting position. What are the advantages and disadvantages of this position compared to the lateral position in this patient?*

C.16. *Which nerves are most commonly missed with axillary brachial plexus block? With interscalene block? With all brachial plexus blocks?*

C.17. *What is the expected duration of brachial plexus block with 30 mL of 1.5% mepivacaine with 5 μg per mL epinephrine?*

C.18. *What is the maximum safe dose of local anesthetic for brachial plexus block?*

D. Postoperative Management

D.1. What regimen would you suggest for postoperative pain management?

D.2. In the postanesthesia care unit, the patient complains of dyspnea. How would you evaluate and manage this?

D.3. On the third postoperative day after removal of the brachial plexus catheter, the patient complains of persistent numbness and paresthesia in the ulnar nerve distribution. What would you tell the patient? How would you manage neurologic dysfunction after brachial plexus block that persists for 1 week?

47 Nerve Blocks of the Lower Extremity

Roniel Weinberg, Melvin La, and Danielle M. Gluck

A. Preoperative Evaluation

A.1. What is the Glasgow Coma Scale and its significance in this patient?

A.2. Should surgery be allowed to proceed in this patient who has a subdural bleed?

A.3. Does the patient's atrial fibrillation need to be addressed prior to surgery, and if so, how?

B. Preoperative Preparation

B.1. What is dabigatran (Pradaxa)? How is its effect measured? How far in advance of elective surgery should it be stopped? Can its effect be reversed?

B.2. What concerns do you have regarding neuraxial anesthesia in this patient who has a subdural hematoma?

B.3. What concerns do you have regarding neuraxial anesthesia in this patient who has prior back surgery?

B.4. The surgeon is willing to wait a few days prior to surgery while the swelling around the injury decreases. When would you feel comfortable proceeding with surgery in this patient?

C. Intraoperative Management

C.1. What two nerve plexuses need to be blocked in this case?

What nerve roots contribute to each plexus? Name the major nerves that come from each plexus.

C.2. *What is the innervation to the medial and lateral aspects of the ankle? What nerves need to be blocked for his surgery?*

C.3. *What nerves are blocked with an ankle block? Would you do an ankle block in this case?*

C.4. *Explain the posterior landmark technique to blocking the lumbar plexus. What motor response would be elicited with a nerve stimulator? At what stimulation level would you feel safe injecting the patient? Why not at a lower level of stimulation? Can ultrasound guidance be utilized for this injection?*

C.5. *What is a fascia iliaca block (three-in-one block)?*

C.6. *Describe the different ultrasound approaches to blocking the saphenous nerve above the knee.*

C.7. *What benefits might a saphenous nerve block above the knee provide compared to a femoral nerve block?*

C.8. *How would pain from a midthigh tourniquet dictate which peripheral nerve blocks to use in this patient? Describe the landmark technique of sciatic nerve block in the gluteal region. What is seen while performing an ultrasound technique to block the sciatic nerve?*

C.9. *Why does a popliteal nerve block have a high failure rate if performed too proximate to the popliteal fossa when using a landmark/nerve stimulator technique? Describe how this can be avoided when using ultrasound-based popliteal block.*

C.10. *What is the IPACK block? In what situations would this block be useful?*

D. Postoperative Pain Management

D.1. *Describe compartment syndrome and how that risk would influence your postoperative plan for peripheral regional analgesia.*

D.2. How would the addition of dexamethasone to your local anesthetic influence the duration of the blocks placed in the OR?

D.3. What is liposomal bupivacaine?

D.4. What benefit would a peripheral nerve catheter provide over a long-acting local anesthetic? Are there any downsides?

D.5. You were able to perform a continuous spinal epidural (CSE) at L3–L4 and used 0.125% bupivacaine via epidural route for postoperative pain control. The patient reports that he is comfortable regarding both his back pain and his ankle pain. What benefit would continuing the patient's methadone confer in this case?

D.6. How can regional analgesia aid in fast-track postoperative care?

48 Complex Regional Pain Syndromes

Mohammad M. Piracha, Neel D. Mehta, Sudhir A. Diwan, and Vinod Malhotra

A. Medical Disease and Differential Diagnosis

A.1. What is the differential diagnosis of pain in this patient?

A.2. What is complex regional pain syndrome (CRPS)?

A.3. What are the two types of CRPS?

A.4. What are the diagnostic criteria for CRPS? What is the incidence of this disease?

A.5. Define allodynia, hyperalgesia, hyperesthesia, and dysesthesia.

A.6. What are the stages of CRPS?

Stage I

Stage II

Stage III

A.7. What are the possible etiologies of CRPS?

A.8. Explain the pathophysiology of the development of CRPS.

A.9. Define sympathetically maintained pain (SMP) and sympathetically independent pain (SIP).

A.10. *How does CRPS differ from neuralgia?*
A.11. *What is central pain? How will you differentiate central pain from CRPS?*
A.12. *Is the social history of this patient relevant to the development of chronic pain syndrome?*

B. Pain Management

B.1. *How will you work up CRPS types I and II?*
B.2. *Describe the sympathetic nerve supply to the arm?*
B.3. *Where is the stellate ganglion located?*
B.4. *What are the anatomic landmarks used in the stellate ganglion block?*
B.5. *What are the clinical signs of stellate ganglion block?*
B.6. *What is Horner syndrome?*
B.7. *After a stellate ganglion block, this patient reports no significant change in the degree of pain despite developing Horner syndrome. Is the pain psychogenic in this patient?*
B.8. *What types of nerve fibers are interrupted in stellate ganglion block?*
B.9. *What is a differential block?*
B.10. *What are the two major classes of local anesthetics? Describe the major differences in their clinical pharmacology.*
B.11. *What factors determine the onset, potency, and duration of a local anesthetic block?*
B.12. *How does the addition of epinephrine to commercially available premixed solutions affect the efficacy of local anesthetics?*
B.13. *How will you treat this patient?*
B.14. *What is the pharmacologic management of CRPS?*
B.15. *What is the role of intravenous regional block (Bier method) in diagnosis and treatment of CRPS?*
B.16. *Compare and contrast the mechanism of actions of ketamine and methadone.*

B.17. What roles does ketamine infusion play in the treatment of CRPS? Is there a guideline for ketamine infusion in treating CRPS?
B.18. What is neuromodulation? What is the role of spinal cord stimulation (SCS) in treating CRPS?
B.19. What is the role of surgical sympathectomy?
B.20. What role does intrathecal (IT) therapy play in managing CRPS?
B.21. If opioids are prescribed as treatment for CRPS patients, what is the Centers for Disease Control and Prevention (CDC) guideline of chronic opioid therapy?

C. Complications

C.1 What are the complications of stellate ganglion block?
C.2 What is the systemic toxicity of local anesthetics?
Central Nervous System Effects
Cardiovascular Effects
C.3 How do you treat the systemic toxicity of local anesthetic drugs?
C.4 What are the possible complications of SCS?
C.5. What are the possible complications of IT therapy?

49 Cancer Pain
Shakil Ahmed and Sudhir A. Diwan

A. Medical Disease and Differential Diagnosis

A.1. What is the definition of pain?
A.2. How significant is the problem of pain in patients with cancer?
A.3. What are the components of cancer pain?
A.4. How does the pain contribute to the suffering of patients with cancer?
A.5. How do psychological factors affect pain in patients with cancer?
A.6. What are the causes of pain in patients with cancer?
A.7. How do you classify pin in patients with cancer?

A.8. *What are the characteristics of pancreatic cancer pain?*
A.9. *How do you assess pain in patients with cancer?*
A.10. *What is the differential diagnosis of abdominal pain?*

B. Pharmacologic Treatment of Pain
B.1. *What is the World Health Organization stepladder approach for cancer pain management?*
B.2. *What class of drugs does morphine sulfate belongs to?*
B.3. *What is the difference between morphine and synthetic opioids?*
B.4. *How does mixed opioid agonist/antagonist differ from opioid agonist?*
B.5. *Describe the role of methadone in the management of cancer pain.*
B.6. *What are the advantages and disadvantages of methadone?*
B.7. *What is the mechanism of action of opioids?*
B.8. *What are the side effects of opioid therapy?*
B.9. *Define tolerance and physical dependence.*
B.10. *How would you treat the side effects of opioid therapy?*
B.11. *What is tramadol? Is it an opioid?*
B.12. *When would you consider adjuvant analgesics as part of the treatment plan?*
B.13. *The patient and his family are worried about addiction. How would you approach this problem?*
B.14. *Describe different routes of opioid administration.*
B.15. *Describe advantages and complications of patient-controlled analgesia (PCA). What is minimum effective analgesic concentration (MEAC)?*
B.16. *What is meperidine? How is it different from other opioids?*
B.17. *What is rotation of opioids? When would you consider rotation of opioids?*

C. Invasive Therapy
C.1. *Describe the role of peripheral nerve blocks in cancer pain management.*

C.2. *Describe the role of celiac plexus block in cancer pain management.*

C.3. *What are the complications of celiac plexus block?*

C.4. *Would you consider neuraxial opioid infusion in this patient? Discuss complications of this procedure.*

C.5. *Which medications can be used intrathecally? What is ziconotide?*

C.6. *What is a Personal Therapy Manager (PTM), and what role does it play in neuraxial pain relief?*

C.7. *Would you consider neuraxial neurolysis in this patient to manage his pain? Discuss advantages and disadvantages of these blocks.*

C.8. *Which neuroablative procedures can be considered in the terminal stage of pancreatic cancer?*

C.9. *Describe the role of radiation therapy in cancer pain.*

D. Nonpharmacologic Management

D.1. *What are the various nonpharmacologic techniques of cancer pain management?*

D.2. *What physical modalities have been successfully tried in cancer pain management?*

D.3. *Describe the role of neuromodulation in cancer pain management.*

D.4. *What psychological techniques have been promoted for comfort care and pain relief?*

D.5. *What are distraction and reframing techniques? What is the role of hypnosis in cancer pain?*

50 Low Back Pain and Sciatica

David Y. Wang

A. Medical Disease and Differential Diagnosis

A.1. *How great an issue is low back pain in the general population?*

A.2. *What is the prevalence of low back pain?*

A.3. *What is the societal cost of low back pain?*

A.4. *What causes low back pain?*
A.5. *What are the risk factors for low back pain?*
A.6. *What are the potential sources of pain in the spine?*
A.7. *What is the anatomy of the intervertebral discs? What is the mechanism of pain from herniated discs?*
A.8. *What is the anatomy of the spinal facets? How do the facet joints cause pain?*
A.9. *What are the important findings through history and physical examination?*
A.10. *What are the appropriate diagnostic studies for low back pain?*
A.11. *What is the differential diagnosis of low back pain?*
A.12. *What are the causes of persistent back pain after multiple spine surgeries?*

B. Management of Low Back Pain and Sciatica
B.1. *What are the noninterventional treatments available?*
B.2. *What traditional interventional treatments are available and how should they be used?*
B.3. *What are some of the recent safety improvements recommended for lumbar epidural steroid injection?*
B.4. *What are some of other approaches in minimally invasive interventions?*
B.5. *What are the concerns about magnetic resonance imaging (MRI) safety in patients with a spinal cord stimulator (SCS)?*
B.6. *When should surgery be considered?*
B.7. *What surgical options are available for the treatment of disc disease?*

51 Perioperative Pain Management
Anuj Malhotra and Vinod Malhotra

A. Perioperative Pain Management for Thoracotomy
A.1. *What would be your advice to the patient about the planned thoracotomy and postoperative pain relief?*

A.2. *How will you decide about the choice of anesthetic technique?*

A.3. *What is chronic postsurgical pain (CPSP)? Does video-assisted thoracic surgery reduce the risk of chronic pain after thoracotomy?*

A.4. *What would be your perioperative analgesic strategy?*

A.5. *Does the choice of analgesic technique influence postoperative outcome?*

A.6. *Does it matter if the epidural catheter is at the thoracic or lumbar level?*

A.7. *Does the choice of drugs influence the efficacy or safety of thoracic epidural analgesia (TEA)?*

A.8. *What are the usual doses and concentrations of the anesthetic combinations commonly employed in epidural analgesia?*

A.9. *If accidental dural puncture occurs during placement of the epidural needle, what steps should be taken?*

A.10. *What are the alternatives to TEA?*

A.11. *What is the usual clinical regimen for intravenous patient-controlled analgesia (IV-PCA) and is special patient monitoring required during its use?*

A.12. *What are the side effects and complications of epidural technique?*

A.13. *What recommendations for placement and removal of epidural catheter will you make if this patient is on antiplatelet or anticoagulant therapy or thromboprophylaxis is planned?*

Prophylactic Unfractionated Heparin
Therapeutic Intravenous Unfractionated Heparin
Preoperative Low Molecular Weight Heparin (Enoxaparin)
Postoperative Low Molecular Weight Heparin
Oral Anticoagulants

Newer Agents

B. Chronic Opioid Therapy and Perioperative Pain Management
   - *B.1. How does chronic opioid therapy influence postoperative pain management?*
   - *B.2. What are the causes for increased postoperative pain and opioid consumption in patients chronically using opioids?*
   - *B.3. What are the main differences between a chronic opioid-consuming patient and a patient who abuses or is addicted to opioids?*
   - *B.4. What issues need to be considered in the opioid-tolerant patient who is scheduled for surgery?*
   - *B.5. What would be your strategy regarding preoperative information and choice of anesthesia technique?*
   - *B.6. What are the choices for perioperative pain management in opioid-tolerant patients?*
   - *B.7. What issues need to be considered before discharging an opioid-tolerant patient?*

C. Perioperative Pain Management for Ambulatory Surgery
   - *C.1. What would be your preoperative considerations and advice to the patient?*
   - *C.2. What are the consequences of inadequate pain management after ambulatory surgery?*
   - *C.3. What is the role of premedication or preoperative analgesic?*
   - *C.4. Does the choice of anesthetic technique influence postoperative pain?*
   - *C.5. Are nonsteroidal anti-inflammatory drugs (NSAIDs) effective? If so, does the choice of drug matter?*
   - *C.6. What is the role of surgical technique in influencing postoperative pain after a laparoscopic cholecystectomy?*
   - *C.7. What would be your strategy for pain control after discharge home?*

D. The Role of an Acute Pain Service (APS)

D.1. What is the extent of the problem, and which patients are at greatest risk of undertreatment?
D.2. What are the consequences of inadequate postoperative pain relief?
D.3. What is the role of an APS in improving postoperative pain management?
D.4. Does an APS improve postoperative outcome?

52 Acupuncture
Yuan-Chi Lin

A. Acupuncture as a Complementary Medical Therapy
A.1. What is acupuncture?
A.2. How is acupuncture practiced? (Video 52.1)
A.3. What are the mechanisms of acupuncture analgesia?
A.4. What were the conclusions of the National Institutes of Health Consensus Conference about acupuncture?
A.5. Can acupuncture be a novel nonopioid alternative pain therapy?

B. Acupuncture for the Treatment of Chronic Conditions
B.1. What are the rationales in integrating acupuncture for the treatment of postoperative nausea and vomiting?
B.2. Can acupuncture be used for the treatment of chemotherapy-induced nausea and vomiting?
B.3. How effective is acupuncture for the management of chronic headache?
B.4. Can acupuncture be used for the treatment of chronic neck and back pain?
B.5. Can acupuncture be used for the treatment of osteoarthritis?
B.6. What role can acupuncture play in the care of patients with cancer?
B.7. Can acupuncture/acupressure be used to decrease anxiety?
B.8. What is ear acupuncture/acupressure? Can it be useful for alleviating anxiety and pain? (Video 52.2)

C. Complications

C.1. *What are the possible complications of acupuncture treatment?*

SECTION 12 Miscellaneous

53 Myasthenia Gravis
James B. Eisenkraft and Bryan S. Carter

A. Medical Disease and Differential Diagnosis
- A.1. *What is MG?*
- A.2. *What is the etiology and pathophysiology of MG?*
- A.3. *Describe the clinical classification of MG.*
- A.4. *How is the diagnosis of MG made?*
- A.5. *What should be considered in the differential diagnosis?*
- A.6. *How does myasthenic syndrome (Lambert-Eaton syndrome) differ from MG?*
- A.7. *What treatments are available for a patient with MG?*
  - Medical Therapy
  - Surgical Therapy

B. Preoperative Evaluation and Preparation
- B.1. *Describe the preoperative evaluation of this patient.*
- B.2. *What preoperative laboratory data are required?*
- B.3. *How should the patient's medications be managed preoperatively?*

C. Intraoperative Management
- C.1. *What are your considerations in the choice of anesthetic technique?*
- C.2. *How should this patient be monitored intraoperatively?*
- C.3. *What anesthetic regimen would you choose for this patient?*
- C.4. *Can neuromuscular blocking drugs be used safely in a patient with MG?*
- C.5. *Should the MG patient who is in remission (i.e., symptom free without treatment) be managed differently?*

D. Postoperative Management

D.1. What factors will help you predict this patient's need for continued intubation or other postoperative ventilatory support?
D.2. How will you determine if this patient's trachea can be safely extubated?
D.3. How will you manage postoperative analgesia?
D.4. How will you define and manage postextubation ventilatory failure in this patient?

54 Malignant Hyperthermia
Henry Rosenberg, Harvey K. Rosenbaum, and Vinod Malhotra

A. Medical Disease and Differential Diagnosis
A.1. What was the problem of concern in this case?
A.2. What is malignant hyperthermia (MH)?
A.3. What are the clinical features of a susceptible patient?
A.4. Does the history of previous uneventful sevoflurane anesthesia reasonably exclude the patient's susceptibility to MH?
A.5. What are the clinical features of the syndrome?
Hyperkalemic Cardiac Arrest
A.6. What are the laboratory findings during an acute crisis of MH?
A.7. What is the incidence of this syndrome?
A.8. What is the mode of inheritance of the disease? Does MH "skip" generations?
A.9. What genetic disorder results in MH susceptibility?
A.10. What is the pathophysiology of the syndrome?
A.11. What laboratory tests can further substantiate the susceptibility of the patient to MH?
Molecular Genetic Testing for MH Susceptibility
A.12. What is neuroleptic malignant syndrome (NMS)?

B. Preoperative Evaluation and Preparation
B.1. How would you prepare this patient for anesthesia and surgery?

B.2. *Is dantrolene prophylaxis indicated?*
B.3. *What laboratory tests would you obtain before surgery?*
B.4. *Is outpatient surgery appropriate for this patient?*
B.5. *In anticipation of general anesthesia, what preparations would you make?*

C. Intraoperative Management
C.1. *What anesthetic techniques and agents would you employ?*
C.2. *Should body (core) temperature be monitored during general anesthesia lasting more than a short time?*
C.3. *What anesthetic agents are contraindicated?*
C.4. *If the surgeon wants to use local anesthesia for a procedure, what agents will you recommend?*
C.5. *What is the significance of masseter muscle spasm occurring after succinylcholine administration?*
C.6. *Twenty minutes into the procedure with sevoflurane anesthesia, the patient developed increasing tachycardia with ventricular premature beats and mottled skin. What emergency measures would you take?*
C.7. *What modalities would you monitor closely during management of the crisis?*
C.8. *What steps should be taken to avoid major morbidity from MH?*
C.9. *How does the new formulation of dantrolene (Ryanodex) compare with the existing formulation of dantrolene (Dantrium or Revonto)?*

D. Postoperative Management
D.1. *What complications may follow this syndrome?*
D.2. *What would be your follow-up in this case?*
D.3. *What would you advise the patient and the family?*
D.4. *What precautions should an MH-susceptible patient take outside of the operating room (OR)?*

55 Postoperative Residual Neuromuscular Weakness and

Prolonged Apnea

Mary So, Danielle McCullough, and David J. Kopman

A. Medical Diseases and Differential Diagnosis

- *A.1. What is the differential diagnosis for postoperative hypoventilation?*
- *A.2. How is residual neuromuscular blockade (NMB) diagnosed?*
- *A.3. What is the order of recovery of voluntary muscle groups from nondepolarizing muscle relaxants?*
- *A.4. What is the mechanism of action of succinylcholine, and how is it metabolized? What are the side effects of succinylcholine?*
- *A.5. If succinylcholine were the only muscle relaxant used during the case and the patient did not exhibit a response to train-of-four (TOF) stimulation, what is the likely diagnosis? How would you confirm it?*
- *A.6. What are acetylcholinesterase and serum cholinesterase? What is the clinical significance of heterozygosity for atypical pseudocholinesterase (PChE)?*
- *A.7. What is the incidence of atypical cholinesterase activity?*
- *A.8. What are some factors that can lower PChE levels?*

B. Intraoperative Management

- *B.1. How is the choice among muscle relaxants made?*
- *B.2. What factors can alter sensitivity to nondepolarizing neuromuscular blockers?*
- *B.3. What are the characteristics of nondepolarizing block?*
- *B.4. What is a TOF stimulus?*
- *B.5. Why is the TOF ratio of clinical importance?*
- *B.6. How do we define adequate recovery of neuromuscular function?*
- *B.7. Are there useful and/or trustworthy clinical tests of neuromuscular recovery?*
- *B.8. How accurate are subjective estimates of the TOF ratio, and what purpose do peripheral nerve stimulator (PNS)*

monitors serve?
B.9. *What is double burst stimulation (DBS)?*
B.10. *What is the posttetanic count (PTC)?*
B.11. *How can the TOF ratio be measured quantitatively?*
B.12. *What are the limitations of acetylcholinesterase antagonists?*
B.13. *Is there anything wrong with administering neostigmine when the TOFC is less than 3?*
B.14. *Is reversal of blockade always necessary?*
B.15. *Is there any way to rapidly antagonize a profound nondepolarizing block?*
C. Postoperative Management
C.1. *What is the incidence of residual NMB in the PACU?*
C.2. *Does undetected postoperative residual neuromuscular block (PORB) have clinical consequences?*
56 Burns
Shreyajit R. Kumar and Anup Pamnani
A. Medical Disease and Differential Diagnosis
A.1. *How do you classify the burn injury?*
A.2. *How do you express the extent of the burn injury?*
A.3. *Should the "rule of nines" be used in children?*
A.4. *What functions does the skin perform?*
A.5. *What pathophysiologic changes accompany major thermal injury?*
A.6. *What is the prognosis for this patient? What major factors affect his prognosis?*
A.7. *What are the common causes of death in burn patients?*
A.8. *Does this patient have a smoke inhalation burn? How do you make the diagnosis?*
A.9. *What is carbon monoxide poisoning? How do you diagnose and treat carbon monoxide poisoning?*
A.10. *What resuscitative measure would you institute immediately in this patient with 40% burns?*

A.11. *What fluid formula would you use?*

Parkland Formula

A.12. *What cardiovascular changes typify the burn injury?*

A.13. *What changes occur in hepatic function? What are the anesthetic implications of such changes?*

A.14. *What are Curling ulcers? How can they be prevented?*

A.15. *What complications are associated with electrical burns?*

B. Preoperative Evaluation and Preparation

B.1. *What preoperative preparations would you order? What are particular concerns in this patient?*

B.2. *What are the various operative and management options available for severely burned patients?*

B.3. *What are the advantages and disadvantages of early tangential excision split-thickness skin grafting (TE/STSG)?*

B.4. *What is this patient's mean arterial blood pressure? How do you calculate it?*

B.5. *Are you concerned about this patient's blood pressure? What treatment would you institute?*

B.6. *This patient was ventilated with respirator settings of tidal volume, 800 mL; respiratory rate, 20 breaths per minute; fraction of inspired oxygen (F_{IO_2}), 60%; and positive end-expiratory pressure, 10 cm H_2O. Arterial blood gas analyses showed the following: pH, 7.24; P_{O_2}, 56 mmHg; P_{CO_2}, 60 mmHg; and oxygen saturation, 80%. How would you interpret these arterial blood gas analysis results? What are the possible causes of high P_{CO_2} and low P_{O_2}?*

B.7. *How do you calculate oxygen content and oxygen delivery? What factors govern the oxygen delivery to the tissues?*

C. Intraoperative Management

C.1. *What monitors would you use in the operating room?*

C.2. *What information can be obtained from an arterial line and a pulmonary artery catheter? How are these calculations*

performed?

C.3. *If the patient had not been intubated, how would you proceed with the anesthetic induction?*

C.4. *Why is awake intubation considered the safest?*

C.5. *What anesthetic agents would you use? Discuss inhalation versus intravenous agents.*

C.6. *Why are you concerned about the patient's body temperature? What is normothermia for a burned patient?*

C.7. *How is temperature best maintained?*

C.8. *What derangements occur with hypothermia?*

C.9. *What muscle relaxant would you use?*

C.10. *Why is succinylcholine contraindicated in burned patients? For how long should it be avoided?*

C.11. *What other adverse effects are associated with succinylcholine?*

C.12. *How are the doses of nondepolarizing muscle relaxants affected by burn injury?*

C.13. *How are the muscle relaxants such as succinylcholine, atracurium, cisatracurium, vecuronium, pancuronium, rocuronium, and curare metabolized and eliminated? Which of them has significant histamine release?*

D. Postoperative Management

D.1. *How would you monitor this patient during transport?*

D.2. *What is meant by diffusion hypoxia? How do you prevent it?*

D.3. *Why do patients often shiver in the recovery room on emergence from anesthesia?*

D.4. *Discuss the causes of oliguria in the recovery room.*

57 Trauma

Rohan K. Panchamia, Jaideep K. Malhotra, and Ralph L. Slepian

A. Medical Disease and Differential Diagnosis

A.1. *How is trauma classified?*

A.2. *What are the injuries associated with thoracic trauma?*

A.3. *What are the injuries associated with cardiac trauma?*

A.4. *What is the pathophysiology of acute pericardial tamponade?*
A.5. *What are the anesthetic implications for treating cardiac tamponade?*
A.6. *How is the initial assessment and management of the trauma patient performed?*
A.7. *What constitutes a primary survey, and what is its objective?*
A.8. *What constitutes a secondary survey, and what is its objective?*
A.9. *What is the definition of massive hemothorax? What are the signs and symptoms of a hemothorax?*
A.10. *What are the indications for a thoracotomy to treat a hemothorax?*
A.11. *How are pneumothoraces categorized?*
A.12. *What is an occult pneumothorax?*
A.13. *If the patient has a widened mediastinum on chest radiograph, what are your concerns?*
A.14. *What are the most commonly injured organs in blunt abdominal trauma?*
A.15. *What is a focused abdominal sonography for trauma (FAST) examination?*
A.16. *What is diagnostic peritoneal lavage (DPL)?*
A.17. *Why was DPL not performed for this patient?*
A.18. *Define shock.*
A.19. *What are the four types of shock?*
A.20. *List the signs and symptoms of shock.*
A.21. *What is the pathophysiology of hypovolemic shock?*
Cardiovascular Derangement
Acid–Base Disturbance
A.22. *How would you classify hemorrhage?*
A.23. *What is the initial treatment of hemorrhagic shock?*
A.24. *Would you choose crystalloid, colloid, or blood products to treat hemorrhagic shock?*

A.25. *Is there a place for dextran or hetastarch (Hespan) in treating hypovolemic shock?*

B. Preoperative Evaluation and Preparation

B.1. *What premedication would you order?*

B.2. *What preoperative testing would you order?*

C. Intraoperative Management

C.1. *How would you monitor this patient?*

C.2. *How would you induce anesthesia?*

C.3. *What technique could you use if single-lung ventilation was indicated?*

C.4. *What agents would you choose to maintain anesthesia?*

C.5. *What muscle relaxant would you choose?*

C.6. *What can be done to decrease the incidence of intraoperative awareness?*

C.7. *Five minutes after intubation, the peak airway pressure increased from 20 to 40 cm H_2O. What are the possible causes?*

C.8. *How would you make a diagnosis of tension pneumothorax?*

C.9. *What is the treatment of tension pneumothorax?*

C.10. *The patient's blood loss was continuing, and the hematocrit was 18%. What type of blood would you give if the type and crossmatch are not completed?*

C.11. *What precautions should be taken if more than 2 units of low titer type O uncrossmatched whole blood are given?*

C.12. *What are the complications associated with any blood transfusion?*

Transfusion Reactions

Transmission of Disease

Microembolization

What is considered a massive transfusion (MT)? What is the Assessment of Blood Consumption (ABC) score?

C.14. *What are the complications associated with an MT?*

C.15. *Can the shift of the oxygen–hemoglobin dissociation curve*

be quantified?

C.16. *How is hypothermia defined?*

C.17. *What are the adverse effects of hypothermia?*

C.18. *What is the treatment of hypothermia?*

C.19. *What are the effects of blood transfusion on the immune system?*

C.20. *What are the guidelines for transfusion of blood products?*

Red Blood Cell Transfusion Criteria
Platelet Transfusion Criteria
Fresh Frozen Plasma Transfusion Criteria
Cryoprecipitate Transfusion Criteria
What are the guidelines for the ratio of plasma/platelet transfusion to packed red blood cells in an MT?

C.22. *If a patient were a member of the Jehovah's Witness religious sect, would you give a blood transfusion?*

C.23. *If a child is a Jehovah's Witness and suffered from hemorrhagic shock, what would you do?*

C.24. *What are the concentrated factors and hemostatic agents available for bleeding patients?*

Recombinant Activated Factor VII (rFVIIa, NovoSeven)
Four-Factor Prothrombin Complex Concentrate
Fibrinogen Concentrates
Tranexamic Acid
What is thromboelastography (TEG) and thromboelastometry? How can they guide transfusion?
Rotation Thromboelastometry
Thromboelastography

D. Postoperative Management

D.1. *What is acute respiratory distress syndrome (ARDS)? What is acute lung injury?*

D.2. *How is ARDS treated?*

D.3. *In the recovery room, you are called to see this patient because of oliguria. How would you evaluate and treat this*

patient?

Prerenal

Renal

Postrenal

D.4. *If this patient had a crush injury and low urine output, what other concerns might you have? What if the patient has dark or "tea-colored" urine?*

58 Scoliosis

Jordan M. Ruby and Victor M. Zayas

A. Medical Disease and Differential Diagnosis

A.1. *What is scoliosis?*

A.2. *What is the most common type of scoliosis?*

A.3. *What are the other types of scoliosis?*

Idiopathic

Neuromuscular

Myopathic

Congenital

Neurofibromatosis

Mesenchymal Disorders

Trauma

A.4. *How is the severity of scoliosis assessed, and why is the severity important?*

A.5. *What are the nonoperative treatment options of scoliosis?*

A.6. *What abnormalities in pulmonary function tests (PFTs) are most commonly seen in scoliosis? What is the cause of these abnormalities?*

A.7. *What is the most common arterial blood gas abnormality seen in scoliosis? What are possible causes for this abnormality?*

A.8. *What abnormalities of ventilatory drive may be associated with scoliosis?*

A.9. *How may the cardiovascular system be affected in patients with scoliosis?*

A.10. *What is the relationship between scoliosis and malignant hyperthermia?*

B. Preoperative Evaluation and Preparation

B.1. *What should the anesthesiologist know about the nature of the spinal curve?*

B.2. *What aspects of the history are most important?*

B.3. *What aspects of the physical examination are most important?*

B.4. *Why is a preoperative neurologic assessment important?*

B.5. *What tests would you order preoperatively?*

B.6. *What is an enhanced recovery after surgery (ERAS) pathway? How has it been applied to the recovery for pediatric patients undergoing posterior spinal instrumentation and fusion?*

B.7. *How will the surgical procedure influence the anesthetic management?*

C. Intraoperative Management

C.1. *What monitoring would you use?*

C.2. *What is the incidence of neurologic complications in scoliosis surgery, and which patients are at highest risk?*

C.3. *What monitoring techniques are used to minimize neurologic complication?*

C.4. *What are somatosensory evoked potentials (SSEPs), and how are they used?*

C.5. *How reliable are SSEPs for predicting spinal injury?*

C.6. *What are motor evoked potentials (MEPs), and how are they used?*

C.7. *How is spinal cord monitoring affected by anesthetic agents? What other factors affect spinal cord monitoring?*

C.8. *What is the optimal anesthetic technique for scoliosis surgery?*

C.9. *What should be done if the SSEPs or MEPs become abnormal during surgery?*

C.10. *How is the "wake-up" test performed? What complications can occur during this test?*

C.11. *Four hours into the surgical procedure, the surgeon reports some bubbling in the thoracic portion of the wound. Shortly thereafter, end-tidal carbon dioxide decreases abruptly from 35 to 18 mmHg, heart rate increases from 80 to 120 beats per minute, blood pressure begins to fall, and arterial saturation decreases to 90%. On auscultation through esophageal stethoscope, you hear a loud gurgling murmur. What is your diagnosis?*

C.12. *How common is significant air embolism during scoliosis surgery?*

C.13. *What should be done if an air embolus is suspected?*

C.14. *What complications occur related to positioning the patient?*

C.15. *What is transfusion-related acute lung injury (TRALI)? How do you distinguish it from transfusion-associated circulatory overload (TACO)?*

C.16. *What techniques can be used to minimize transfusion requirements?*

D. Postoperative Management

D.1. *When would you extubate the patient?*

D.2. *What should be done to optimize pulmonary status?*

D.3. *What laboratory tests should be ordered postoperatively?*

D.4. *What fluid therapy would you use postoperatively?*

D.5. *What complications may occur following scoliosis surgery?*

D.6. *Upon arrival to the recovery room, you notice that the urine appears to be tea colored. What is your diagnosis, and how should this be managed?*

D.7. *How would you manage this patient's pain, nausea, and vomiting postoperatively?*

59 Hypoxia and Equipment Failure

James B. Eisenkraft and Garrett W. Burnett

A. Medical Disease and Differential Diagnosis

A.1. What is hypoxia, and what is hypoxemia?

A.2. Is the partial pressure of oxygen in arterial blood (Pa_{O_2}) related to age?

A.3. Was this patient hypoxemic?

A.4. What is a pulse oximeter, and what is a hemoximeter?

A.5. How does a pulse oximeter work?

A.6. How is a two-wavelength pulse oximeter calibrated by the manufacturer?

A.7. What may affect the accuracy of a two-wavelength pulse oximeter?

A.8. How do the dyshemoglobins, methemoglobin (metHb), and carboxyhemoglobin (Hb_{CO}) affect Sp_{O_2} readings?

A.9. What is a capnometer, and what is capnography? Of what value are they in patient monitoring?

A.10. What is meant by the term end-tidal carbon dioxide (Et_{CO_2})?

A.11. What is the appearance of a normal capnogram, and what is its significance?

A.12. What are mainstream and sidestream capnometers?

A.13. Show some common capnograms and provide a differential diagnosis of each event.

A.14. What is the arterial–alveolar difference in carbon dioxide (CO_2)?

A.15. What are some of the important safety features of the contemporary anesthesia workstation?

Features Intended to Prevent Human Error

Features to Correct for Use Error

Monitoring Systems

Alarm Systems

A.16. What are the common sites for gas leakage?

A.17. How is the anesthesia machine checked for leaks?

B. Preoperative Evaluation and Preparation

B.1. *What should be included in the equipment checkout in preparation for anesthesia?*

- *Emergency ventilation equipment*
- *High-pressure system*
- *Low-pressure systems*
- *Scavenging system*
- *Breathing system*
- *Manual and automatic ventilation systems*
- *Monitors*
- *Final position*

B.2. *What emergency equipment should be easily available to the anesthesiologist?*

B.3. *How should this patient be premedicated?*

C. Intraoperative Management

C.1. *How should this patient be monitored?*

- *Oxygenation*
- *Ventilation*
- *Circulation*
- *Body temperature*

C.2. *Following uncomplicated induction of anesthesia and endotracheal intubation, the procedure begins. Upon insufflation of the abdomen with CO_2, the SpO_2 decreases to 78%. What acute diagnostic and therapeutic interventions would you perform?*

C.3. *The endotracheal tube was withdrawn 2 cm. Squeezing the reservoir bag in the circle breathing system failed to generate positive pressure in the circuit. What are the common sites for gas leaks in the circle breathing system?*

C.4. *The patient was taken out of Trendelenburg position. Direct laryngoscopy revealed the endotracheal tube to be supraglottic. Additionally, green secretions were noted to be pooled in the posterior pharynx. What should be done next?*

D. Postoperative Management

D.1. *What criteria would you use for tracheal extubation?*

D.2. *What are the causes of postoperative hypoxemia?*

D.3. *What is the difference between shunt, ventilation/perfusion mismatch, and dead space?*

D.4. *Postoperatively, the patient developed hypoxia and pulmonary edema. What is the differential diagnosis of pulmonary edema? What is the most likely cause of pulmonary edema in this patient?*

D.5. *How should the ventilator be set if mechanical ventilation is required postoperatively?*

D.6. *If this patient had acute respiratory distress syndrome (ARDS) secondary to aspiration, besides low-tidal volume ventilation, what other changes in routine therapy should be considered?*

D.7. *What therapies routinely administered by the anesthesiologist may cause acute lung injury?*

D.8. *What methods of oxygen administration may be used postoperatively?*

60 Electroconvulsive Therapy

Patricia Fogarty Mack

A. Medical Disease and Differential Diagnosis

A.1. *What are the indications for ECT?*

A.2. *Are there any contraindications to ECT?*

A.3. *What is the mechanism of action of ECT?*

B. Preoperative Evaluation and Preparation

B.1. *How would you assess the cardiac status of this patient?*

B.2. *How should his anticoagulation be managed during ECT?*

B.3. *What implications do his history of sleep apnea have on management of ECT?*

B.4. *How does his history of TIA and carotid endarterectomy impact your preoperative evaluation?*

B.5. *Is ECT contraindicated in a patient with a permanent pacemaker or implantable cardioverter-defibrillator?*

B.6. *Are there any psychiatric medications he is taking that would impact your anesthetic care?*

C. Intraoperative Management

C.1. *Describe the hemodynamic and cardiac response to ECT in a typical patient.*

C.2. *Is an arterial line warranted in this patient?*

C.3. *By what means would you attempt to maximize hemodynamic stability?*

C.4. *Describe the cerebral hemodynamic effects of ECT.*

C.5. *How would you proceed with an anesthetic induction for this procedure?*

C.6. *How do you intend to manage his airway during each treatment?*

D. Postoperative Management

D.1. *The patient is extremely agitated upon emergence. Discuss the risk factors for postictal agitation (PIA) as well as the therapeutic options.*

D.2. *After three consecutive uneventful inpatient treatments, the psychiatrist asks if the patient may undergo ECT as an outpatient. Would you agree to this plan?*

61 Ambulatory Surgery

Melinda Randall and Hugh C. Hemmings Jr.

A. Medical Disease and Differential Diagnosis

A.1. *Is this patient morbidly obese?*

A.2. *What medical conditions may be associated with obesity and morbid obesity?*

A.3. *Is there a link to a decline in memory and thinking with anesthesia and surgery?*

B. Preoperative Evaluation and Preparation

B.1. *What advantages does outpatient surgery offer?*

B.2. *What are the goals of the preoperative evaluation of the surgical outpatient?*

B.3. *In order to thoroughly screen for disease, should one put all*

outpatients through a full battery of laboratory testing?

- *B.4. What preoperative laboratory testing is necessary for surgical outpatients?*
- *B.5. Which outpatients should receive a preoperative chest roentgenogram?*
- *B.6. In which patients is an electrocardiogram (ECG) necessary before outpatient anesthesia and surgery?*
- *B.7. Would age or physical status influence the decision to perform outpatient surgery?*
- *B.8. What patients are considered inappropriate for ambulatory surgery?*
- *B.9. What questions are critically important to ask this patient when obtaining her history?*
- *B.10. What instructions should the patient be given with regard to continuing or discontinuing lisinopril in the perioperative period?*
- *B.11. What is an enhanced recovery after surgery (ERAS) protocol, and how would you apply it in the outpatient setting?*
- *B.12. How would you premedicate this patient?*
- *B.13. Should every outpatient receive prophylaxis against aspiration pneumonitis?*
- *B.14. Is an overnight fast justified for all outpatients?*

C. Intraoperative Management

- *C.1. What are the important considerations in choosing an anesthetic technique for outpatient surgery?*
- *C.2. How would you monitor this patient?*
- *C.3. What is the bispectral index (BIS) monitor, and what information does it convey?*
- *C.4. What benefits might be derived from using a BIS monitor?*
- *C.5. Is BIS monitoring applicable to children?*
- *C.6. What are the major limitations of BIS monitoring?*
- *C.7. What does a BIS reading of 56 mean?*

C.8. *What anesthetic agents would you use to induce and maintain general anesthesia in this patient?*
C.9. *Under what circumstances might spinal anesthesia be appropriate for outpatient surgery?*

D. Postoperative Management
D.1. *What are the common causes of nausea and vomiting in outpatients?*
D.2. *How would you pharmacologically prevent PONV in the susceptible ambulatory patient?*
D.3. *How is postoperative pain treated?*
D.4. *What criteria would you use to establish that a patient can be safely discharged after ambulatory surgery?*
D.5. *How would you decide when to discharge a patient after regional anesthesia?*
D.6. *What instructions should be given to an ambulatory surgical patients upon discharge?*

62 Magnetic Resonance Imaging
Jayanth Swathirajan, Dana L. Gurvitch, and Hugh C. Hemmings Jr.

A. Medical Disease and Differential Diagnosis
A.1. *What is MRI, and how does it work?*
A.2. *What are some advantages of MRI?*
A.3. *What are some disadvantages associated with MRI? What are some safety concerns?*
A.4. *How do you manage patients with implanted devices?*
A.5. *What are the biologic effects of clinical MRI?*
A.6. *What are the anesthetic considerations for this procedure?*
A.7. *What is intraoperative MRI (iMRI)? What is real-time MRI, and in what setting can this be used?*

B. Preoperative Evaluation and Preparation
B.1. *What type of patients may require sedation or general anesthesia for MRI?*
B.2. *Do all children require sedation for MRI?*
B.3. *What preoperative laboratory testing would you require for*

this patient?

B.4. How would you premedicate this patient? What are some options that can be used to premedicate other patients for MRI?

C. Intraoperative Management

C.1. What are some of the anesthetic options for this patient?

C.2. How is an MRI conducted?

C.3. How would you monitor this patient?

C.4. What special considerations apply to monitoring equipment used during MRI?

C.5. How would you induce and maintain general anesthesia in this patient?

C.6. What are ways to maintain the airway during an MRI scan?

C.7. During the scan, you notice loss of end-tidal carbon dioxide. You immediately go into the scanner, remove the patient from the MRI scanner and initiate bag ventilation. However, you are still unable to ventilate the patient, and asystole follows. What do you do next?

C.8. What is the risk to the patient of gadolinium administration in the presence of acute renal insufficiency?

D. Postoperative Management

D.1. How will you recover the patient from anesthesia?

63 Morbid Obesity, Obstructive Sleep Apnea, and Bariatric Anesthesia

Jon D. Samuels and Fun-Sun F. Yao

A. Medical Disease and Differential Diagnosis

A.1. What problems exist with this patient? The patient asks you if he is high risk. What is the evidence? Is surgical therapy a safe and viable alternative for this patient?

A.2. Define the terms overweight, obesity, MO, super obesity (SO), super-SO (SSO), normal weight, ideal body weight (IBW), and lean body weight (LBW). What is the impact of obesity on society?

A.3. *What is OSA? What are the risk factors for OSA?*

A.4. *How is OSA diagnosed? What is a sleep study, or PSG? How are results obtained from a PSG used to grade the severity of OSA? What are the subtypes of OSA? Are there genetic disorders with a predisposition to OSA? What is the role of OSA screening tests in the preoperative setting?*

A.5. *How does OSA differ in the pediatric population in clinical presentation and pathogenesis?*

A.6. *What is the Pickwickian syndrome (PS)? What is obesity hypoventilation syndrome (OHS)? Describe the pathogenesis of severe OSA.*

A.7. *What is the association between obesity and OSA? What is the etiology of OSA in severe obesity?*

A.8. *What are the anesthetic implications of OSA?*

A.9. *What type of metabolic problems would you expect to find in morbidly obese patients? What are the roles of leptin and ghrelin in obesity?*

A.10. *Describe the changes that occur in the following respiratory parameters in morbidly obese patients:*

A.11. *What changes occur in Pa_{O_2} and Pa_{CO_2} in morbidly obese patients?*

A.12. *What changes occur in intrapulmonary shunt (Q_S/Q_T) and dead space (V_D/V_T) in MO? Describe the Shunt equation and the physiologic dead space, or Bohr equation.*

A.13. *What changes occur in the cardiovascular system of the obese patient? Discuss cardiac output, blood volume, blood pressure, and pulmonary arterial pressure.*

A.14. *Are there any other disease entities commonly associated with obesity? What is their relationship?*

A.15. *What anatomic changes that affect the airway are associated with MO and OSA?*

A.16. *What derangements of the gastrointestinal system are*

associated with MO?

B. Preoperative Evaluation and Preparation

- *B.1. How would this patient be optimized for surgery preoperatively? Would you use preoperative screening questionnaires to diagnose OSA? Summarize the workup for this patient.*
- *B.2. One of the recent developments in bariatric surgery is that many patients are receiving prebariatric screening procedures performed in the endoscopy suite. Describe the anesthetic considerations.*
- *B.3. Summarize the evidence-based workup, risk, chance of various adverse outcome, and expected length of stay for this patient.*
- *B.4. What is the role of enhanced recovery after surgery (ERAS) in bariatric surgery? How does the public find a quality bariatric surgery team and surgical facility? What is the role of robotics in bariatric surgery?*
- *B.5. Would you premedicate the patient?*
- *B.6. Describe the mechanism of action of each premedication in the ENERGY protocol.*
- *B.7. How would you adjust doses of anesthetics in the morbidly obese?*

C. Intraoperative Management

- *C.1. How would you monitor this patient?*
- *C.2. The American Society of Anesthesiologists' (ASA) Difficult Airway Algorithm (DAA) provides a guideline for management of the difficult airway. How do the comorbidities of MO and OSA modify implementation of the algorithm?*
- *C.3. Why is it important to preoxygenate the obese patient? How would you do it? Compare the effectiveness of the four-maximum-breath and 3-minute techniques. What is the importance of continuous positive airway pressure (CPAP)*

during the induction of general anesthesia? Describe use of the nasal CPAP mask in the induction of general anesthesia.

- *C.4. There are many new airway devices on the marketplace. Which of these devices have been particularly successful on the morbidly obese or OSA patient?*
- *C.5. How would you induce anesthesia? Describe the intubation technique.*
- *C.6. How would you maintain general anesthesia? What agents would you choose? How would you prepare for emergence?*
- *C.7. Which muscle relaxants would you use?*
- *C.8. Is postoperative pain severe after bariatric surgery? What are the pain generators? What is the role of regional anesthesia to decrease opioid requirements for bariatric surgery? What are the advantages and disadvantages of regional anesthesia? What are some of the newer techniques available?*
- *C.9. What is the pathophysiology of pneumoperitoneum (PNP)? What is the effect on the cardiopulmonary system? How does it change perioperative care? What are the optimal ventilator strategies for morbidly obese patients undergoing bariatric surgery?*
- *C.10. What are the devices that anesthesiologists place in the upper gastrointestinal canal during laparoscopic bariatric surgery? Are there risks associated with placement and management of these devices?*
- *C.11. When will you extubate this patient? Describe weight-based extubation criteria.*
- *C.12. What is apneic oxygenation?*
- *C.13. What is diffusion hypoxia (DH)? How do you prevent it?*

D. Postoperative Management

- *D.1. What are the early postoperative complications of bariatric surgical procedures?*
- *D.2. What are the late complications of bariatric surgical*

procedures?
D.3. What is the effect of position on respiratory function in the obese patient?
D.4. How would you prevent postoperative atelectasis?
D.5. How long would you prescribe supplementary oxygen postoperatively?
D.6. How would you control postoperative pain?
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Preface

Important advances in surgical procedures and in the clinical practice of anesthesiology have prompted the production of a new edition of this text. The book has been published in five languages: English, German, Japanese, Chinese, and Portuguese. The remarkable popularity of the first eight editions in the anesthesiology community both in the United States and abroad encouraged us to update and expand its subject matter. The ninth edition is written to further improve anesthesia management for sophisticated modern surgery.

As with our previous editions, *Yao & Artusio's Anesthesiology: Problem-Oriented Patient Management* was written to present a group of important clinical entities covering the most critical anesthetic problems. It is intended to provide logical and scientific fundamentals for individualized patient management.

In this ninth edition, *Yao & Artusio's Anesthesiology: Problem-Oriented Patient Management* is organized by organ systems into 12 sections consisting of 63 chapters. Each chapter begins with a brief case presentation, followed by essential problems of each disease covering four areas: (1) pathophysiology and differential diagnosis, (2) preoperative evaluation and preparation, (3) intraoperative management, and (4) postoperative anesthetic management. Using a question-and-answer format, the book is designed to stress anesthetic problems and to give the anesthesiologist the opportunity to organize his or her own ideas of patient care. A reasonable answer, with updated references, follows each question.

To maintain the fresh quality of the textbook, the ninth edition has been

updated with significant newer content and contributions by new authors. The text originally reflected the clinical experience of the Department of Anesthesiology at Weill Cornell Medicine—NewYork-Presbyterian Hospital. In this edition, experts from other prestigious institutions have shared their evidence-based invaluable experience and practice to make this book more universally acceptable and applicable. The material in the book is prepared for the education of the trainee as well as the practicing anesthesiologist; it also serves as a review source for continuing education. The question-and-answer format, combined with current references, enhances its educational value.

We welcome comments, criticisms, and suggestions for future editions.

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SECTION 1 The Respiratory System

1 Asthma and Chronic Obstructive Pulmonary Disease

Jaroslav K. Usenko and Fun-Sun F. Yao

A 55-year-old man with cholelithiasis is scheduled for laparoscopic cholecystectomy. He has a long history of asthma, has smoked two packs of cigarettes a day for the past 30 years, and reports dyspnea with moderate exertion (walking uphill). He sleeps on two pillows. There is no peripheral edema. Arterial blood gas (ABG) on room air shows the following: pH, 7.36; P_{CO_2}, 60 mmHg; P_{O_2}, 70 mmHg; and CO_2 content, 36 mEq per L.

A. Medical Disease and Differential Diagnosis

1. What is the differential diagnosis of dyspnea?
2. What is the prevalence of asthma and chronic obstructive pulmonary disease (COPD)?

3. What is the etiology of asthma?
4. Discuss the pathogenesis of asthma. How is asthma distinguished from COPD?
5. What are the triggers of bronchospasm?
6. What is the universal finding in ABGs during asthmatic attacks: hypoxemia or CO_2 retention?
7. Describe the abnormalities seen in spirometry, lung volumes, and lung capacities during an asthmatic attack.

B. Preoperative Evaluation and Preparation

1. How would you evaluate the patient preoperatively? What preoperative workup would you order?
2. How would you distinguish obstructive lung disease from restrictive lung disease by spirometry?
3. Define normal lung volumes and lung capacities. Give normal values for an average adult male.
4. What are flow–volume loops? Draw flow–volume loops for a healthy subject and patients with COPD, restrictive lung disease, fixed obstruction of the upper airway, variable extrathoracic obstruction, and variable intrathoracic obstruction.
5. Define closing volume (CV) and closing capacity (CC). What is the normal value of CV?
6. Why is the functional residual capacity (FRC) important in oxygenation?
7. How are FRC and CC affected by age and posture? How are they affected by anesthesia?
8. Give the equations for shunt ($\dot{Q}_S/\dot{Q}_T$) and dead space/tidal volume (V_D/V_T). What are their normal values?
9. Interpret the following ABG: pH, 7.36; P_{CO_2}, 60 mmHg; P_{O_2}, 70 mmHg; and CO_2 content, 36 mEq per L.
10. What are the common physiologic causes of hypoxemia?
11. How would you prepare this asthmatic patient with COPD for

surgery?

12. The patient comes to your perioperative clinic 2 weeks before surgery. He wants to know if his smoking puts him at increased risk during surgery. What do you tell him? Should he quit now?
13. You discover that the patient had a recent upper respiratory infection (URI), would you postpone surgery? For how long?
14. What medications would you expect the patient to have taken in the past or be taking at the present time?
15. The patient was on 20 mg of prednisone per day for 5 days as part of the treatment of an asthma exacerbation 3 months ago. He is currently not on steroids. Should the patient receive stress-dose steroids?
16. Should patients with reactive airway disease receive preoperative steroids?
17. What is the onset of action of intravenous steroid therapy in asthma?

C. Intraoperative Management

1. If the patient had a severe asthmatic attack in the operating room before the induction of anesthesia, would you proceed with the anesthetic or postpone the surgery?
2. The patient did not have an asthmatic attack in the operating room and you proceed with induction. How would you induce anesthesia? Would you use a supraglottic airway instead of an endotracheal tube?
3. Would you use propofol for induction of anesthesia?
4. Would you use thiopental, methohexital, etomidate, or ketamine for induction?
5. Would you administer lidocaine for intubation?
6. If this is an emergency surgery and rapid sequence induction is indicated, how would you induce anesthesia in this patient?
7. Could a regional technique be used for this surgery? Discuss

the advantages and disadvantages of neuraxial anesthesia in this patient for this surgery.

8. Would you choose an inhalational or an intravenous technique for maintenance of anesthesia?
9. What mechanisms produce bronchodilation from volatile anesthetics?
10. Which muscle relaxants would you use? Why?
11. How will you ventilate the patient? Will you use positive end-expiratory pressure (PEEP)? How can you detect the presence of auto-PEEP on your ventilator?
12. What is the differential diagnosis of intraoperative bronchospasm?
13. In the middle of surgery, peak inspiratory pressures (PIPs) suddenly increase. How do you manage this?
14. How would you give β_2-agonists? What is their mechanism of action on asthma?
15. If the patient does not respond to the aforementioned treatment and becomes cyanotic, what would you do?
16. The asthmatic attack was relieved with your treatment, and the surgery was completed. Following emergence, the patient was found to be hypoventilating. What are the common causes of hypoventilation? What will be your approach to treat hypoventilation?
17. Would you consider a deep extubation in this patient?
18. If the patient cannot be extubated, what measures can you take to reduce the likelihood of bronchospasm with an endotracheal tube in place?

D. Postoperative Management

1. In patients with asthma and COPD, are there special considerations for the use of opioids and nonsteroidal anti-inflammatory drugs (NSAIDs) for postoperative pain control?
2. Would you consider using a regional technique for analgesia?

3. The patient was breathing well and was extubated. Would you place this patient on supplemental oxygen in the recovery room? How much?
4. The patient is hypoventilating in postanesthesia care unit (PACU). Would you initiate noninvasive ventilation (NIV)?

A. Medical Disease and Differential Diagnosis

A.1. What is the differential diagnosis of dyspnea?

Dyspnea is a symptom of a broad array of underlying conditions. Although the differential diagnosis is extensive, pulmonary and cardiac conditions account for as many as 85% of the underlying causes of dyspnea. Pulmonary causes include asthma, COPD, interstitial lung disease, and chest wall disease (kyphoscoliosis). Cardiac causes include left heart failure, sometimes called cardiac asthma, and pericardial disease (restrictive pericarditis, cardiac tamponade). Dyspnea can also be due to anemia, deconditioning, and psychological causes.

In this patient, with known asthma, the most likely causes of dyspnea are pulmonary. In patients such as this one with a considerable smoking history, concomitant COPD and asthma is common, and airway obstruction with both reversible and irreversible components is frequently seen.

Jameson JL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:226–229, 1957–1969, 1990–1998.

A.2. What is the prevalence of asthma and chronic obstructive pulmonary disease (COPD)?

Asthma is one of the most common chronic diseases globally and currently affects up to 334 million people. The global incidence of asthma has been increasing for the past three decades. The prevalence of asthma in the United States is 8.2%

of the adult population and 9.5% of children. It occurs at all ages, with a peak in children aged 5 to 9 years. In childhood, there is a 10:7 male/female preponderance, which is reversed in adulthood (6.5:10 male/female).

The greatest modifiable risk factor for asthma is smoking. Nonmodifiable risk factors include income (inversely proportional), ethnicity (Whites and Hispanics have a reduced risk, increased prevalence in African Americans), and environmental exposure.

In the United States, deaths from asthma are rare, with an age-adjusted rate of 11 per million in 2010. However, the annual rate of death from asthma is approximately 15-fold higher in adults older than 65 years than in children (37.2 vs. 2.6 per million).

COPD affects more than 200 million people in the world. In the United States, 14.1% of smokers carry a diagnosis of COPD, 7.1% of former smokers, and 2.9% of never smokers. The majority (71.2%) of COPD patients carry the diagnosis of at least one comorbidity and have a significantly higher rate of hyperlipidemia, hypertension, coronary artery disease, diabetes, cancer, stroke, and chronic kidney disease than patients without COPD.

Centers for Disease Control and Prevention. Asthma facts: CDC's National Asthma Control Program grantees. Published 2013. http://www.cdc.gov/asthma/reports_publications.htm. Accessed December 21, 2018.

Cunningham TJ, Ford ES, Rolle IV, et al. Associations of self-reported cigarette smoking with chronic obstructive pulmonary disease and co-morbid chronic conditions in the United States. *COPD*. 2015;12:276–286.

Forum of International Respiratory Societies. The global impact of respiratory disease—second edition. Published 2017. https://www.firsnet.org/publications/the-global-impact-of-respiratory-disease. Accessed December 21, 2018.

A.3. What is the etiology of asthma?

Asthma is a heterogeneous disease with complex, multifactorial etiologies. The common denominator that underlies the asthmatic diathesis is a nonspecific hyperirritability of the tracheobronchial tree. Although asthma can be subdivided according to several clinical, physiologic, and pathologic variables, traditionally asthma is classified into two groups: atopic (allergic, extrinsic) and nonatopic (nonallergic, intrinsic). Atopic asthma is usually associated with a personal or family history of allergic diseases, positive skin reactions to extracts of airborne antigens, and increased levels of immunoglobulin E (IgE) in the serum. Most patients with asthma have the atopic type. Patients with nonatopic asthma have negative skin tests to common inhalant allergens and normal serum concentrations of IgE. The patients with nonatopic asthma usually show later onset of disease, and may be aspirin-sensitive.

Jameson JL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:1957–1969, 1990–1998.

McCracken JL, Veeranki SP, Ameredes BT, et al. Diagnosis and management of asthma in adults: a review. *JAMA*. 2017;318:279–290.

Olin JT, Wechsler ME. Asthma: pathogenesis and novel drugs for treatment. *BMJ*. 2014;349:g5517.

A.4. Discuss the pathogenesis of asthma. How is asthma distinguished from COPD?

Asthma is a chronic disease characterized by reversible expiratory airflow obstruction resulting from narrowing of the airways in response to various stimuli and a nonspecific hyperirritability of the tracheobronchial tree.

COPD is characterized by persistent respiratory symptoms and airflow limitation that is not fully reversible.

In asthma, exposure to an initiating stimulus triggers inflammatory cells (mast cells, eosinophils, T lymphocytes, macrophages, basophils, neutrophils, and platelets) and

structural cells (epithelial cells, fibroblasts, and airway smooth muscle cells) to release various mediators that lead to bronchospasm, vascular congestion, increased capillary permeability (edema of bronchial mucosa), and thick tenacious secretions.

The net result is a reduction in airway diameter, an increase in airway resistance, decreased forced expiratory volumes and flow rates, hyperinflation of the lungs and thorax, increased work of breathing, alterations in respiratory tract muscle function, mismatched ventilation/perfusion, and altered blood gases.

In COPD, goblet cell hypertrophy, activation of inflammatory cells (lymphocytes, neutrophils, and macrophages), and alteration in function of structural cells lead to increased mucus production, airway fibrosis, loss of alveolar attachments, and pulmonary vascular remodeling. The net result is hypersecretion of mucus, emphysema with peripheral airway collapse, impaired gas exchange, pulmonary hypertension, and right ventricular dysfunction. The minority of COPD cases are a result of a genetic deficiency in antitrypsin levels, leading to an imbalance between antiproteinases and increased lung parenchymal destruction.

Although asthma and COPD are distinct syndromes, some patients, such as this patient with extensive smoking history, have features of COPD, such as irreversible airflow limitation. Additionally, although airway hyperresponsiveness to a variety of exogenous stimuli is one of the defining features of asthma, many patients with COPD also have airway hyperresponsiveness.

Jameson JL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:1957–1969, 1990–1998.

A.5. What are the triggers of bronchospasm?

- *Allergens*. Inhaled allergens activate mast cells with bound IgE directly leading to the immediate release of bronchoconstrictor mediators. This early response is reversed by bronchodilators. Common allergens are house dust mites (*Dermatophagoides* species), pet dander, grass pollen, ragweed, and tree pollen.
- *Infections*. Respiratory tract infections are among the most common triggers of acute severe asthma exacerbations.
- *Pharmacologic agents*. Drugs that can trigger bronchospasm include β-adrenergic antagonists, aspirin and other NSAIDs, and sulfiting agents (food preservatives). All nonspecific β-blockers should be avoided in asthmatics because their use can lead to severe bronchospasm. The ultra–short-acting β_1 selective antagonists landiolol and esmolol can be safely used perioperatively in patients with airway hyperreactivity. Aspirin-sensitive asthma is a well-defined phenotype of asthma that affects a small proportion of asthmatics. Because asthma can be triggered by cyclooxygenase (COX)-1 inhibitors, all nonselective COX inhibitors (aspirin, ibuprofen, ketorolac) should be avoided, but selective COX-2 inhibitors (celecoxib) are safe to use. Theoretically, reversal of neuromuscular blockade with anticholinesterase drugs could precipitate bronchospasm due to stimulation of postganglionic cholinergic receptors in airway smooth muscle. Adequate dosing of a concomitant anticholinergic is necessary to avoid this complication. Alternatively, sugammadex may be used for reversal of rocuronium-induced neuromuscular blockade.
- *Environment and air pollution*. Increased levels of sulfur dioxide, ozone, diesel particulates, and nitrogen oxides are associated with increased asthma symptoms. Dry, cold air can also trigger bronchospasm in susceptible individuals.
- *Occupational factors*. Various compounds used in industry

can cause asthma in susceptible individuals. Various names have been applied to this condition, such as meat wrapper's asthma, baker's asthma, and woodworker's asthma.

- *Exercise*. Asthma can be induced or made worse by physical exertion. The mechanism is linked to hyperventilation, which results in increased osmolality in airway lining fluid and triggers mast cell mediator release, resulting in bronchoconstriction.
- *Emotional stress*. Psychological factors can induce bronchoconstriction through the cholinergic reflex pathway.

Carron M, Zarantonello F, Tellaroli P, et al. Efficacy and safety of sugammadex compared to neostigmine for reversal of neuromuscular blockade: a meta-analysis of randomized controlled trials. *J Clin Anesth*. 2016;35:1–12.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:15–32.

Jameson JL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:1957–1969.

Yamakage M, Iwasaki S, Jeong SW, et al. Beta-1 selective adrenergic antagonist landiolol and esmolol can be safely used in patients with airway hyperreactivity. *Heart Lung*. 2009;38:48–55.

A.6. What is the universal finding in ABGs during asthmatic attacks: hypoxemia or CO_2 retention?

Hypoxemia is a universal finding during asthmatic attacks. Frank ventilatory failure with CO_2 retention is relatively uncommon because CO_2 has a diffusion capacity that is 20 times higher than that of oxygen. During acute asthmatic attacks, most patients try to overcome airway obstruction and hypoxia by hyperventilation. This results in hypocarbia and respiratory alkalosis. CO_2 retention is a late finding and indicates severe and prolonged airway obstruction, as in status asthmaticus.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:15–32.

Jameson JL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:1957–1969.

A.7. Describe the abnormalities seen in spirometry, lung volumes, and lung capacities during an asthmatic attack.

There is a substantial reduction in forced expiratory volume in 1 second (FEV_1) but less reduction in forced vital capacity (FVC), giving a decreased FEV_1/FVC ratio. Forced expiratory flow at 25% to 75% ($FEF_{25\%–75\%}$) is sharply reduced as well. $FEF_{25\%–75\%}$ (also referred to as the maximum midexpiratory flow rate or MMEFR) is the forced expiratory flow rate during 25% to 75% of the vital capacity (VC). Unlike the FEV_1, the $FEF_{25\%–75\%}$ is independent of patient effort. Other classic spirometry findings include a decreased expiratory reserve volume (ERV), whereas the residual volume (RV), FRC, and total lung capacity (TLC) are increased.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:15–32.

Jameson JL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:1957–1969.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57–i65.

B. Preoperative Evaluation and Preparation

B.1. How would you evaluate the patient preoperatively? What preoperative workup would you order?

Preoperative evaluation of patients with asthma and COPD focuses on the assessment of disease severity, the effectiveness of current medical management, and the potential need for additional therapy before surgery. The history should include assessment of exercise tolerance, recent or current respiratory

infections, sputum quantity and quality, known triggers of attacks, most recent exacerbations, current medications and time of last use, smoking history, and prior surgical and anesthetic history.

A focused cardiopulmonary exam should occur, which should focus on detecting signs of acute bronchospasm, active lung infection, and right heart failure. Note the patient's general appearance and observe the patient's breathing. Look for use of accessory muscles, pursed-lip exhalation, or cyanosis. Auscultation of the lungs can reveal wheezing, adventitious lung sounds, and hyperinflation. Auscultation of the heart may reveal a split second heart sound typical of cor pulmonale or the murmur of tricuspid or pulmonary regurgitation present in some patients with long-standing pulmonary hypertension. Additionally, jugular venous distension, peripheral edema, and hepatic enlargement may be present. Cachexia may also be seen.

Laboratory testing is guided by the history and physical examination. For major surgery, it is reasonable to obtain a complete blood count, serum electrolytes, electrocardiogram, and chest radiograph. Additionally, these patients should have a room air Spo_2. It is not recommended to routinely perform pulmonary function tests. However, if the worsening of disease severity is elicited from the history and physical examination, additional diagnostic tests may include a computed tomography scan of the chest, echocardiogram, detailed lung volume testing, and a room air ABG.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:15–32.

Lakshminarasimhachar A, Smetana GW. Preoperative evaluation: estimation of pulmonary risk. *Anesthesiol Clin*. 2016;34:71–88.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57–i65.

B.2. How would you distinguish obstructive lung disease from restrictive lung disease by spirometry?

Table 1.1 summarizes the distinctions between the two types of lung diseases. In restrictive lung disease (e.g., pulmonary fibrosis and ankylosing spondylitis), the FVC is low because of limited expansion of the lungs or chest wall, although the FEV_1 is often not reduced proportionately, because airway resistance is normal. Therefore, the FEV_1/FVC percentage is normal or high.

TABLE 1.1 Differences between Obstructive and Restrictive Lung Diseases

	Obstructive	Restrictive
Vital capacity	N or ↓	↓
Total lung capacity	N or ↓	↓
Residual volume	↑	↓
FEV_1/FVC	↓	N or ↑
Maximum midexpiratory flow rate	↓	N
Maximum breathing capacity	↓	N

↓, decreased; ↑, increased; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; N, normal.

In obstructive lung disease, the FEV_1/FVC is grossly reduced because the airway resistance is high. Normally, FEV_1 is more than 80% of FVC, and VC should be more than 80% of predicted value. The predicted values depend on body size, age, and sex. The FEV_1/FVC is less than 0.70 in COPD. The severity of airflow limitation in COPD is determined by the FEV_1. Patients with an FEV_1 less than predicted but greater than or equal to 80% of predicted are considered to have mild COPD (Global Initiative for Chronic Obstructive Lung Disease [GOLD] 1). Those with FEV_1 greater than or equal to 50% but less than 80% of predicted are classified as having moderate

COPD (GOLD 2). Severe cases of COPD have an FEV_1 that is greater than or equal to 30% but less than 50% of predicted (GOLD 3). Finally, patient with an FEV_1 that is less than 30% of predicted have very severe COPD (GOLD 4).

The TLC is increased in obstructive lung disease and decreased in restrictive lung disease. However, TLC cannot be obtained by routine screening spirometry.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:361–383.

Jameson JL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:1943–1944.

Vogelmeier CF, Criner GJ, Martinez FJ, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017 report. GOLD executive summary. *Am J Respir Crit Care Med*. 2017;195:557–582.

B.3. Define normal lung volumes and lung capacities. Give normal values for an average adult male.

There are four basic "volumes" and four derived "capacities" that are combinations of these volumes (**Fig. 1.1**).

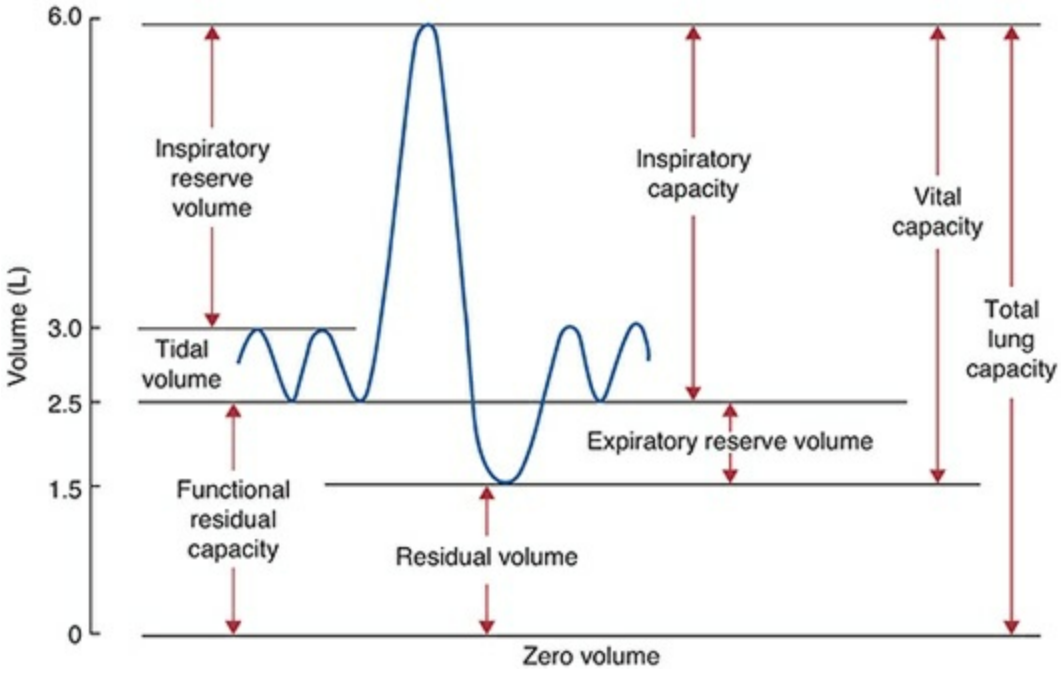

FIGURE 1.1. Lung volumes and lung capacities.

V_T is the volume of air inhaled or exhaled during normal breathing. Normal V_T is 500 mL or approximately 6 to 8 mL per kg.

Inspiratory reserve volume (IRV) is the maximum volume of gas that can be inhaled following a normal inspiration while at rest. Normal IRV is 2,500 to 3,500 mL.

ERV is the maximum volume of gas that can be exhaled after a normal expiration. Normal ERV is 1,200 mL.

RV is the volume of gas remaining in the lungs after a forced exhalation. Normal RV is 1,200 mL.

VC is the maximum amount of gas that can be exhaled after a maximum inhalation. VC is the sum of V_T, ERV, and IRV. Normal VC is 4,500 mL or approximately 60 to 70 mL per kg.

Inspiratory capacity (IC) is the maximum amount of gas that can be inhaled from the resting expiratory position after a normal exhalation. It is the sum of V_T and IRV. Normal IC is 3,500 mL.

FRC is the remaining lung volume at the end of a normal quiet expiration. It is the sum of RV and ERV. Normal FRC is 2,500 mL or 30 to 40 mL per kg.

TLC is the lung volume at the end of a maximum inspiration. It is the sum of VC and RV. Normal TLC is 5,000 to 6,000 mL for an adult man and 4,000 to 5,000 mL for an adult woman.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:361–383, 1710.

Jameson JL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:1945–1950.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:26–29.

B.4. What are flow–volume loops? Draw flow–volume

loops for a healthy subject and patients with COPD, restrictive lung disease, fixed obstruction of the upper airway, variable extrathoracic obstruction, and variable intrathoracic obstruction.

Flow–volume loops provide a graphic analysis of flow at various lung volumes. To perform the test, subjects are asked to inhale maximally (to TLC) and then exhale as forcefully and maximally as possible (to RV). This cycle is repeated. The flow (liters per second) is plotted on the y-axis and volume (liters) on the x-axis (**Fig. 1.2A**). The test requires a compliant patient for accurate results—the majority of the test is effort dependent, including the entire inspiratory curve and both ends of the expiratory curve (near TLC and RV). The forced expiratory flow during 25% to 75% of VC ($FEF_{25\%–75\%}$) is reflective of the small- to medium-sized airways and is considered a relatively effort-independent value.

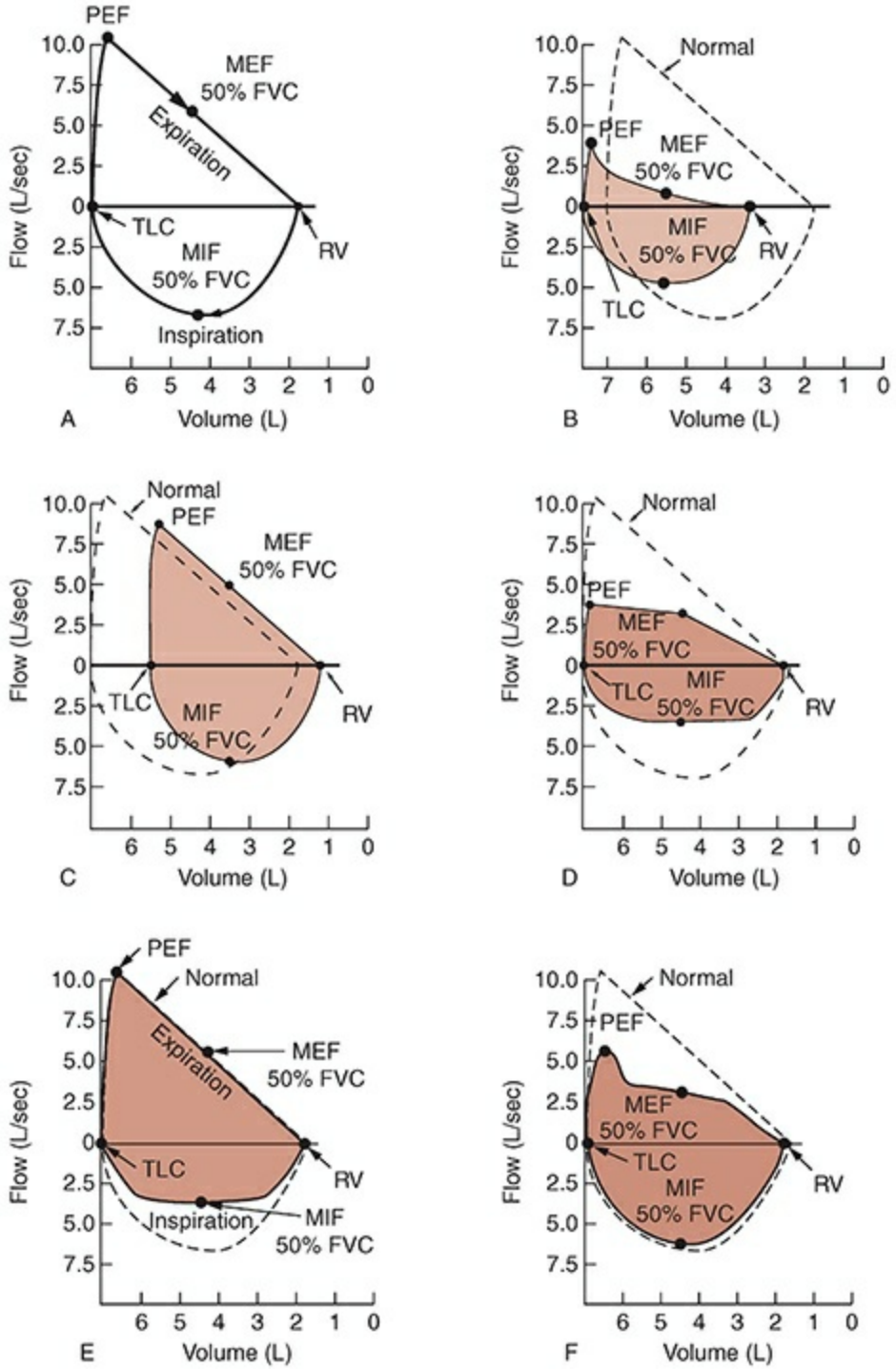

FIGURE 1.2. Flow–volume loops in a healthy person (A), a patient with obstructive lung disease (B), a patient with restrictive lung disease (C), a patient with a fixed obstruction (D), a patient with a variable extrathoracic obstruction (E), and a patient with a variable intrathoracic obstruction (F). FVC, forced vital capacity; MEF, maximal expiratory flow; MIF, maximal inspiratory flow; PEF, peak expiratory flow; RV, residual volume; TLC, total lung capacity. (*From the Merck Manual Professional Version [known as the Merck Manual in the United States and Canada and the MSD Manual in the rest of the world], edited by Robert Porter. Copyright 2019 by Merck Sharp &*

Dohme Corp., a subsidiary of Merck & Co, Inc, Kenilworth, NJ. Available at http://www.msdmanuals.com/professional. *Accessed November 11, 2014.*)

Normal flow–volume loop (**Fig. 1.2A**). Inspiratory limb of loop is symmetric and convex. Expiratory limb is linear. Airflow at the midpoint of IC and airflow at the midpoint of expiratory capacity are often measured and compared. Maximal inspiratory flow (MIF) at 50% FVC is greater than maximal expiratory flow (MEF) at 50% FVC because dynamic compression of the airways occurs during exhalation.

Obstructive disorder (e.g., emphysema, asthma) (**Fig. 1.2B**). Although all airflow is diminished, expiratory prolongation predominates, and MEF < MIF. Peak expiratory flow (PEF) is sometimes used to estimate degree of airway obstruction but depends on patient effort.

Restrictive disorder (e.g., interstitial lung disease, kyphoscoliosis) (**Fig. 1.2C**). The loop is narrowed because of diminished lung volumes. Airflow is greater than normal at comparable lung volumes because the increased elastic recoil of lungs holds the airways open.

Fixed obstruction of the upper airway (e.g., tracheal stenosis, goiter) (**Fig. 1.2D**). The top and bottom of the loops are flattened so that the configuration approaches that of a rectangle. Fixed obstruction limits flow equally during inspiration and expiration, and MEF = MIF.

Variable extrathoracic obstruction (e.g., unilateral vocal cord paralysis, vocal cord dysfunction) (**Fig. 1.2E**). When a single vocal cord is paralyzed, it moves passively with pressure gradients across the glottis. During forced inspiration, it is drawn inward, resulting in a plateau of decreased inspiratory flow. During forced expiration, it is passively blown aside, and expiratory flow is unimpaired. Therefore, MIF 50% FVC < MEF 50% FVC.

Variable intrathoracic obstruction (e.g., tracheomalacia) (**Fig.**

1.2F). During a forced inspiration, negative pleural pressure holds the floppy trachea open. With forced expiration, loss of structural support results in tracheal narrowing and a plateau of diminished flow. Airflow is maintained briefly before airway compression occurs.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:361–383.

Jameson JL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:1945–1950.

The Merck Manual: Professional Edition. http://www.merckmanuals.com/professional/pulmonary_disorders/tests_of_pul volume_loop.html?qt=flow%20volume%20loops&alt=sh. Accessed December 21, 2018.

B.5. Define closing volume (CV) and closing capacity (CC). What is the normal value of CV?

CC is the lung volume at which the small airways in the dependent parts of the lung begin to close. CC is the sum of CV and RV. CV is the volume above the RV at which small airways begin to close during expiration. It can be measured during the single-breath nitrogen test (Fig. 1.3) or with an inert tracer gas such as helium, xenon, or argon.

In healthy young people, CV is approximately 10% of the VC, or 400 to 500 mL. CV and CC increase with age. CV is increased in patients with small airway disease and in chronic smokers.

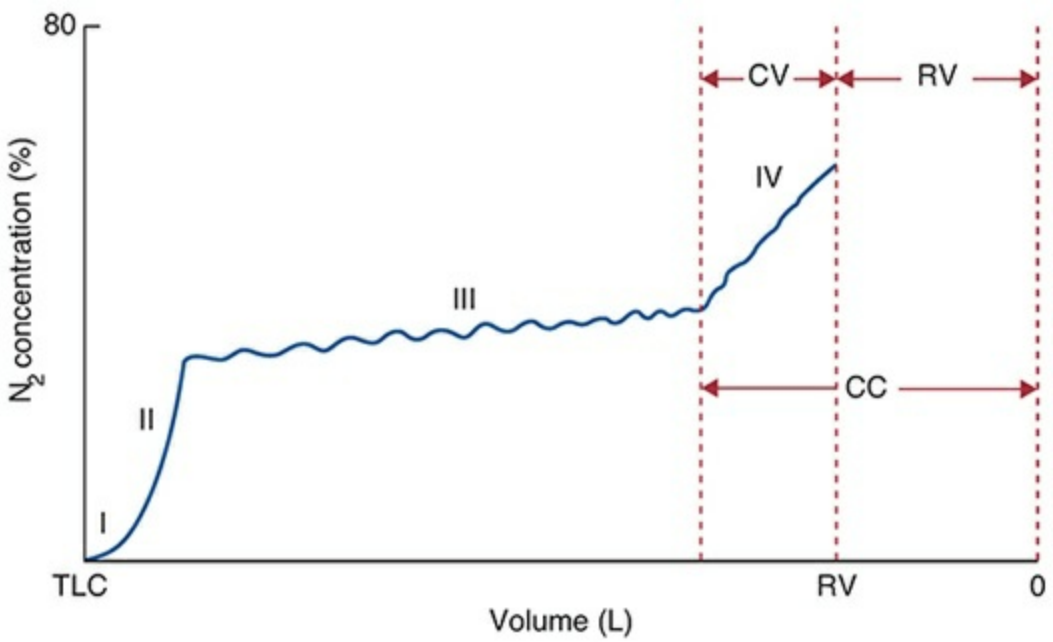

FIGURE 1.3. Closing volume (CV) measurement by single-breath nitrogen test. CC, closing capacity; RV, residual volume; TLC, total lung capacity.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:362.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:26–29.

B.6. Why is the functional residual capacity (FRC) important in oxygenation?

In a healthy young adult, FRC is above CC (FRC > CV + RV). Increases in CC and/or decreases in FRC can result in CC exceeding FRC and subsequent closure of the small airways during certain periods of normal tidal ventilation. Airway closure produces shunting, with perfusion of unventilated alveoli. Therefore, shunt ($\dot{Q}_S/\dot{Q}_T$) is increased and arterial oxygenation is decreased.

Perfusion to the lung occurs in both inspiratory and expiratory phases of respiration. The FRC, or lung volume remaining at end expiration, provides surface area for gas exchange during this phase of respiration. The greater the FRC, the more oxygenation occurs. Patients in the supine position, under

general anesthesia, or with acute respiratory distress syndrome all have decreased FRC to varying degrees. PEEP increases FRC, improving oxygenation in the expiratory phase and reducing small airway collapse.

FRC can be measured by helium dilution, nitrogen washout, or body plethysmography.

Buist AS. New tests to assess lung function. The single-breath nitrogen test. *N Engl J Med*. 1975;293:438–440.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:37–38.

B.7. How are FRC and CC affected by age and posture? How are they affected by anesthesia?

Posture has a dramatic effect on FRC. When a patient goes from upright to the supine position, FRC decreases approximately 30%. Body position does not affect CC.

Conversely, age has a greater effect on CC than on FRC. CC increases with age, whereas FRC does not change or increases only slightly. Therefore, CC will exceed FRC in healthy adults over the age of 44 years when in the supine position and in healthy adults over the age of 70 years in the upright position.

During general anesthesia, FRC is reduced approximately 20%, whether breathing is controlled or spontaneous. The anatomic basis of the FRC reduction under anesthesia is not well understood. Traditionally, it was thought to be due to the cephalad shift of the diaphragm, induced by anesthesia and muscle paralysis. Although the role of the anatomic position of the diaphragm remains debatable, the current understanding is that FRC is reduced due to loss of respiratory muscle tone.

CC was previously reported to be unchanged during anesthesia, but later studies concluded that CC reduced in parallel to FRC during anesthesia.

Bergman NA, Tien YK. Contribution of the closure of pulmonary units to

impaired oxygenation during anesthesia. *Anesthesiology*. 1983;59:395–401.

Gilmour I, Burnham M, Craig DB. Closing capacity measurements during general anesthesia. *Anesthesiology*. 1976;45:477.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:357–358, 1655–1662, 2105.

Juno P, Marsh HM, Knopp TJ, et al. Closing capacity in awake and anesthetized-paralyzed man. *J Appl Physiol*. 1978;44:238.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:26–29, 37–38, 296–299.

Wahba RWM. Perioperative functional residual capacity. *Can J Anaesth*. 1991;38:384–400.

B.8. Give the equations for shunt (Qs/Qt) and dead space/tidal volume (Vd/Vt). What are their normal values?

$$\text{QS/QT} = \frac{\text{CcO}_2 - \text{CaO}_2}{\text{CcO}_2 - \text{C}\bar{\text{v}}\text{O}_2} \qquad \text{VD/VT} = \frac{\text{PaCO}_2 - \text{P}\bar{\text{E}}\text{CO}_2}{\text{PaCO}_2}$$

where CcO_2, CaO_2, and $C\bar{v}O_2$ are oxygen contents in pulmonary capillary, arterial, and mixed venous blood, respectively; QT is cardiac output; QS is shunt blood; and $PaCO_2$ and $P\bar{E}CO_2$ are partial pressures of CO_2 in arterial blood and the mixed expired gases, respectively.

Normal QS/QT is 4% to 5%, and VD/VT is approximately 0.3.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:374–376.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:122–124.

B.9. Interpret the following ABG: pH, 7.36; PCO_2, 60 mmHg; PO_2, 70 mmHg; and CO_2 content, 36 mEq per L.

The fraction of inspired oxygen (FIO_2) is essential to evaluate PaO_2. Assume the blood sample is obtained while the patient is

breathing room air. The blood gases show mild hypoxemia and respiratory acidosis, compensated by metabolic alkalosis. The blood gases are compatible with COPD.

Jameson JL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:1990–1998.

B.10. What are the common physiologic causes of hypoxemia?

From the shunt equation, arterial oxygen content is related to the change in pulmonary capillary oxygen content, venous oxygen content, and venous admixture. It is easier to classify hypoxemia into the following three categories.

Decreased pulmonary capillary oxygen tension

- Hypoventilation
- Low F_{IO_2}
- Ventilation/perfusion mismatch from pulmonary parenchymal change
- Diffusion abnormality (rare)

Increased shunting

- Either intrapulmonary or cardiac

Reduced venous oxygen content

- Congestive heart failure—low cardiac output
- Increased metabolism—fever, hyperthyroidism, shivering
- Decreased arterial oxygen content—anemia

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:354–383, 2592–2593.

Jameson JL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:234–236.

B.11. How would you prepare this asthmatic patient with COPD for surgery?

The goal of preoperative preparation is to optimize the patient for surgery and to decrease the risk of postoperative pulmonary complications (PPCs). This patient's risk factors for PPCs include preexisting pulmonary disease, cigarette smoking, abdominal surgery, and general anesthesia.

Preoperative strategies that have proven to reduce PPC rates include smoking cessation (see section B.12), optimizing airflow limitation in patients with obstructive lung disease (such as this patient), and treating respiratory tract infections, if present.

The severity of airflow limitations is assessed during preoperative evaluation and laboratory and diagnostic studies (see section B.1). Airflow limitation can be optimized by continuation of anti-inflammatory and bronchodilator therapy up to the time of surgery. Additional therapy, such as systemic corticosteroids may need to be initiated in patients with poorly controlled symptoms.

Elective surgery should not be performed in the presence of active respiratory infection and symptoms should be actively treated until the patient is back to baseline status.

Additionally, preoperative lung expansion maneuvers, such as deep breathing exercises, incentive spirometry, and chest physiotherapy are of proven benefit in reducing PPC rates.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:15–32.

Lakshminarasimhachar A, Smetana GW. Preoperative evaluation: estimation of pulmonary risk. *Anesthesiol Clin*. 2016;34:71–88.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57–i65.

B.12. The patient comes to your perioperative clinic 2 weeks before surgery. He wants to know if his smoking puts him at increased risk during surgery. What do you tell him? Should he quit now?

Smoking results in increased levels of carboxyhemoglobin, lower oxygen content, and decreased delivery of oxygen by hemoglobin to the tissues. These effects are dramatically improved with as little as 12 hours of smoking cessation.

Smoking also increases the risk of PPCs, which include respiratory failure, unplanned intensive care unit (ICU) admission, pneumonia, airway events during anesthesia, and increased need for postoperative respiratory support. Smokers have an increased rate of wound-related complications and decreased bone healing after surgery. Although a cessation period of at least 8 weeks prior to surgery is optimal and results in improved mucociliary clearance, decreased sputum production, and a relative risk reduction in PPCs, it is highly recommended for patients to stop smoking at any time prior to surgery.

A persistent misconception in our specialty is that short-term smoking cessation (<4 weeks) is detrimental to the patient. Some have argued that a patient smoking 2 weeks before surgery should continue smoking to avoid *increased* risks associated with cessation. There is now a preponderance of evidence that debunks this myth. Short-term smoking cessation is *not* a risk factor for long-term perioperative complications. In contrast, the long-term detrimental effects of continued smoking are well known. Anesthesiologists should be aware that admission for surgery can be a powerful motivator for patients to quit smoking, providing a "teachable moment" for smoking cessation and frequently resulting in successful, long-term cessation. Therefore, this patient should be counseled to quit smoking as soon as possible.

Myers K, Hajek P, Hinds C, et al. Stopping smoking shortly before surgery and postoperative complications. *Arch Intern Med*. 2011;171(11):983–989.

Turan A, Mascha EJ, Roberman D, et al. Smoking and perioperative outcomes. *Anesthesiology*. 2011;114:837–846.

Warner DO. Perioperative abstinence from smoking: physiologic and clinical consequences. *Anesthesiology*. 2006;104:356–367.

Yu S, Warner DO. Surgery as a teachable moment for smoking cessation. *Anesthesiology*. 2010;112:102–107.

B.13. You discover that the patient had a recent upper respiratory infection (URI), would you postpone surgery? For how long?

Respiratory tract infections are the most common stimuli that trigger acute exacerbations of asthma. Even healthy subjects have transiently increased airway responsiveness to nonspecific stimuli following a viral infection. It is unclear how long surgery should be delayed following a URI because airway hyperreactivity can last 2 to 8 weeks after the infection in both healthy subjects and patients with asthma. Cohen and Cameron reported that a child with a URI having endotracheal anesthesia has an 11-fold increased risk of respiratory complications. In addition, Tait and Knight found that laryngospasm and bronchospasm were significantly increased in healthy children 2 weeks after a URI. However, the data are controversial. A frequently cited retrospective study by Warner et al. found no increase in intraoperative bronchospasm in patients with well-controlled asthma and a recent URI.

In this patient presenting for elective surgery with multiple risk factors for PPCs, postponing surgery at least 2 weeks after clinical recovery from the URI is reasonable.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:851.

Cohen MM, Cameron CB. Should you cancel the operation when a child has an upper respiratory infection? *Anesth Analg*. 1991;72:282–288.

Tait AR, Knight PR. Intraoperative respiratory complications in patients with upper respiratory tract infections. *Can J Anaesth*. 1987;34:300–303.

Warner DO, Warner MA, Barnes RD, et al. Perioperative respiratory complications in patients with asthma. *Anesthesiology*. 1996;85:460–467.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57–i65.

B.14. What medications would you expect the patient to have taken in the past or be taking at the present time?

The main drugs for asthma and COPD can be divided into rescue medications (bronchodilators) and controllers (for maintenance).

Patients with infrequent asthma symptoms are placed solely on a short-acting β_2-agonist (SABA). Alternatively, anticholinergic inhalers such as ipratropium may be given, although their slower onset of action makes them less preferred.

Patients with increased risk for exacerbations (including smokers) and/or those with frequent symptoms should be placed on controller therapy with a low-dose inhaled corticosteroid (ICS). In patients with severe symptoms, a long-acting β_2-agonist or a high-dose ICS are added. Acute exacerbations are treated with a short course of oral corticosteroids.

Theophylline was a widely prescribed oral controller medication for asthma but has fallen out of favor secondary to its narrow therapeutic index, multiple drug interactions, and side effect profile. It may be prescribed in patients with COPD. Patients taking theophylline require routine level testing. They should continue theophylline in the perioperative period to avoid an asthma or COPD exacerbation secondary to withdrawal.

Other oral medications targeting the inflammatory component of asthma include the mast cell stabilizer cromolyn, the anti-IgE antibody omalizumab, and leukotriene receptor antagonists such as zafirlukast and montelukast. The phosphodiesterase-4 inhibitor roflumilast may be added to the treatment regimens of patients with severe COPD.

Global Initiative for Asthma. Global strategy for asthma management and

prevention. Published 2018. http://www.ginasthma.org/. Accessed January 11, 2019.

Global Initiative for Asthma. Global strategy for the diagnosis, management, and prevention of COPD. Global Initiative for Chronic Obstructive Lung Disease. Published 2018. http://www.goldcopd.org/. Accessed January 11, 2019.

Jameson JL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:1957–1969, 1990–1998.

B.15. The patient was on 20 mg of prednisone per day for 5 days as part of the treatment of an asthma exacerbation 3 months ago. He is currently not on steroids. Should the patient receive stress-dose steroids?

Patients on chronic steroid therapy may experience hypothalamic-pituitary-adrenal (HPA) axis suppression that can result in decreased cortisol (hydrocortisone) production, a process known as secondary adrenal insufficiency. The concern is that inadequate cortisol production in response to the stress of surgery can manifest as full-blown adrenal crisis in the perioperative period. The anesthesiologist must decide whether to administer stress-dose steroids to mitigate this rare but potentially life-threatening complication of chronic steroid use. However, the decision is not always clear-cut because even the recommendations found in most textbooks are inconsistent and lacking in class A and B evidence. Additionally, there is no universally agreed on dose or duration of exogenous steroids required to cause HPA axis dysfunction, although prednisone 20 mg per day for 2 weeks within the previous 6 months has been cited.

Given this patient's short duration of prednisone treatment, he should not require administration of stress-dose steroids. However, 100 mg of hydrocortisone intravenous (typical stress-dose for this type of surgery) should be available in the

operating room in case hypotension attributable to adrenal insufficiency occurs during surgery.

Another consideration is whether the patient will receive prophylaxis for postoperative nausea/vomiting (PONV) with dexamethasone. Dexamethasone has 30 times glucocorticoid potency of hydrocortisone, so even a modest PONV dose of 4 mg of dexamethasone is equivalent to the usual stress dose of hydrocortisone. Because there is no mineralocorticoid deficiency in secondary adrenal insufficiency, dexamethasone's absence of mineralocorticoid activity is not an issue.

Liu MM, Reidy AB, Saatee S, et al. Perioperative steroid management: approaches based on current evidence. *Anesthesiology*. 2017;127:166–172.

Wax DB. One size fits all for stress-dose steroids. *Anesthesiology*. 2018;128:680–681.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57–i65.

B.16. Should patients with reactive airway disease receive preoperative steroids?

The increasing understanding of the inflammatory component of reactive airway disease has led to greater appreciation of the importance of steroids in preventing and treating exacerbations. In wheezing patients, oral methylprednisolone 40 mg daily for 5 days before surgery has been shown to decrease postintubation bronchospasm. The oft-cited concern that steroids increase the rate of wound complications is not well founded. A study of patients with asthma treated with steroids preoperatively found no increase in the incidence of wound infections or wound-healing problems.

Patients with poorly controlled asthma presenting for surgery with high risk of PPCs (open aortic aneurysm repair, thoracic, upper abdominal) that will require endotracheal intubation must be treated with utmost caution, and may benefit from

preoperative optimization of pulmonary function with a short course of systemic steroids. On the other hand, patients with mild, well-controlled disease should not require such treatment.

Bishop MJ. Preoperative corticosteroids for reactive airway? *Anesthesiology*. 2004;100:1047–1048.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:20–22.

Silvanus M-T, Groeben H, Peters J. Corticosteroids and inhaled salbutamol in patients with reversible airway obstruction markedly decrease the incidence of bronchospasm after tracheal intubation. *Anesthesiology*. 2004;100:1052–1057.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57–i65.

B.17. What is the onset of action of intravenous steroid therapy in asthma?

Parenteral steroids remain a mainstay of the treatment of acute asthma. Although the bronchial effects of intravenous steroids are not immediate and are typically seen 4 to 6 hours after initial administration, their administration is nonetheless indicated with severe bronchospasm that has not resolved despite intense optimal bronchodilator therapy.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:19.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57–i65.

C. Intraoperative Management

C.1 If the patient had a severe asthmatic attack in the operating room before the induction of anesthesia, would you proceed with the anesthetic or postpone the surgery?

First, medical treatment should be given to relieve the asthmatic

attack. Elective surgery should be postponed, the patient reevaluated carefully, and his asthma better optimized. In the case of emergency surgery, such as acute appendicitis, the surgery can be performed after the asthmatic attack is successfully treated. Regional anesthesia, if feasible, should be considered. During surgery, the medical treatment should be continued.

Dewachter P, Mouton-Faivre C, Emala CW, et al. Case scenario: bronchospasm during anesthetic induction. *Anesthesiology*. 2011;114:1200–1210.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57–i65.

C.2. The patient did not have an asthmatic attack in the operating room and you proceed with induction. How would you induce anesthesia? Would you use a supraglottic airway instead of an endotracheal tube?

The principles of anesthetic management for the asthmatic patient are threefold: to block airway reflexes before laryngoscopy and intubation, to relax airway smooth muscle, and to prevent release of biochemical mediators.

Before induction of general anesthesia, the patient should take two or three puffs of albuterol from a metered-dose inhaler (MDI). Propofol is often used for induction of hemodynamically stable asthmatic patient. Ketamine may be chosen in a hemodynamically unstable patient with asthma (see sections C.3 and C.4). Then, oxygen and a potent inhalation agent, such as sevoflurane, are administered by mask to achieve an adequate depth of anesthesia that suppresses hyperreactive airway reflexes sufficiently to permit tracheal intubation without triggering bronchospasm. The lesser pungency of sevoflurane (compared with desflurane and isoflurane) may decrease the likelihood of coughing, which can induce bronchospasm.

Muscle relaxants that do not release histamine, such as cisatracurium and rocuronium, can be used to facilitate endotracheal intubation. Prior to intubation, lidocaine may be administered (see section C.5).

Avoidance of intubation altogether is another approach. A supraglottic airway provides a unique opportunity for the clinician to control the airway without having to introduce a foreign body into the trachea. Kim and Bishop demonstrated a reversible increase in airway resistance in intubated patients under isoflurane anesthesia and showed that this increase was not present with supraglottic airway use. Therefore, it may be an ideal airway tool in the patient with asthma not at risk for reflux and aspiration.

Laparoscopic surgeries using a supraglottic airway have been reported by multiple centers for both gynecologic surgeries and cholecystectomies. Insufflation of the abdomen and manipulation of the bowel places these patients at increased aspiration risk. However, the use of a specialized supraglottic airway such as LMA ProSeal can mitigate these effects by allowing for placement of an orogastric tube for drainage of the stomach and a larger cuff size that reduces both the risk for gastric inflation and aspiration of refluxed gastric contents.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:775–776.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:20–22.

Kim ES, Bishop MJ. Endotracheal intubation, but not laryngeal mask airway insertion, produces reversible bronchoconstriction. *Anesthesiology*. 1999;90:391–394.

Maltby JR, Beriault MT, Watson NC, et al. The LMA-ProSeal is an effective alternative to tracheal intubation in laparoscopic cholecystectomy. *Can J Anaesth*. 2002;49:857–862.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57–i65.

C.3. Would you use propofol for induction of anesthesia?

Propofol may be the induction agent of choice for the hemodynamically stable patient with reactive airways. In comparison to induction with thiopental, thiamylal, or methohexital, 2.5 mg per kg propofol induction resulted in a significantly lower incidence of wheezing after tracheal intubation in asthmatic patients. The incidence of wheezing was 0%, 45%, and 26% in patients who received propofol, a thiobarbiturate, and oxybarbiturate, respectively. Another study in unselected patients found a significantly lower respiratory resistance after tracheal intubation following induction with propofol than with thiopental or etomidate. Nevertheless, propofol-induced bronchospasm has been reported in patients with allergic rhinitis and should be used with caution in patients with a high allergic component.

Eames WO, Rooke GA, Wu RS, et al. Comparison of the effects of etomidate, propofol, and thiopental on respiratory resistance after tracheal intubation. *Anesthesiology*. 1996;84:1307–1311.

Nishiyama T, Hanaoka K. Propofol-induced bronchoconstriction: two case reports. *Anesth Analg*. 2001;93:645–646.

Pizov R, Brown RH, Weiss YS, et al. Wheezing during induction of general anesthesia in patients with and without asthma. A randomized, blinded trial. *Anesthesiology*. 1995;82:1111–1116.

C.4. Would you use thiopental, methohexital, etomidate, or ketamine for induction?

Thiopental and thiamylal are thiobarbiturates that have been demonstrated to release histamine. Methohexital and pentobarbital are oxybarbiturates that have not been shown to release histamine. This suggests that the sulfur atom is important in barbiturate-induced histamine release. Moreover, thiobarbiturates, but not oxybarbiturates, have been shown to lead to a thromboxane-mediated tracheal constriction in guinea pigs. For these reasons, methohexital may be preferred as the

induction agent in patients with extreme sensitivity to histamine (asthmatics) or increased histamine releasability (atopics).

Because it provides only a light plane of anesthesia, airway instrumentation under thiopental anesthesia alone may trigger bronchospasm. However, it may be used cautiously in asthmatics provided that an adequate depth of anesthesia is achieved before airway stimulation.

Etomidate has not been shown to release histamine, does not depress myocardial function, and provides hemodynamic stability in critically ill patients. Both etomidate and thiopental afford no protection against wheezing after intubation and are therefore inferior to propofol in this regard.

Ketamine produces bronchodilation both through neural mechanisms and through release of catecholamines. In an actively wheezing patient, ketamine is the induction agent of choice, particularly with unstable hemodynamics.

Eames WO, Rooke GA, Wu RS, et al. Comparison of the effects of etomidate, propofol, and thiopental on respiratory resistance after tracheal intubation. *Anesthesiology*. 1996;84:1307–1311.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:21.

Pizov R, Brown RH, Weiss YS, et al. Wheezing during induction of general anesthesia in patients with and without asthma. A randomized, blinded trial. *Anesthesiology*. 1995;82:1111–1116.

C.5. Would you administer lidocaine for intubation?

The administration of intravenous lidocaine 1 to 1.5 mg per kg several minutes prior to intubation to prevent reflex-induced bronchospasm is a long-standing practice. However, some caution is required, as paradoxical bronchospasm has been demonstrated in patients with asthma. It appears that while intravenous lidocaine reduces airway responsiveness to drugs and stimuli that cause bronchospasm, lidocaine on its own does not reduce baseline airway tone, and may actually increase it.

Therefore, intravenous lidocaine should be administered with care in these patients.

Alternatively, topical endotracheal spray of lidocaine can be used. However, inhalation of lidocaine is itself irritating and can *provoke* bronchospasm in a patient with asthma. If lidocaine spray is used to tropicalize the airway, an adequate depth of anesthesia should be achieved before lidocaine is administered.

Burches BR Jr, Warner DO. Bronchospasm after intravenous lidocaine. *Anesth Analg*. 2008;107:1260–1262.

Chang HY, Togias A, Brown RH. The effects of systemic lidocaine on airway tone and pulmonary function in asthmatic subjects. *Anesth Analg*. 2007;104:1109–1115.

Maslow AD, Regan MM, Israel E, et al. Inhaled albuterol, but not intravenous lidocaine, protects against intubation-induced bronchoconstriction in asthma. *Anesthesiology*. 2000;93:1198–1204.

McAlpine LG, Thomson NC. Lidocaine-induced bronchoconstriction in asthmatic patients. Relation to histamine airway responsiveness and effect of preservative. *Chest*. 1989;96:1012–1015.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57–i65.

C.6. If this is an emergency surgery and rapid sequence induction is indicated, how would you induce anesthesia in this patient?

All the precautions to prevent aspiration of gastric contents and asthmatic attack must be considered simultaneously. Rapid sequence induction and tracheal intubation is necessary to prevent aspiration. However, light anesthesia may precipitate severe bronchospasm.

Prior to induction, inhalation of β_2-agonists such as albuterol should be administered. The patient should then be adequately denitrogenated with 100% oxygen administered by mask. Preoxygenation is particularly important because mask ventilation is usually not performed in rapid sequence induction.

Preoxygenation is administered for three minutes of normal V_T breathing, or for eight deep breaths over 1 minute.

Propofol is the induction agent of choice in a hemodynamically stable patient with asthma. Ketamine and etomidate are alternatives to propofol in a patient at risk of hemodynamic instability. It is important to note that in a patient with depleted sympathetic reserve, ketamine administration may result in hypotension.

Intravenous lidocaine is a useful adjunct drug to prevent reflex bronchospasm, particularly in emergency situations when deep anesthesia cannot be achieved before intubation (see section C.5).

Traditionally, opioids were not used as part of rapid sequence induction. However, opioids reduce cardiovascular effects associated with laryngoscopy and suppress cough reflex. They also reduce the dose of induction agent required to achieve adequate depth of anesthesia. Therefore, administration of opioids that do not release histamine, such as fentanyl and remifentanil, should be considered.

Muscle relaxant is administered after the induction agent to achieve optimal intubating conditions. Unless contraindicated, succinylcholine should be used because it provides excellent intubating conditions within 30 to 60 seconds of administration. Rocuronium 1.2 mg per kg is an alternative to succinylcholine but results in much longer neuromuscular block.

In a patient with asthma, efforts to achieve adequate depth of anesthesia necessary to minimize bronchospasm may result in hypotension. Therefore, medications to treat hypotension, such as phenylephrine, should be immediately available.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:21–22.

Tanoubi I, Drolet P, Donati F. Optimizing preoxygenation in adults. *Can J Anaesth*. 2009;56:449–466.

Tran DT, Newton EK, Mount VA, et al. Rocuronium versus succinylcholine for rapid sequence induction intubation. *Cochrane Database Syst Rev*. 2015;(10):CD002788.

Wallace C, McGuire B. Rapid sequence induction: its place in modern anaesthesia. *Contin Educ Anaesth Crit Care Pain*. 2014;14:130–135.

Weiskopf RB, Bogetz MS, Roizen MF, et al. Cardiovascular and metabolic sequelae of inducing anesthesia with ketamine or thiopental in hypovolemic swine. *Anesthesiology*. 1984;60:214–219.

C.7. Could a regional technique be used for this surgery? Discuss the advantages and disadvantages of neuraxial anesthesia in this patient for this surgery.

For laparoscopic surgery, regional anesthesia can be used. Typically, this is performed with epidural or combined spinal–epidural anesthesia, which allows for repeated dosing to obtain an adequate level and duration of anesthesia. Laparoscopic surgery requires a T4 to T5 dermatomal level. Even with adequate analgesia to this dermatome, patients will often complain of shoulder pain, which can be treated with intravenous narcotic administration. The advantages of regional anesthesia include the avoidance of instrumenting the airway, a decrease in the resultant risk of bronchospasm, and the ability to maintain the epidural postoperatively to reduce or even eliminate the need for postoperative narcotics.

However, the high level required for laparoscopic surgery has multiple effects on the respiratory system. First, patients with a high blockade lose sensory input from chest wall movement, and patients feel dyspneic, even in the presence of normal respiratory function. This feeling of dyspnea can be anxiety producing and in a patient with asthma can lead to bronchospasm.

More important, however, high levels of neuraxial anesthesia should be avoided in patients with severe respiratory disease who require accessory muscle contribution in order to maintain adequate ventilation. These patients will have reduced

expiratory flow and minute ventilation under high neuraxial blockade and can become hypoxic and hypercarbic.

Newer surgical techniques, including the natural orifice transluminal endoscopic surgery (NOTES), are being developed for minimally invasive cholecystectomy. These procedures may be done with a lower dermatomal level.

Donmez T, Erdem VM, Uzman S, et al. Laparoscopic cholecystectomy under spinal-epidural anesthesia vs. general anaesthesia: a prospective randomised study. *Ann Surg Treat Res*. 2017;92:136–142.

Vretzakis G, Bareka M, Aretha D, et al. Regional anesthesia for laparoscopic surgery: a narrative review. *J Anesth*. 2014;28:429–446.

C.8. Would you choose an inhalational or an intravenous technique for maintenance of anesthesia?

For maintenance of anesthesia, inhalation agents such as sevoflurane and isoflurane can be used. These agents are thought to be superior to desflurane because of its pungent odor that may cause airway irritation and trigger bronchospasm. At lower doses (<1.0 minimum alveolar concentration), the inhaled anesthetics inhibit chemically induced tracheal contractions in the order: *enflurane* ≥ *isoflurane* > *sevoflurane*. More recent clinical observations in humans indicate that sevoflurane at 1.1 minimum alveolar concentration may be the most effective agent, particularly in the presence of airway instrumentation. In addition, sevoflurane may have a more rapid onset of bronchodilation than isoflurane.

Desflurane has been shown to cause elevations in airway resistance and tissue mechanical parameters, with markedly enhanced airway narrowing in children with asthma or a recent URI. Therefore, desflurane should be avoided in children with susceptible airways.

Nitrous oxide can also be used, provided that the patient does not have pulmonary hypertension, a condition commonly

present in patients with COPD.

For scenarios that require avoidance of inhaled anesthetics, such as patients with history of malignant hyperthermia or cases that require monitoring of motor and somatosensory evoked potentials, intravenous anesthetics can be used for maintenance. Bronchodilating properties of propofol make it a choice intravenous anesthetic for patients with obstructive lung disease. Opioids without histamine-releasing effects and ketamine can be used as adjuncts to the intravenous technique.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:478–479, 490–491.

Rock GA, Choi JH, Bishop MJ. The effect of isoflurane, halothane, sevoflurane, and thiopental/nitrous oxide on respiratory system resistance after tracheal intubation. *Anesthesiology*. 1997;86:1294–1299.

von Ungern-Sternberg BS, Saudan S, Petak F, et al. Desflurane but not sevoflurane impairs airway and respiratory tissue mechanics in children with susceptible airways. *Anesthesiology*. 2008;108:216–224.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57–i65.

C.9. What mechanisms produce bronchodilation from volatile anesthetics?

The volatile anesthetics relax airway smooth muscle primarily by directly reducing smooth muscle contractility and indirectly by inhibiting the reflex neural pathways. Direct effects of the volatile anesthetics partially depend on intact bronchial epithelium, suggesting that epithelial damage or inflammation secondary to asthma or a respiratory infection may lessen their bronchodilating effect.

The mechanisms responsible for the direct relaxation effects involve decreases in intracellular calcium, an important regulator of smooth muscle reactivity. Several intracellular mediators responsible for mobilization of calcium ions are potential sites for the action of volatile anesthetics, but the

predominant mechanism appears to be inhibition of cell membrane–associated voltage-dependent calcium channels, an action that decreases entry of calcium ions into the cytosol. Volatile anesthetic–induced increases in cyclic 3′,5′ adenosine monophosphate (cAMP) cause decreases in free intracellular calcium by stimulating efflux of calcium and increasing uptake of calcium into the sarcoplasmic reticulum. This action contributes to airway smooth muscle relaxation. In addition, volatile anesthetics reduce calcium sensitivity as a result of inhibition of protein kinase C activity and inhibition of G protein function.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:478–479.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:543–546.

C.10. Which muscle relaxants would you use? Why?

Any muscle relaxants that do not release histamine, such as cisatracurium, vecuronium, rocuronium, and pancuronium may be used. Atracurium causes histamine release, especially in high doses, and should be avoided. Succinylcholine can cause slight histamine release, but there is no evidence that succinylcholine is associated with increased airway resistance in patients with asthma.

It may be advantageous to avoid the long-acting pancuronium and instead to use muscle relaxants of intermediate duration of action because the earlier recovery from neuromuscular blockade may allow avoidance of reversal with an anticholinesterase, which, theoretically, could precipitate bronchospasm due to stimulation of postganglionic cholinergic receptors in airway smooth muscle. However, avoidance of anticholinesterase antagonism requires monitoring with a quantitative peripheral nerve stimulator to ensure adequate

spontaneous recovery, defined as a train-of-four (TOF) ratio greater than 0.90. If anticholinesterase is used, adequate dosing of a concomitant anticholinergic is necessary. Alternatively, sugammadex may be used for reversal of rocuronium-induced neuromuscular blockade.

Basta SJ. Modulation of histamine release by neuromuscular blocking drugs. *Curr Opin Anaesthesiol*. 1992;5:572.

Brull SJ, Kopman AF. Current status of neuromuscular reversal and monitoring: challenges and opportunities. *Anesthesiology*. 2017;126:173–190.

Carron M, Zarantonello F, Tellaroli P, et al. Efficacy and safety of sugammadex compared to neostigmine for reversal of neuromuscular blockade: a meta-analysis of randomized controlled trials. *J Clin Anesth*. 2016;35:1–12.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:814–815.

C.11. How will you ventilate the patient? Will you use positive end-expiratory pressure (PEEP)? How can you detect the presence of auto-PEEP on your ventilator?

There are competing interests involved in managing the ventilation of this patient with COPD undergoing laparoscopic surgery. PIPs should be kept at a minimum, end-expiratory time needs to be adequate to overcome air trapping, and hypercarbia from insufflation with CO_2 must be compensated for.

A pressure control ventilation mode would be preferable to volume control because it results in lower PIPs at similar VTs. However, the laparoscopic technique leads to increasing airway resistance and increasing PIPs, so the VTs must be watched closely because they will decrease with insufflation of the abdomen and PIP set on the ventilator will need to be increased as the case proceeds.

High PIP should be avoided, especially in patients with emphysema and blebs, because a pneumothorax can result from

barotrauma. PIP should never be greater than 50 cm H_2O, and plateau pressures should be kept below 30 cm H_2O to minimize barotrauma.

The inspiratory-to-expiratory time ratio (I:E ratio) can be increased in order to reduce PIP. However, in this patient, the I:E ratio will likely need to be *reduced* in order to allow for complete expiration in the setting of expiratory obstruction and avoid air trapping. Allowing for an adequate expiratory time is a key component in the ventilatory management of patients with obstructive pulmonary disease.

Adequate minute ventilation will need to be maintained and should be increased, as the case proceeds and insufflated CO_2 is absorbed into the bloodstream and exhaled through the alveoli. Minute ventilation may need to increase as much as 60% in order to maintain normocarbia. Absorbed CO_2 can result in hypercapnia that lingers well into the postoperative period.

Achieving adequate minute ventilation with sufficient expiratory time and reasonable PIP can be a difficult task. In patients with severe pulmonary disease, it may be impossible. In this scenario, alternatives to traditional laparoscopy should be discussed with the surgeon. Gasless laparoscopic techniques that do not require insufflation of the abdomen are preferable, when feasible. These techniques utilize abdominal wall lifting to avoid necessitating a pneumoperitoneum.

The application of PEEP during positive pressure ventilation is a controversial issue. This type of PEEP is also referred to as extrinsic PEEP and must be differentiated from intrinsic or auto-PEEP. Intrinsic PEEP occurs in patients with COPD or asthma because outflow obstruction leads to air trapping. In ventilators equipped with an expiratory hold control, intrinsic PEEP can be measured during positive pressure ventilation. PEEP applied by the ventilator should be subtracted from the airway pressure

measured during the expiratory hold time in order to obtain intrinsic PEEP. When extrinsic PEEP is lower than intrinsic PEEP, it can improve ventilation, especially in the spontaneously ventilating patient. Extrinsic PEEP reduces the amount of negative pressure required to generate a breath and therefore reduces the work of breathing.

However, extrinsic PEEP that exceeds intrinsic PEEP can worsen air trapping and hyperinflation. Excessive PEEP also results in decreased venous return, decreased left ventricular compliance, and increased pulmonary capillary resistance. All of these changes lead to hypotension.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:379.

Reddy RM, Guntupalli KK. Review of ventilatory techniques to optimize mechanical ventilation in acute exacerbation of chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis*. 2007;2(4):441–452.

Slinger P. Don't make things worse with your ventilator settings: how you manage the lungs during the perioperative period affects postoperative outcomes. In: *IARS 2013 Review Course Lectures*. San Francisco, CA: International Anesthesia Research Society; 2013:38–46.

C.12. What is the differential diagnosis of intraoperative bronchospasm?

The causes of intraoperative wheezing and increased airway pressure include the following:

- Mechanical obstruction of endotracheal tube
  - Kinking
  - Secretions or blood
  - Overinflation of tracheal tube cuff
- Inadequate depth of anesthesia
  - Active expiratory efforts
- Pulmonary edema
- Pneumothorax (especially consider in a patient with emphysema and blebs)

- Aspiration pneumonitis
- Pulmonary embolism
- Endobronchial intubation
- Acute asthmatic attack
- Anaphylaxis

Anaphylaxis is a rare event but should be considered in all patients with intraoperative bronchospasm. The most common causes of intraoperative allergies include neuromuscular blocking drugs (NMBDs), latex, and antibiotics. Cardiovascular (hypotension) and cutaneous (flushing, urticaria) manifestations along with bronchospasm are the most common presenting signs of anaphylaxis during anesthesia. In the setting of bronchospasm with hypotension, even without cutaneous signs, anaphylaxis is high on the differential. Administration of likely inciting agents should cease; epinephrine 5 to 10 μg, diphenhydramine, and steroids should be given. An infusion of epinephrine may be necessary. A tryptase level should be sent to confirm the diagnosis, and the patient should be notified in writing of the potential reaction so that follow-up allergy testing can be obtained.

Hepner DL, Castells MC. Anaphylaxis during the perioperative period. *Anesth Analg*. 2003;97:1381–1395.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:22.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57–i65.

C.13. In the middle of surgery, peak inspiratory pressures (PIPs) suddenly increase. How do you manage this?

Elevation of PIPs is one of the signs of intraoperative bronchospasm. One of the most common causes of bronchospasm during surgery is inadequate depth of anesthesia. The patient with asthma has an extremely sensitive

tracheobronchial tree. When the level of anesthesia is too light, the patient may develop straining or coughing as a result of the foreign body (endotracheal tube) in the trachea and then bronchospasm. Therefore, during surgery, the initial treatment of bronchospasm is to increase F_{IO_2} and deepen anesthesia while investigating other potential causes of bronchospasm (see section C.12).

First, increase the F_{IO_2} and bag ventilate in order to manually assess pulmonary compliance. Check the anesthesia circuit and the endotracheal tube for kinking and any other visible obstruction. Auscultate the lungs to assess for wheezing. Bilaterally diminished or absent breath sounds can be an ominous sign suggesting critically low airflow, which can occur during severe bronchospasm or a mechanical obstruction of the tube. Unilaterally decreased breath sounds may indicate a main-stemmed endotracheal tube or, rarely, a pneumothorax. Once bronchospasm is confirmed, prior to deepening anesthesia, take a blood pressure. If normal or high, deepen anesthesia by increasing the concentration of inhalation agents, such as sevoflurane or isoflurane, which are direct bronchodilators, or administer an incremental dose of propofol. This has the advantage of deepening anesthesia without relying on alveolar ventilation (which is decreased during bronchospasm) for administration. Likewise, in a patient with a low to normal blood pressure, an incremental dose of ketamine both deepens anesthesia and bronchodilates.

Second, relieve mechanical stimulation. Pass a catheter through the endotracheal tube to suction secretions and determine whether there is an obstruction or kinking of the tube. Occasionally, the endotracheal tube slips down and stimulates the carina of the trachea, causing severe bronchospasm during light anesthesia. The cuff of the endotracheal tube can be deflated, the tube moved back 1 to 2 cm, and the cuff reinflated.

Surgical stimulation, such as traction on the mesentery, intestine, or stomach, should be stopped temporarily because it stimulates a vagal reflex and can cause bronchospasm.

Third, start medical intervention if the previously mentioned treatment does not break the bronchospasm or anesthesia cannot be deepened secondary to hypotension. The cornerstone of the treatment of intraoperative bronchospasm is inhalation of β_2-agonists such as albuterol, which induce further bronchodilation even in the presence of adequate inhalational anesthesia. Because of rain-out in the endotracheal tube, a large dose (8 to 10 puffs) should be given to achieve adequate therapeutic levels. If bronchospasm continues despite optimal bronchodilation therapy, high-dose intravenous corticosteroids are indicated (see sections B.16 and B.17). Epinephrine 5 to 10 μg can be given intravenously, but caution should be taken as it can exacerbate tachycardia and tachyarrhythmias. Alternatively, a continuous infusion of epinephrine 0.5 to 2 μg per minute in adults can provide maintenance bronchodilation with fewer adverse effects.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:22.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57–i65.

C.14. How would you give β_2-agonists? What is their mechanism of action on asthma?

Historically, it was fashionable to treat episodes of severe asthma with intravenous sympathomimetics such as isoproterenol. This approach no longer appears justifiable. Isoproterenol infusions can induce ventricular arrhythmias during halothane anesthesia and is clearly associated with myocardial damage. Even the intravenous administration of β_2-selective agents such as terbutaline and albuterol offers no advantage over the inhaled route.

β_2-Agonists such as albuterol, levalbuterol, and terbutaline may be administered through MDI adapters or small-volume jet nebulizers to the anesthetic circuit. Because MDI adapters are not very efficient in the intubated patient due to rain-out in the endotracheal tube, 8 to 10 puffs are needed to break acute bronchospasms.

Adrenergic stimulants produce bronchodilation through action on β-adrenergic receptors. β-Agonists increase intracellular cAMP by activating adenyl cyclase, which produces cAMP from adenosine triphosphate. Increased cAMP promotes bronchial relaxation and inhibits the release of mediators from mast cells (**Fig. 1.4**).

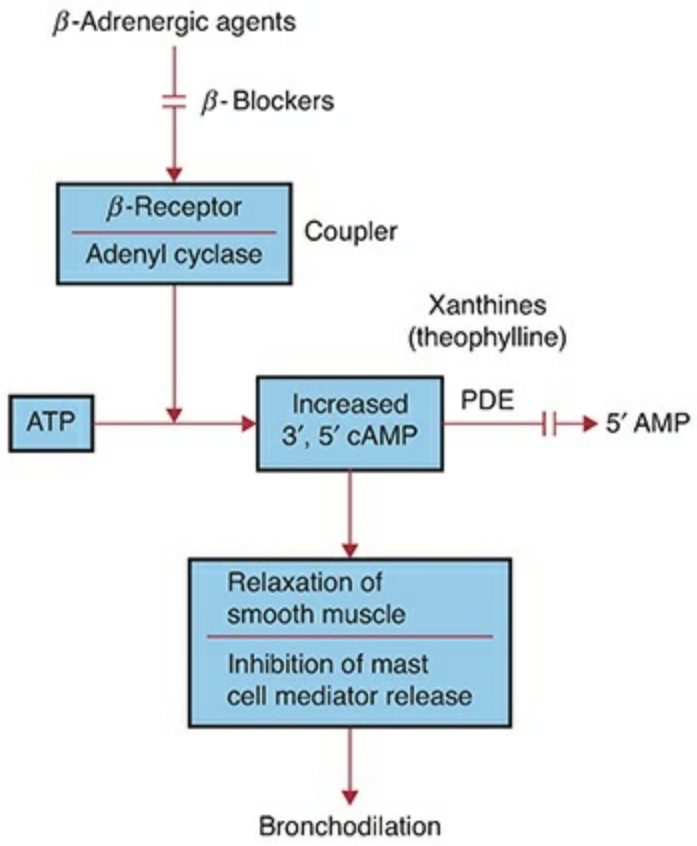

FIGURE 1.4. Cyclic adenosine monophosphate (cAMP) pathways involved in bronchodilator action. 3′,5′, cAMP, cyclic 3′,5′ adenosine monophosphate; AMP, adenosine monophosphate; ATP, adenosine triphosphate; PDE, phosphodiesterase. (*Reprinted with permission from Hirshman C. Airway reactivity in humans. Anesthetic implications.* Anesthesiology. *1983;58:170–177.)*

Fanta CH. Asthma. *N Engl J Med*. 2009;360:1002–1014.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:19–22.

Jameson JL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:1957–1969.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57–i65.

C.15. If the patient does not respond to the aforementioned treatment and becomes cyanotic, what would you do?

The ABG values should be determined immediately. In a severe, prolonged asthmatic attack, there will be combined respiratory and metabolic acidosis resulting from CO_2 retention and lactic acidosis from tissue hypoxia. Hypercarbia, hypoxemia, and acidemia promote arrhythmias and impair the response to bronchodilator therapy. Sodium bicarbonate ($NaHCO_3$) should be given to correct the acidosis because β-agonists are not effective in severe acidosis. At the same time, bronchodilator therapy should be continued or increased.

A patient with severe, refractory bronchospasm may require ventilation with a ventilator equipped to generate very high inspiratory pressures. An ICU ventilator can generate inspiratory pressures as high as 120 cm H_2O. Most anesthesia machines cannot deliver adequate alveolar ventilation because the circuit has too much compressible volume (tubing compliance) and the ventilator does not have sufficient driving power. The major disadvantage of an ICU ventilator is its inability to use inhalational anesthetics. Some newer anesthesia machines incorporate an ICU-type ventilator with vaporizers and oxygen mixers. They may be ideal for this situation.

Heliox is a helium/oxygen mixture that, secondary to its lower density to air, can permit higher flow rates at lower pressures, theoretically improving delivery of oxygen during bronchospasm. A major limitation is that heliox mixtures can

only provide 21% to 30% oxygen. Also, although heliox facilitates ventilation, it does not reverse the underlying bronchospasm. Reports on the perioperative use of heliox remain limited.

Finally, although not available at all centers, venovenous extracorporeal membrane oxygenation (VV-ECMO) may be established in order to adequately oxygenate the blood when all other measures have failed. ECMO is expensive, requires specially trained personnel, and is an invasive treatment modality associated with a number of potential complications. However, it is a potentially lifesaving measure that should be considered in select cases of severe, refractory hypoxemia secondary to respiratory disease.

Katz JA, Kallet RH, Alonso JA, et al. Improved flow and pressure capabilities of the Datex-Ohmeda SmartVent anesthesia ventilator. *J Clin Anesth*. 2000;12:40–47.

Lazarus SC. Clinical practice. Emergency treatment of asthma. *N Engl J Med*. 2010;363:755–764.

Liu LL, Aldrich JM, Shimabukuro DW, et al. Special article: rescue therapies for acute hypoxemic respiratory failure. *Anesth Analg*. 2010;111:693–702.

Marks JD, Schapera A, Kraemer RW, et al. Pressure and flow limitations of anesthesia ventilators. *Anesthesiology*. 1989;71:403–408.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57–i65.

C.16. The asthmatic attack was relieved with your treatment, and the surgery was completed. Following emergence, the patient was found to be hypoventilating. What are the common causes of hypoventilation? What will be your approach to treat hypoventilation?

The following are common causes of apnea or hypoventilation at the end of surgery:

- Respiratory center depression by inhalational anesthetics,

opioids, or mechanical hyperventilation (low P_{CO_2})

- Peripheral blockade by muscle relaxants
- Hypothermia

This list of the common causes of postoperative hypoventilation can be used to guide the systematic approach for the diagnosis and management. Measuring the temperature can easily diagnose hypothermia, and residual neuromuscular blockade can be assessed by a response to peripheral nerve stimulator. If hypothermia and residual neuromuscular blockade are ruled out, then hypoventilation is likely due to residual anesthetics and opioids. This can be managed by waiting longer or by pharmacologic reversal (if deemed appropriate) of opioid or benzodiazepine effect.

Management of residual neuromuscular blockade requires extra care in patients with reactive airway disease. In a patient with severe asthma, avoiding the use of an anticholinesterase, such as neostigmine, to reverse a nondepolarizing relaxant may be beneficial because neostigmine may trigger bronchospasm by cholinergic and prosecretory effects. However, any hypoventilating patient without adequate recovery (defined as TOF ratio greater than 0.90 when measured with a peripheral nerve stimulator) should be reversed.

If reversal is required, larger than customary doses of glycopyrrolate or atropine should be administered to minimize the possibility of bronchospasm. Although atropine or glycopyrrolate given simultaneously with neostigmine may prevent bronchospasm, the duration of action of neostigmine can outlast that of a vagolytic agent, especially in the presence of renal insufficiency, and lead to delayed bronchospasm. Intraoperatively, it is advisable to use inhalation agents to potentiate relaxants and to use smaller amounts of intermediate-acting relaxants for surgery. Alternatively, sugammadex may be safely used for reversal of rocuronium-induced neuromuscular

blockade (see section C.10).

Finally, if the patient does not appear to have any of the aforementioned causes of hypoventilation but is still inadequately ventilating, extubation should be delayed.

Brull SJ, Kopman AF. Current status of neuromuscular reversal and monitoring: challenges and opportunities. *Anesthesiology*. 2017;126:173–190.

Carron M, Zarantonello F, Tellaroli P, et al. Efficacy and safety of sugammadex compared to neostigmine for reversal of neuromuscular blockade: a meta-analysis of randomized controlled trials. *J Clin Anesth*. 2016;35:1–12.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2592–2593.

Hazizaj A, Hatija A. Bronchospasm caused by neostigmine. *Eur J Anaesthesiol*. 2006;23:85–86.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57–i65.

C.17. Would you consider a deep extubation in this patient?

To avoid bronchospasm triggered by coughing and straining caused by laryngeal and pharyngeal reflexes during emergence and extubation, patients may be extubated at surgical (deep) levels of anesthesia. However, the risks of aspiration, airway obstruction, and hypoventilation should be weighed against the benefits. With a history of severe COPD, chronic hypoxemia, and CO_2 retention, the patient is not a good candidate for extubation while deeply anesthetized. A systematic approach for emergence and extubation is illustrated in **Figure 1.5**. However, the guidelines do not include all possible patient-surgical-anesthetic conditions. Certainly, the practitioner's clinical judgment is of utmost importance regarding the decision to extubate.

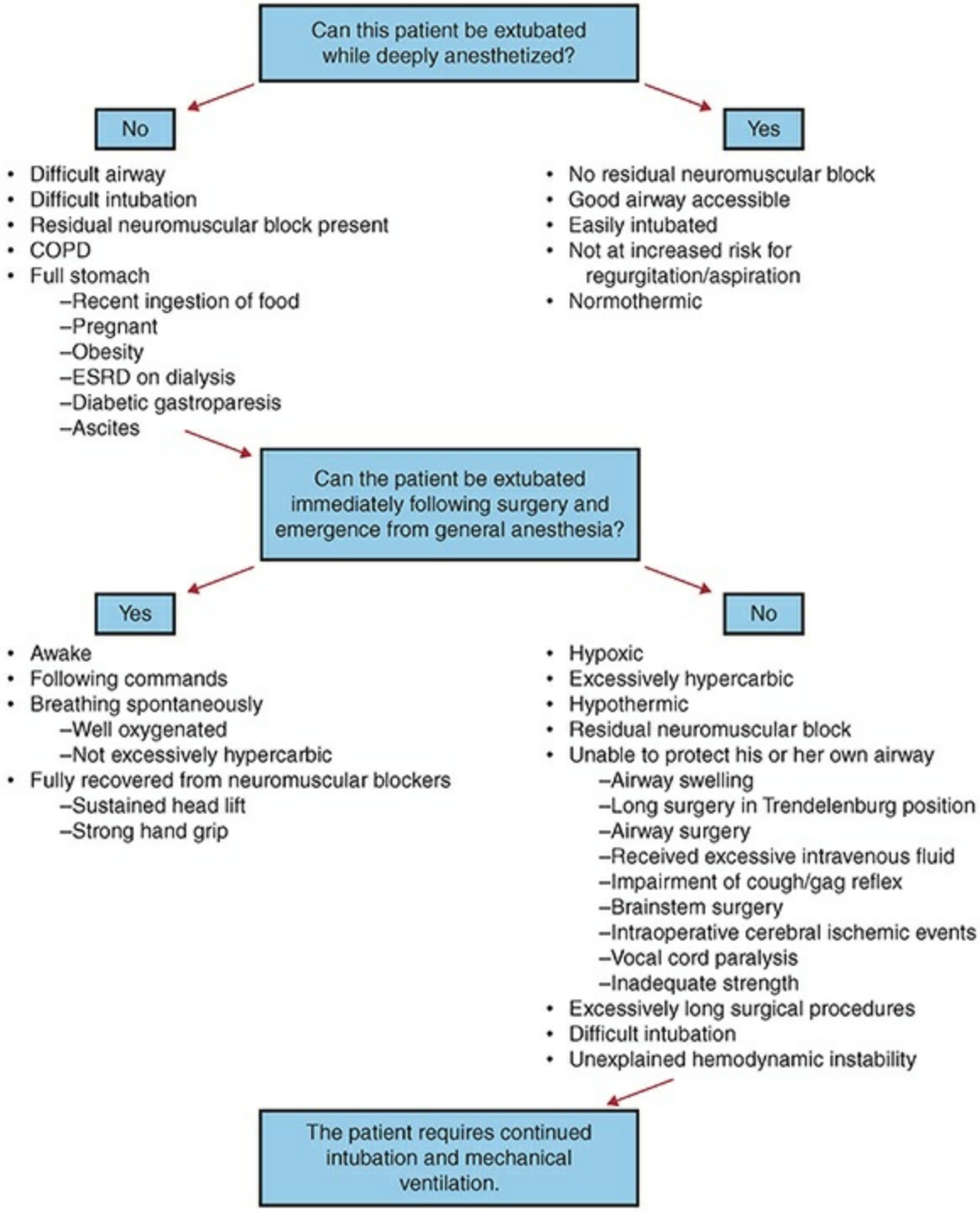

FIGURE 1.5. A systematic approach to emergence and extubation. COPD, chronic obstructive pulmonary disease; ESRD, end-stage renal disease.

Lien CA, Koff H, Malhotra V, et al. Emergence and extubation: a systemic approach. *Anesth Analg*. 1997;85:1177.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57–i65.

C.18. If the patient cannot be extubated, what measures can you take to reduce the likelihood of bronchospasm with an endotracheal tube in place?

Loading doses of lidocaine, followed by continuous infusion, as described in section C.5, may be administered intravenously to prevent bronchoconstriction induced by stimulation of the trachea by the endotracheal tube. β_2-Agonists such as albuterol may be administered through MDI adapter to prevent bronchospasm. Dexmedetomidine, which has a favorable profile, including anxiolysis, sympatholysis, and drying of secretions without respiratory depression, can be used to sedate an agitated patient with asthma who does not meet extubation criteria. Alternatively, if there are no contraindications, a supraglottic airway may be used to replace the endotracheal tube for control of ventilation and to avoid tracheal stimulation.

Groeben H, Mitzner W, Brown RH. Effects of the alpha2-adrenoceptor agonist dexmedetomidine on bronchoconstriction in dogs. *Anesthesiology*. 2004;100:359–363.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:21–22.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57–i65.

D. Postoperative Management

D.1. In patients with asthma and COPD, are there special considerations for the use of opioids and nonsteroidal anti-inflammatory drugs (NSAIDs) for postoperative pain control?

Morphine is avoided because of possible histamine release and increased central vagal tone, which may cause bronchospasm. Meperidine causes histamine release more frequently than do

most other opioids and should be avoided as well. Fentanyl, on the other hand, is an appropriate choice for patients with asthma or other bronchospastic diseases because of its antimuscarinic, antihistaminergic, and antiserotoninergic actions. Effective analgesia is especially important in patients with respiratory disease because poor pain control may compromise respiration further due to splinting of the thoracic cage and decreased ability to cough. However, narcotics should be titrated very carefully to avoid dose-dependent respiratory depression.

An estimated 4% to 11% of asthmatics have a sensitivity toward NSAIDs, known as aspirin-sensitive respiratory disease (ASRD). NSAIDs block the cyclooxygenase-mediated conversion of arachidonic acid to prostaglandins, thereby shunting arachidonic acid toward the formation of bronchoconstricting leukotrienes. Patients with ASRD are more likely to have an irreversible component to their obstructive airway disease, more likely to have frequent exacerbations, and more likely to have had a history of severe attacks and oral steroid use. Persistent rhinorrhea, nasal polyps, and nasal congestion are common symptoms. Most patients with ASRD are unaware of the diagnosis. If a focused preoperative history reveals any of the aforementioned symptoms, NSAIDs should be avoided.

Farooque SP, Lee TH. Aspirin-sensitive respiratory disease. *Annu Rev Physiol*. 2009;71:465–487.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2553–2556, 2614–2638.

Jameson JL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:1957–1969.

D.2. Would you consider using a regional technique for analgesia?

Were this surgery to be accomplished laparoscopically, a

regional technique for analgesia is typically not necessary. However, in a patient with severe respiratory disease, the complete avoidance of systemic narcotics may be desired in order to reduce the risk of PPCs. In this case, epidural analgesia is preferred. The epidural may be placed before surgery and may be used as an adjunct or alternative to general anesthesia (see section C.7). The complete analgesia that can be obtained with epidural anesthesia allows for patients to avoid "splinting" secondary to abdominal pain and improves postoperative respiratory recovery.

Contraindications to epidural anesthesia include patient refusal and anticoagulation. In patients unable to receive neuraxial anesthesia, an alternative is the transversus abdominis plane (TAP) block. A study of 43 patients undergoing laparoscopic cholecystectomy showed decreased postoperative opiate use and mean discharge time from PACU in patients receiving a TAP block as compared to those with conventional port site infiltration. A TAP block consists of two to four injections of local anesthetic (typically bupivacaine, ropivacaine, or liposomal bupivacaine) providing 12 to 36 hours of pain relief. Unlike an epidural, once the block is performed and following a period of adequate postblock monitoring, no special equipment is necessary and patients can be discharged home. However, a TAP block only covers surgical incision pain and does not affect internal surgical pain. Therefore, a multimodal pain regimen will still be required.

Tolchard S, Davies R, Martindale S. Efficacy of the subcostal transversus abdominis plane block in laparoscopic cholecystectomy: comparison with conventional port-site infiltration. *J Anaesthesiol Clin Pharmacol*. 2012;28(3):339–343.

Vretzakis G, Bareka M, Aretha D, et al. Regional anesthesia for laparoscopic surgery: a narrative review. *J Anesth*. 2014;28:429–446.

D.3. The patient was breathing well and was extubated.

Would you place this patient on supplemental oxygen in the recovery room? How much?

Administration of oxygen to patients with severe COPD can lead to hypercapnia. This was traditionally attributed to the impairment of hypoxic respiratory drive and subsequent hypoventilation. Although there is a transient reduction in minute ventilation when high-flow oxygen is administered to patients with COPD, this does not appear to play a major role in oxygen-induced hypercapnia.

The primary mechanism responsible for hypercapnia with oxygen administration in patients with COPD appears to be ventilation/perfusion mismatch. Under normal conditions, hypoxic pulmonary vasoconstriction helps minimize ventilation/perfusion mismatch. Oxygen therapy may abolish hypoxic pulmonary vasoconstriction in poorly ventilated areas, increasing blood flow to these areas, and decreasing blood flow to other lung regions with normal or high ventilation:perfusion ratios. These areas will then contribute further to alveolar dead space causing an increase in P_{CO_2}.

Although uncontrolled oxygen therapy in patients with COPD is potentially harmful, hypoxemic patients should receive oxygen. A carefully titrated oxygen therapy to achieve saturations of 88% to 92% is recommended.

Abdo WF, Heunks LM. Oxygen-induced hypercapnia in COPD: myths and facts. *Crit Care*. 2012;16:323.

Decalmer S, O'Driscoll BR. Oxygen: friend or for in peri-operative care? *Anaesthesia*. 2013;68:8–12.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:399–400.

D.4. The patient is hypoventilating in postanesthesia care unit (PACU). Would you initiate noninvasive ventilation (NIV)?

NIV refers to delivery of ventilatory support via the patient's upper airway using a mask or a similar device. NIV respiratory support ranges from continuous positive airway pressure (CPAP) to bilevel positive airway pressure (BIPAP). NIV has been shown to be safe and effective in patients with COPD and should be readily available in PACU to treat postoperative respiratory distress. Judicious use of NIV may reduce reintubation rates after surgery.

Glossop AJ, Shephard N, Bryden DC, et al. Non-invasive ventilation for weaning, avoiding reintubation after extubation and in the postoperative period: a meta-analysis. *Br J Anaesth*. 2012;109:305–314.

Jaber S, Chanques G, Jung B. Postoperative noninvasive ventilation. *Anesthesiology*. 2010;112:453–461.

2 Bronchoscopy, Mediastinoscopy, and Thoracoscopy

Alessia Pedoto, Paul M. Heerdt, and Fun-Sun F. Yao

A 60-year-old man has suffered from cough, intermittent hemoptysis, and weight loss for 2 months. He has smoked one pack of cigarettes per day for 40 years. A chest radiograph 1 month ago revealed a right middle lobe infiltrate that was treated with antibiotics without clinical improvement. Subsequent evaluation revealed a mass. He is now scheduled for fiberoptic bronchoscopy, possible mediastinoscopy, and possible video-assisted thoracoscopic (VATS) lobectomy.

A. Medical Disease and Differential Diagnosis

1. How is the diagnosis of lung cancer made? What is your prediction for the most likely type of malignancy?
2. What are the less common manifestations of bronchogenic carcinoma?
3. The patient has a long history of cigarette smoking. What is the significance of this finding?

B. Preoperative Evaluation and Preparation

1. How would you evaluate the patient prior to surgery?

2. What are the pulmonary function guidelines that indicate an increased risk for morbidity and mortality?
3. What are the preoperative concerns of induction immunotherapy?

C. Intraoperative Management

1. How would you premedicate, monitor, and anesthetize this patient?
2. How many types of bronchoscopes are available and what are the intraoperative considerations of each one?
3. What are the indications for cervical mediastinoscopy? Are there potential complications?
4. The decision was made to proceed with a robotic right middle lobectomy. How would this alter your management?
5. What are the indications for single-lung ventilation and how can it be accomplished?
6. What are the contraindications to the use of double-lumen endotracheal tubes (DLTs)?
7. Would you use a right- or left-sided DLT?
8. How do you know that the tube is in the correct position?
9. How many types of bronchial blockers are available? What are the advantages and disadvantages of bronchial blockers?
10. How will systemic oxygenation be monitored during single-lung ventilation? What is the mechanism of pulse oximetry?
11. The patient was placed in the lateral decubitus position. Describe the effects of lateral positioning on pulmonary blood flow and respiration.
12. What is hypoxic pulmonary vasoconstriction (HPV)?
13. What are the effects of anesthetic agents on HPV and their clinical implications?
14. Discuss pulmonary blood flow distribution, shunt flow, and partial pressure of oxygen in the arterial blood (Pa_{O_2}) (fractional inspired O_2 concentration [F_{IO_2}] = 1.0) during

single-lung ventilation in the lateral position.

15. How could you improve oxygenation during single-lung ventilation?
16. A right middle lobectomy was performed. Would you extubate the trachea at the end of the procedure?

D. Postoperative Management

1. What are the immediate life-threatening complications that follow lobectomy or pneumonectomy?
2. Why is it important to control postoperative pain? How would you achieve this goal?

A. Medical Disease and Differential Diagnosis

A.1. How is the diagnosis of lung cancer made? What is your prediction for the most likely type of malignancy?

The initial presenting symptoms in patients with lung cancer are constitutional and nonspecific, mainly related to metastatic disease. Nonproductive cough, dyspnea, hemoptysis, and chest pain, along with an unresolved lung infiltrate on chest radiography, should suggest carcinoma. In the attempt to make an early diagnosis, the American Cancer Society has issued preliminary guidelines for screening high-risk patients using low-dose computed tomography (LDCT) imaging. Recommended candidates include subjects aged between 55 and 77 years with a smoking history of at least 30 packs per year, who are current smokers or quit within the past 15 years. The main limitation of this test is the 23.3% incidence of false-positive results, which may lead to further testing including surgical biopsy. Biomarkers from large airway epithelial cells or buccal mucosal biopsies are being investigated and may represent early diagnostic options in the future. Currently, the

initial diagnosis and staging are done in the operating room and include flexible bronchoscopy with airway washings and brush biopsy, possibly followed by ultrasound-guided transbronchial biopsy (endobronchial ultrasound [EBUS]) for mediastinal lymph node biopsy. Additional areas for biopsy include palpable lymph nodes in the neck or axilla, needle aspiration biopsy, cervical mediastinoscopy, and possibly exploratory thoracoscopy or thoracotomy. An extensive evaluation must be performed to exclude metastases that would contraindicate major surgery.

Cancers of the lung account for 12% of all malignancies and nearly 18% of cancer-related deaths worldwide. Bronchogenic carcinomas are the most common tumors requiring surgical resection and can be classified into four major types: small cell, large cell, squamous cell, and adenocarcinoma. For surgical purposes, lung tumors are classified as non–small cell or small cell. The former is amenable to surgical resection, whereas the latter tends to be nonresectable and is medically treated.

Further subclassification of lung tumors involves the TNM classification in which *T* designates tumor site, size, and local extent; *N* the presence and location of regional lymph node involvement; and *M* the presence of distal metastases beyond the ipsilateral hemithorax. This system is used for staging bronchogenic carcinomas and helps predict the response to therapy. In general, small cell carcinomas that have spread beyond possible resection by the time of presentation are primarily managed with chemotherapy, with or without radiation, and are associated with a 5-year survival of approximately 20%. In contrast, non–small cell cancers found to be localized at the time of presentation should be considered for primary resection. The 5-year survival can be as high as 85% for small tumors without regional lymph node involvement or metastases (stage I). Approximately 45% of patients present

with circumscribed extrapulmonary disease or lymphatic spread to the ipsilateral mediastinal or subcarinal lymph nodes (stage IIIa). Their 5-year postresection survival is less than 20%.

Ettinger DS, Wood DE, Aisner DL, et al. Non–small cell lung cancer, version 5.2017, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2017;15:504–535.

Hirsch FR, Scagliotti GV, Mulshine JL, et al. Lung cancer: current therapies and new targeted treatments. *Lancet*. 2017;389(10066):299–311.

Kritek PA, Levy BD. Approach to the patient with disease of the respiratory system. In: Jameson JL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:278.

Masters GA, Johnson DH, Temin S. Systemic therapy for stage IV non-small-cell lung cancer: American Society of Clinical Oncology clinical practice guideline update. *J Oncol Pract*. 2016;12(1):90–94.

Smith RA, Andrews KS, Brooks D, et al. Cancer screening in the United States, 2018: a review of current American Cancer Society guidelines and current issues in cancer screening. *CA Cancer J Clin*. 2018;68:297–316. doi:10.3322/caac.21446.

Vachani A, Sequist LV, Spira A. AJRCCM: 100-year anniversary. The shifting landscape for lung cancer: past, present, and future. *Am J Respir Crit Care Med*. 2017;195(9):1150–1160.

A.2. What are the less common manifestations of bronchogenic carcinoma?

Other manifestations of lung tumors are primarily related to mass effects or altered metabolism. In addition to bronchial obstruction (evident in this patient) occasionally leading to postobstructive pneumonia, mass effects include invasion into the chest wall and pleura, compression of great vessels (e.g., superior vena cava syndrome) and heart, tracheobronchial displacement, and/or paresis of the recurrent laryngeal or phrenic nerves and the sympathetic chain. *Pancoast syndrome* can present with pain and upper extremity weakness secondary to invasion of the brachial plexus as well as the first and second thoracic and eighth cervical nerve roots. Recognized *metabolic manifestations* of small cell lung tumors include symptoms

resembling those of Cushing syndrome (from ectopic adrenocorticotropic hormone production), carcinoid syndrome, hypercalcemia and hypophosphatemia (resulting from ectopic parathyroid hormone or parathyroid hormone–related peptides), hypokalemia (caused by ectopic adrenocorticotropic hormone secretion), and hyponatremia (from inappropriate secretion of antidiuretic hormone and possibly atrial natriuretic factor). *Neurologic paraneoplastic syndromes* include Eaton-Lambert myasthenic syndrome, peripheral motor and sensory neuritis, cerebellar degeneration, retinopathy, limbic encephalopathy, and autonomic neuropathy. An autoimmune process has been suggested for these findings, and it seems to be more common in patients with limited disease.

Extrathoracic spread of the tumor can affect the bones, liver, adrenal glands, intra-abdominal and subcutaneous lymph nodes, brain, and spinal cord, contributing to the nonspecific presentation of the cancer.

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Kritek PA, Levy BD. Approach to the patient with disease of the respiratory system. In: Jameson JL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:278.

A.3. The patient has a long history of cigarette smoking. What is the significance of this finding?

Cigarette smoking remains the leading cause of lung cancer in the United States. Tobacco exposure is linked to chronic obstructive pulmonary disease (COPD), which includes chronic bronchitis and emphysema, and is strongly associated with an increased incidence of stroke, myocardial infarction, and cancer (lung, oral cavity, larynx, and esophagus). Pulmonary hypertension from chronic hypoxemia and subsequent cor pulmonale may also occur.

Eight percent to 17% of patients with lung cancer who are scheduled for surgical resection are still smoking at the time of surgery. Current tobacco use increases the risk of postoperative respiratory failure, pneumonia, aspiration, air leak, and atelectasis as well as 1-year mortality. Preoperative smoking cessation is strongly recommended, but it is unclear how long is needed before surgery to see a significant reduction in postoperative complications. Carboxyhemoglobin concentrations decline substantially within 12 hours of smoking cessation. Four weeks of abstinence decrease the incidence of postoperative respiratory complications, probably because of an improved mucociliary function. However, because continuous local tumor growth and metastatic spread may preclude resectability, a prolonged period of preoperative abstinence may not be practical. Nonetheless, smoking cessation at any time prior to surgery is still strongly recommended. A combined approach including counseling and polypharmacology has been shown to increase the success rate and decrease relapses after hospital discharge.

Lugg ST, Tikka T, Agostini PJ, et al. Smoking and timing of cessation on postoperative pulmonary complications after curative-intent lung cancer surgery. *J Cardiothorac Surg*. 2017;12:52.

Turan A, Koyuncu O, Egan C, et al. Effect of various durations of smoking cessation on postoperative outcomes: a retrospective cohort analysis. *Eur J Anaesthesiol*. 2018;35:256–265.

B. Preoperative Evaluation and Preparation

B.1. How would you evaluate the patient prior to surgery?

The main goal of preoperative evaluation is to identify in advance those at risk for major postoperative complications and optimize their functional status. The first step should include a complete history, physical examination, and laboratory tests

(e.g., complete blood count, basic metabolic profile, coagulation study, electrocardiogram, chest radiography, and computed tomographic imaging). A positive smoking history, especially if current, and in the presence of cough, sputum production, orthopnea, and dyspnea, requires further investigation. An abnormal exercise tolerance, such as the inability to climb at least three flights of stairs or walk for 6 minutes, may indicate a compromised cardiorespiratory function and the inability to tolerate the stress of anesthesia and surgery. In this subgroup of patients, further cardiopulmonary function testing may be indicated to define cardiac disease or customize a prehabilitation program. A brief review of symptoms, physical limitations, interval changes, and airway anatomy is usually performed before entering the operating room.

In addition to routine preoperative testing, patients scheduled for lung resection usually undergo pulmonary function testing to help define the relative risks of the planned resection. *Respiratory function* can be assessed by the following:

- **Respiratory mechanics** is evaluated via forced vital capacity (FVC), forced expiratory volume in the first second (FEV_1), and the ratio between residual volume and total lung capacity (RV/TLC). Flow–volume loops may be helpful to document the location of the obstruction (small vs. large airway) and its severity. Post-bronchodilator FEV_1 and FEV_1/FVC paired with clinical symptoms are used to determine the severity of COPD.
- **Cardiopulmonary reserve** evaluation includes maximal oxygen uptake ($\dot{V}O_{2max}$), stair climbing, 6-minute walk, and shuttle walk. In case of poor performance in these tests, cardiopulmonary exercise tolerance testing (CPET) can be added to identify patients who are not surgical candidates. $\dot{V}O_{2max}$ is the gold standard for aerobic capacity and

cardiorespiratory fitness. Patients with $\dot{V}O_{2max}$ value less than 10 mL/kg/min are at increased risk for postoperative morbidity and mortality.

- **Lung parenchymal function** include diffusing lung capacity for carbon monoxide (DLCO), Pa_{O_2}, and partial pressure of arterial carbon dioxide (Pa_{CO_2}). Predicted postoperative DLCO and FEV_1 less than 40% to 44% are significant independent predictors for increased postoperative morbidity and mortality.

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Carli F, Silver JK, Feldman LS, et al. Surgical prehabilitation in patients with cancer. *Phys Med Rehabil Clin N Am*. 2017;28:49–64.

Hata A, Sekine Y, Koh E, et al. Preoperative exercise testing is a better predictor of postoperative complications than pulmonary function testing for patients with lung cancer. *Open J Thorac Surg*. 2015;5:15–20.

Licker M, Triponez F, Diaper J, et al. Preoperative evaluation of lung cancer patients. *Curr Anesthesiol Rep*. 2014;4:124–134.

Ravenel JG, ed. *Lung Cancer Imaging: Contemporary Medical Imaging*. New York: Springer Science; 2013:69–78.

Spyratos D, Zarogoulidis P, Porpodis K, et al. Preoperative evaluation for lung cancer resection. *J Thor Dis*. 2014;6(2):S162.

B.2. What are the pulmonary function guidelines that indicate an increased risk for morbidity and mortality?

The reported mortality from lung resection is between 2% and 4%, mainly as a result of pneumonia, respiratory failure, bronchopleural fistula, empyema, and pulmonary embolism. Respiratory insufficiency occurs in approximately 5% of patients following lung resection and is associated with a 50% mortality rate. Advanced age and the associated increased

incidence of concomitant nonpulmonary disease seem to contribute to this outcome. An increased risk of postoperative complications can be predicted by the following:

- **Spirometry:** Spirometric parameters, such as FEV_1/FVC ratio and FEV_1 (reflective of the degree of airway obstruction), as well as static volumes (such as inspiratory and TLC), are used to define the severity of COPD. Several studies have indicated a strong correlation between predicted postoperative FEV_1 and DLCO and a respective increase in morbidity and mortality, especially for open procedures and extensive dissection. Concerning values are summarized in **Table 2.1**.

TABLE 2.1 Minimal Pulmonary Function Test Criteria for Various-Sized Pulmonary Resections

Test	Unit	Normal	Pneumonectomy	Lobectomy	Biopsy or Segmental
MBC	Liters per minute	>100	>50	>40	>25
MBC	Percentage predicted	100%	>50%	>40%	>25%
FEV_1	Liters	>4	>2.1–1.7	>1.2–1.0	>0.6–0.9
FEV_1	Percentage	>80% FVC	>50% FVC	>40% FVC	>40% FVC
$FEV_{25\%–75\%}$	Liters	>2	>1.6	>0.6–1.6	>0.6

FEV_1, forced expiratory volume in first second; $FEV_{25\%–75\%}$, forced expiratory volume from 25% to 75% of forced vital capacity; FVC, forced vital capacity; MBC, maximum breathing capacity.

- **Arterial blood gases:** Historically, hypercapnia ($PaCO_2$ greater than 45 mmHg) was considered an exclusion criterion for lung resection. However, no independent correlation has been found with an increased mortality. Patients who are hypercapnic often have a low predicted postoperative FEV_1 and an abnormal exercise capacity, which may preclude

surgery. Preoperative hypoxemia (Pa_{O_2} less than 50 mmHg and percentage of available hemoglobin saturated with oxygen [Sa_{O_2}] less than 90%) has been associated with an increased risk of postoperative complications. However, baseline hypoxemia can be the result of ventilatory mismatch caused by obstructive tumors that once resected may theoretically improve gas exchange.

Other factors influencing outcome include patient comorbidities and functional status, the extent and location of the proposed surgical resection, and whether the patient has undergone preoperative induction chemotherapy. Improvements in both surgical and anesthesia techniques have broadened the criteria for surgical respectability. As evident from lung volume reduction studies, patients with severely impaired pulmonary function (e.g., FEV_1 less than 1 L) can still undergo surgical resection with general anesthesia without prohibitive risk for postoperative complications. Moreover, the development of minimally invasive surgical techniques has raised the question of whether standard selection criteria should always be adopted.

Although preoperative pulmonary function tests are valid indices of physiologic performance, the actual predictive utility of a range of values for a single parameter is poorly defined. Overall, emphasis has been directed toward integrating multiple aspects of the preoperative evaluation (e.g., spirometry, ventilation-perfusion scanning, extent of planned resection, patient functional status) into the estimate of postoperative function. “Enhanced Recovery After Surgery” (ERAS) protocols have contributed to improve outcomes. Multimodal analgesia, early ambulation, and thromboprophylaxis are among the recommendation for the perioperative period that have affected outcome after major lung resection in patients at high risk.

Batchelor TJP, Rasburn NJ, Abdelnour-Bertchtold E, et al. Guidelines for

enhanced recovery after lung surgery: recommendations of the Enhanced Recovery after Surgery (ERAS®) Society and the European Society of Thoracic Surgeons (ESTS). *Eur J Cardiothoracic Surg*. 2019;1(55):91–115.

Fernandez FG, Kosinski AS, Furnary AP, et al. Differential effects of operative complications on survival after surgery for primary lung cancer. *J Thorac Cardiovasc Surg*. 2018;155:1254–1264.

Gao SJ, Corso CD, Wang EH, et al. Timing of surgery after neoadjuvant chemoradiation in locally advanced non–small cell lung cancer. *J Thorac Oncol*. 2017;12(2):314–322.

B.3. What are the preoperative concerns of induction immunotherapy?

Chemotherapy and high-dose stereotactic radiation have been used in the preoperative period after diagnosis and staging of lung cancer with an increase in survival when started in the early stages (IB-IIIA). In the past decade, the approach to chemotherapy has changed with an increased use of immunomodulators that affect the autoimmune response in favor of the organism. Lung cancer cells abound of programed death (PD)-1 and programmed death-ligand 1 (PD-L1) receptors, which upon activation, decrease the function of the killer T cells. Drugs that inhibit these receptors (also known as check point inhibitors, such as pembrolizumab, nivolumab, cemiplimab, atezolizumab, avelumab, and durvalumab) can increase the T-cell immune response toward cancer cells. This treatment modality has shown a very good oncologic response and outcome. However, a new toxic profile has emerged secondary to the overwhelming inflammation and autoimmune process, ranging from mild reaction to life-threatening conditions. Concerning **side effects** include skin reactions (diffuse rash), enteritis and diarrhea, hypothyroidism, hypophysitis, and adrenal insufficiency as well as hepatic insufficiency. *Endocrine and hepatic* side effects may be so severe to warrant delaying surgery to allow optimization. *Grade 3 to 4 toxicity* usually requires prednisone 1 to 2 mg/kg/day, gradually tapered to

symptoms improvement and discontinuation of the immunotherapy. Anti-tumor necrosis factor-α (TNF-α) inhibitors are added in case of suboptimal response to steroids. *Interstitial pneumonitis* has been reported in patients receiving phosphoinositol 3-kinase inhibitors. When severe, it warrants intensive care unit admission and high-dose corticosteroids (1 to 2 mg/kg/day) with further immunosuppression in refractory cases. *Cytokine release syndrome* (CRS) can present with encephalopathy, mental status changes, and cerebellar disease. In this subpopulation, surgery should be delayed. CRS is a major concern in recipients of chimeric antigen receptor–modified T-cell lymphocytes and checkpoint inhibitors. Altered cerebellar function, mental status, and seizures have been described after its use.

Hirsch FR, Scagliotti GV, Mulshine JL, et al. Lung cancer: current therapies and new targeted treatments. *Lancet*. 2017;389(10066):299–311.

Kroschinsky F, Stölzl F, von Bonin S, et al; and Intensive Care in Hematological and Oncological Patients Collaborative Group. New drugs, new toxicities: severe side effects of modern targeted and immunotherapy of cancer and their management. *Crit Care*. 2017;21(1):89.

Vachani A, Sequist LV, Spira A. AJRCCM: 100-year anniversary. The shifting landscape for lung cancer: past, present, and future. *Am J Respir Crit Care Med*. 2017;195(9):1150–1160.

C. Intraoperative Management

C.1. How would you premedicate, monitor, and anesthetize this patient?

Patients usually arrive at the hospital on the day of surgery, making traditional oral or parenteral premedication before transport to the operating room largely obsolete. Bronchoscopy and mediastinoscopy are generally ambulatory procedures, necessitating a relatively rapid hospital discharge.

EBUS-guided lymph node biopsy has become more popular

in the past decade as a minimally invasive, highly accurate alternative to cervical mediastinoscopy for staging of lung cancer. It is usually performed either under sedation or general anesthesia. When combined with esophageal ultrasound-guided biopsies, it allows staging of the entire mediastinal lymphatic chain (from station 1 through 11, including 8 and 9, accessible via esophageal approach). On-site cytologic exam is usually performed during the procedure. Mediastinal, hilar, lobar, and interlobar lymph nodes are accessible with this technique with a complication rate of 1.4%. Coughing (if the airway is not adequately topicalized) and bronchospasm are common perioperative complications. The incidence of pneumothorax is rare and depends on the location of the lymph node to biopsy or the presence of bullous disease rather than the type of anesthesia and the ventilation modality. Bleeding is also a rare instance, therefore not requiring aggressive reversal of preoperative anticoagulation as generally required for a mediastinoscopy.

Cervical mediastinoscopy is now reserved for small lymph nodes not readily accessible via EBUS or in the presence of inconclusive results. During mediastinoscopy, intermittent compression or occlusion of the innominate artery can occur. Therefore, the blood pressure cuff should be placed on the left arm and the pulse oximeter on the right hand. In the case of innominate artery compression, a dampening of the pulse oximetry trace will be evident, whereas blood pressure measurements will remain accurate. Although rare, injury to vascular structures (such as the azygos veins and innominate artery) can occur, potentially necessitating a median sternotomy. Patient positioning and placement of electrocardiography leads should be considered accordingly. Arterial access is not routinely used for this procedure unless the patient has clinical indications for continuous hemodynamic monitoring. In this case, the catheter should be placed in the left radial artery as

well to avoid falsely low readings related to innominate artery compression. Noninvasive continuous blood pressure monitoring can be used as an alternative. Artifacts related to compression of the reading site, especially if the arms are tucked, will affect the accuracy and precision of the monitoring, making it the main limitation to its use. Body temperature should be monitored and a warming blanket applied. Despite the potential of being a short procedure, hypothermia can occur, especially in elderly patients. Induction, maintenance of anesthesia, and muscle relaxation can be achieved with relatively short-acting agents. Propofol is frequently used for induction of general anesthesia followed by rocuronium, vecuronium, or cisatracurium to facilitate tracheal intubation via a single-lumen endotracheal tube (ETT). Anesthesia can be maintained with a potent inhalational agent in oxygen or air if adequate oxygen saturation can be maintained. Two to 3 μg per kg of fentanyl often provides sufficient analgesia for the procedure. Local anesthetic can be infiltrated in the wound by the surgeon at the beginning or at the end of the procedure. Nonsteroidal anti-inflammatory drugs (NSAIDs) may be used as adjuvant agents, in addition to intravenous acetaminophen, if not contraindicated. Finally, many clinicians choose to avoid the use of nitrous oxide because of the potential for the mediastinoscope to enter the pleural space and create a pneumothorax. The advent of sugammadex has allowed to prolong patient paralysis until the end of the procedure. Recommended reversal doses are based on the train of four (2 milligram per kilogram for two or more twitches, 4 milligram per kilogram in case of no twitches). Hypersensitivity reactions as well as anaphylaxis have been reported with the use of sugammadex and should be considered when the medication is administered.

procedures: a review of advanced diagnostic and therapeutic bronchoscopy. *Can J Anaesth*. 2018;65:822–836.

Eapen G, Shah AM, Lei X, et al. Complications, consequences and practice patterns of endobronchial ultrasound-guided needle aspiration. *Chest*. 2013;143:1044.

Harris CL, Toloza EM, Klapman JB, et al. Minimally invasive mediastinal staging of non-small-cell lung cancer: emphasis on ultrasonography-guided fine needle aspiration. *Cancer Control*. 2014;21:15.

Kim SH, Lilot M, Sidhu KS, et al. Accuracy and precision of continuous noninvasive arterial pressure monitoring compared with invasive arterial pressure: a systematic review and meta-analysis. *Anesthesiology*. 2014;120(5):1080–1097.

Miyazaki Y, Sunaga H, Kida K, et al. Incidence of anaphylaxis associated with sugammadex. *Anesth Analg*. 2018;126(5):1505–1508.

Rami-Porta R, Call S. Invasive staging of mediastinal lymph nodes: mediastinoscopy and remediastinoscopy. *Thorac Surg Clin*. 2012;22:177–189.

Zafirova Z, Dalton A. Neuromuscular blockers and reversal agents and their impact on anesthesia practice. *Best Practice Res Clin Anaesthesiol*. 2018;32(2):203–211.

Zhang R, Ma Y, Xu G, et al. Endobronchial ultrasound-guided transbronchial needle aspiration and cervical mediastinoscopy for mediastinal staging of non-small cell lung cancer: a retrospective comparison study. *J Thorac Dis*. 2018;10(3):1951–1959.

C.2. How many types of bronchoscopes are available and what are the intraoperative considerations of each one?

Four types of bronchoscopes are currently in use: flexible fiberoptic, EBUS bronchoscope, rigid ventilating, and rigid Venturi.

The *flexible fiberoptic bronchoscope* can be used either in sedated patients under local anesthesia (allowing examination of vocal cords movements) or under general anesthesia with a supraglottic airway device or an ETT. For the awake or sedated examination, viscous lidocaine can be gargled to anesthetize the upper airway and a 2% or 4% lidocaine solution inhaled via nebulizer mask to reach the lower airway. Bilateral superior

laryngeal nerve blocks and transtracheal block can be added; however, they are not as popular as in the past due to potential complications. Intravenous sedation can be achieved with 0.5-mg increments of midazolam, 10 μg of remifentanil boluses or propofol infusion. Alternatively, dexmedetomidine (as a bolus of 0.5 to 1 μg per kg over 10 minutes followed by a continuous infusion of 0.2 to 1.5 μg/kg/hr) can also be used, with the main advantage of causing amnesia without impaired ventilation. When compared to propofol, the main disadvantage of dexmedetomidine seems to be the prolonged recovery time, limiting its use in the ambulatory setting. If the oropharynx is adequately anesthetized, a supraglottic airway device can be inserted without discomfort in sedated patients and used to assist ventilation at higher F_{IO_2} concentrations.

EBUS can be done with either sedation or general anesthesia, depending on the number and locations of the lymph nodes to biopsy. Good topical anesthesia is paramount to prevent coughing and bronchospasm. The EBUS bronchoscope is a 6.9-mm outer diameter flexible bronchoscope with a latex balloon tip, coupled with a 7.5-MHz convex ultrasound probe. When the balloon is inflated with normal saline, it allows a tight adhesion to the airway wall facilitating ultrasound identification of the lymph nodes. A 21-gauge needle is used through a dedicated channel in the bronchoscope for real-time biopsy. Color Doppler is available to differentiate the lymph nodes from vascular structures. In the sedated patient, or in the presence of a supraglottic airway device, attention should be used to avoid vocal cord trauma, due to the positioning of the optical view at a 30-degree angle. Intravenous steroids may be used to prevent inflammation and edema. In nonintubated patients, local anesthetic toxicity may result from larger doses necessary to tolerate the longer procedure and abolish the cough reflex. If an ETT is used, an 8.5 is recommended to accommodate the

bronchoscope and ventilate. In the presence of precarinal lymphadenopathy, the ETT may require placement high in the trachea, potentially leaving the balloon between vocal cords. Trauma may occur with prolonged procedures or in the absence of paralysis. Other rare complications associated with the technique include pneumo- and hemomediastinum, pneumothorax, mediastinitis, and bacteremia.

Rigid bronchoscopy usually necessitates general anesthesia. Although spontaneous ventilation has been used, the risk of tracheal trauma is high with coughing. Therefore, muscle relaxation is commonly used unless contraindicated. The rigid ventilating bronchoscope has a side-port adapter that can be attached either to the anesthesia circuit or the jet ventilator, allowing the delivery of a high flow rate. A variable air leak usually exists around the bronchoscope, so high flow rates of inspired gases or packing of the oropharynx are needed. Significant loss of volatile anesthetic into the operating room environment needs to be considered; thus, the use of total intravenous technique is a good alternative.

The *rigid Venturi-effect bronchoscope* relies on an intermittent high flow (20 to 60 L per minute), high pressure (50 psi) oxygen jet to entrain air and insufflate the lungs. The jet is delivered through a reducing valve (25 psi) into a 16- or 18-gauge needle inside and roughly parallel to the lumen of the bronchoscope. Major disadvantages of this technique are the lack of control of the inspired oxygen concentration and the inability to administer inhaled anesthetics. Accordingly, anesthesia should be maintained by intravenous techniques. Inadequate ventilation (with resultant hypercapnia) can also occur.

Rigid bronchoscopic procedures can be relatively short. If sugammadex is available, patients can be fully paralyzed and reversed at the end of the case. Otherwise, continuous

succinylcholine infusion is an alternative even though rarely used nowadays. When followed by another procedure (such as the mediastinoscopy scheduled for this patient), an intermediate-duration nondepolarizing muscle relaxant is often desirable.

José RJ, Shaefi S, Navani N. Anesthesia for bronchoscopy. *Curr Opin Anesthesiol*. 2014;27:453–457.

Metha AC, Jain P, eds. *Interventional Bronchoscopy: A Clinical Guide*. New York: Springer Science; 2013:85–106.

C.3. What are the indications for cervical mediastinoscopy? Are there potential complications?

For many years, cervical mediastinoscopy was the gold standard for evaluating disease in the mediastinum and the staging of lung cancer. However, with the introduction of EBUS, cervical mediastinoscopy has become less common. Independent of the technique used, if lymph nodes are positive for malignancy by frozen section, the patient is probably not a candidate for surgical resection at the time of biopsy.

Conventional cervical mediastinoscopy involves a small incision at the sternal notch for the insertion of the mediastinoscope and sampling of lymph nodes. The pleural space is generally not entered intentionally, and, therefore, a chest tube is not indicated. Occult pneumothorax can occur as a complication, so a chest radiograph is usually obtained before discharge. Complications during mediastinoscopy are relatively rare (1% to 2%) and generally result from trauma to adjacent structures (pleura, trachea, esophagus, superior vena cava, azygos vein, innominate artery, pulmonary artery, and aorta) or nerve injury (recurrent laryngeal or phrenic nerve). Should a major vascular structure be perforated, blood loss can be rapid and profound, necessitating emergent sternotomy. Because packing or vascular clamps may be applied to the superior vena cava, clinicians should always have a plan for establishing

venous access in the lower extremity.

Kaplan JA, Slinger PD, eds. *Thoracic Anesthesia*. 3rd ed. Philadelphia, PA: Churchill Livingstone; 2011:155–168.

Wells FC, Coonar AS, eds. *Thoracic Surgical Techniques*. New York: Springer; 2018:191–194.

C.4. The decision was made to proceed with a robotic right middle lobectomy. How would this alter your management?

Robotic thoracic procedures present some unique challenges when compared to VATS despite both being minimally invasive.

In both cases, patients are **positioned** in the lateral decubitus and the bed may be flexed. However, for robotic cases, the bed may also be rotated 90 to 180 degrees from the original position to allow docking of the robot and hence far away from the anesthesiologist. Extensions for the intravenous tubing and the breathing circuit may be necessary. Special care is required for the upper arm, which is suspended and sometimes abducted to facilitate the robotic arms motion. Unnatural positioning with stretching of the brachial plexus can lead to potentially permanent damage. Direct injury can also result from the robotic arms resting on the patient's arm or head.

Optimal **lung isolation** and **collapse** are needed to enhance lung visualization during the case and allow full motion of the instruments in the chest cavity. Because this space remains partially closed, lung collapse is slower than for the open approach. Carbon dioxide (CO_2) insufflation may be used to expedite the process. Left DLTs are commonly used due to less chance of displacement and the ability to quickly collapse the lung. Once the patient is positioned and the robot docked, it may be difficult to gain access to the airway. Bronchial blockers may be an alternative, but they may require repositioning during the

case.

Intravenous access should be placed before final positioning and draping because patient access will be limited. Although not uniformly regarded as necessary for lung resection via thoracotomy, an **arterial catheter**, generally in the dependent radial artery, may be beneficial in patients undergoing robotic procedures for hemodynamic monitoring especially if the chest will be insufflated with CO_2. This "iatrogenic tension pneumothorax" can be associated with a transient increase in peak airway pressures and a decrease in venous return with significant hypotension and decreased lung compliance. In most cases, this is transient and effectively treated with pressors and/or temporary decrease of the insufflation pressures. Suggested insufflation pressure should be less than 10 to 15 mmHg, whereas peak inspiratory pressures should be less than 30 cm H_2O. Minute ventilation should be adjusted to maintain normocapnia while complying with protective lung ventilation guidelines.

Hemodynamic compromise can also be caused by unexpected bleeding, arrhythmias, or, in rare cases, contralateral pneumothorax (more common during robotic esophagectomy). Bleeding can be more difficult to control in robotic cases than VATS because the robotic arms limit the access to the chest, causing delays in making an incision or performing CPR. Helpful maneuvers to decrease bleeding involve increasing the CO_2 insufflation pressure (potentially worsening systemic hypotension) and allowing periods of apnea to decrease mediastinal movement and facilitate compression/clipping of the source of bleeding.

Robotic resections tend to take longer than open procedures or VATS, with duration influenced by experience of the surgical team and the need for added equipment. As a consequence,

exposure to anesthesia and lung collapse may be prolonged, and intraoperative costs are increased.

Campos JA. Update on lung separation techniques. *Rev Mex Anestesiol*. 2011;34:S270–S277.

Campos J, Ueda K. Update on anesthetic complications of robotic thoracic surgery. *Minerva Anestesiol*. 2014;80(1):83–88.

Deen SA, Wilson JL, Wilshire CL, et al. Defining the costs of care for lobectomy and segmentectomy: a comparison of open, video-assisted thoracoscopic, and robotic approaches. *Ann Thorac Surg*. 2014;97(3):1000–1007.

Kroh M, Chalikonda S, eds. *Essentials of Robotic Surgery*. New York: Springer; 2015:165–177.

Walsh AM, Losher J. Arterial oxygenation and management of hypoxemia during VATS. *Curr Opin Resp*. 2014;4:170–176.

C.5. What are the indications for single-lung ventilation and how can it be accomplished?

Absolute and relative indications for lung separation are listed in **Table 2.2**. Several techniques can be used to provide single-lung ventilation, including DLTs, bronchial blocking catheters passed inside or outside an ETT, bronchial blocking catheters incorporated within an ETT (Univent® ETT, Teleflex, Triangle Park, NC), or conventional ETTs placed endobronchially. Newer DLTs include the VivaSight®, ET (ETView Medical Ltd, Misgav, Israel), a left DLT with a high-resolution built-in video camera at the tip of the tracheal lumen that provides a continuous view of the airway; the Silbroncho® (Teleflex, Triangle Park, NC) left DLT constructed of silicone with a wire reinforced tip; and the Cliny® (Create Medic Co, Ltd, Yokohama, Japan) right DLT, a device with an oblong cuff and two ventilation slots for the right upper lobe. Currently, DLTs remain the most common method for achieving lung isolation. Although DLTs of variable design and material have been used in the past (e.g., Robertshaw, Carlens, and White), the models

most commonly used today are disposable and made of polyvinylchloride. Such a tube was chosen for this procedure. Several manufacturers produce right and left DLTs that are available in six sizes: 28, 32 (only one manufacturer), 35, 37, 39, and 41 French (size in French = 3.14 × external diameter in millimeters or 4 × the internal diameter + 2). Although the general rule is that average-sized Caucasian men usually accommodate a 39 French and average-sized women a 37 French.

TABLE 2.2 Indications for Single-Lung Ventilation

Absolute	
1. To isolate from spillage or contamination	• Infection: bronchiectasis and lung abscess • Massive hemorrhage
2. To control the distribution of ventilation	• Bronchopleural fistula • Bronchopleural cutaneous fistula • Giant unilateral lung cyst or bulla • Tracheobronchial tree disruption or trauma • Surgical procedures on major conducting airway (i.e., pneumonectomy or sleeve resection) • Life-threatening hypoxemia resulting from unilateral lung disease • Unilateral bronchopulmonary lavage (pulmonary alveolar proteinosis)
3. To facilitate surgical exposure	• Video- and robotic-assisted thoracoscopic surgery
Relative	
1. Facilitation of surgical exposure—high priority	• Thoracic aortic aneurysm • Pneumonectomy • Upper lobectomy • Mediastinal exposure • Pulmonary resection via median sternotomy
2. Facilitation of surgical exposure—low priority	• Esophageal resection • Middle and lower lobectomies and segmental resection • Procedures on the thoracic spine
3. Severe hypoxemia resulting from unilateral lung disease	

A variety of techniques have been described based on measurements of airway size derived from radiographic or computed tomographic imaging, but these have been questioned across gender and ethnicity. A properly sized DLT should pass atraumatically through the glottis, advance easily into the trachea and bronchus, and exhibit an air leak when the bronchial cuff is deflated.

Bronchial blockers (see section C.9) are a good option for lung isolation in patients who have difficult airways, when postoperative mechanical ventilation is needed, in case of a fresh tracheostomy, or in the pediatric population. Lobar blockade can also be accomplished by using a blocker, especially after pneumonectomy or in case one-lung ventilation (OLV) is not tolerated. Disadvantages of blockers include slow lung collapse, especially in patients with severe COPD, dislodgment of the catheter tip during surgical manipulation of the hilum or being stapled in the bronchial stump.

Independent of the technique chosen, single-lung ventilation is associated with certain disadvantages and complications. The most notable is the large and variable alveolar-to-arterial oxygen tension difference ($P_{[A-a]}O_2$) that occurs because of continued perfusion to the nondependent nonventilated lung. The incidence of severe hypoxemia and hypercarbia is relatively small and often the result of DLT malposition resulting from overinflation of the endobronchial cuff, surgical manipulation of the bronchus, or head extension/flexion during positioning in the lateral decubitus. Traumatic laryngitis and tracheobronchial rupture secondary to bronchial cuff overinflation, forceful placement, or airway pathology have also been reported as potential complication of DLT placement.

Campos JA. Update on lung separation techniques. *Rev Mex Anestesiol*. 2011;34:S270–S277.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1663–1700.

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Pedoto A. How to choose the double-lumen tube size and side: the eternal debate. *Anesthesiol Clin*. 2012;4:671–681.

C.6. What are the contraindications to the use of double-lumen endotracheal tubes (DLTs)?

Placement of a DLT should be carefully considered in the following situations:

- Patients whose upper airway anatomy may preclude safe insertion such as recessed jaw, prominent teeth, bull neck, anterior larynx, mandibular surgery, and neck radiation
- Patients with lesions along the pathway of the tube that could be traumatized, such as airway stricture or endoluminal tumors
- Small patients for whom a 35 or 32 French tube is too large to fit comfortably through the larynx and a 28 French tube is considered too small
- Critically ill patients already intubated who cannot tolerate cessation of mechanical ventilation and positive end-expiratory pressure (PEEP) for a short time.

Under these circumstances, single-lung ventilation can be achieved via an endobronchial blocker. Endobronchial placement of a single-lumen tube for lung isolation is an alternative but suboptimal option. The tip of the ETT can cause direct distal airway trauma, whereas significant airway compression with potential mucosal ischemia may occur if the cuff bulges at carina. When placed on the right side, the right upper lobe will be occluded by the cuff of the tube, preventing the ability to ventilate.

Campos JA. Update on lung separation techniques. *Rev Mex Anestesiol*. 2011;34:S270–S277.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1663–1700.

Licker M, Le Guen M, Diaper J, et al. Isolation of the lung: double-lumen tubes and endobronchial blockers. *Trends Anaesth Crit Care*. 2014;4:47–54.

C.7. Would you use a right- or left-sided DLT?

A left-sided DLT is preferred for most procedures. The left mainstem bronchus is much longer than the right (approximately 5.0 to 5.5 cm vs. 1.5 to 2.0 cm), allowing small movements of the tube without obstructing a bronchial division. The variable origin of the right upper lobe (1.5 to 2.0 cm below carina) may complicate maintaining a good placement of a right-sided tube. Nevertheless, in an institution where the use of right-sided DLTs is routine, no difference was found in the incidence of hypoxemia, hypercarbia, or high airway pressures between patients managed with left or right DLTs, even when infrequent users were studied. A right-sided DLT is specifically indicated in the case of pathology involving the left mainstem bronchus, such as large exophytic lesions, significant bronchial stenosis, tracheobronchial disruption, endobronchial stent, and distortion by an adjacent tumor or a thoracoabdominal aneurysm. Other indications include left pneumonectomy, sleeve resection, or lung transplantation to avoid the presence of a foreign body in the surgical field that could be included in the staple line or prevent suturing of the lung. At the end of a pneumonectomy, the stump can be protected from positive pressure ventilation by leaving the tracheal side clamped until the patient returns to spontaneous ventilation; for a left lung transplant or a sleeve resection, the right lung can be ventilated when the bronchus is open during the reconstruction phase. The only absolute contraindication for right-sided DLTs use is the presence of an anomalous takeoff of the right upper bronchus above the

tracheal carina, commonly referred to as a "pig bronchus." The presence of any right mainstem lesion may also preclude the use of this lung isolation device.

Campos JA. Lung isolation. In: Slinger P, ed. *Principle and Practice of Anesthesia for Thoracic Surgery*. Cham, Switzerland: Springer; 2019:283–309.

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Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1663–1700.

Pedoto A. How to choose the double lumen-tube size and side: the eternal debate. *Anesthesiol Clin*. 2012;4:671–681.

C.8. How do you know that the tube is in the correct position?

Recommended insertion techniques for a DLT include direct laryngoscopy followed by fiberoptic guidance in the appropriate mainstem. Blind insertion may cause the potential of airway injury. Auscultation alone is unreliable to confirm the position of a DLT especially in the presence of a baseline decrease in breath sounds, such as in case of COPD. The position of the device should be reconfirmed once the patient is in the lateral decubitus prior to lung collapse.

During bronchoscopy, the tracheal cartilaginous rings are anterior and the tracheal membrane is posterior. Therefore, right versus left can be discerned by the relationship of the mainstem bronchi to the anterior cartilaginous rings and the posterior membrane (**Fig. 2.1A**). In addition, the right upper lobe takeoff (which usually arises from the lateral aspect of the right mainstem bronchus, just below the tracheal carina) is a useful landmark when the airway anatomy has been obscured by bleeding, edema, or radiation-induced changes or has been distorted by extrinsic compression. Left DLT position and depth

are confirmed by inserting the fiberoptic bronchoscope in the tracheal lumen. The entire right mainstem bronchus should be visible, and the tracheal lumen orifice of the DLT should be 1 to 2 cm above the tracheal carina. When properly positioned, the upper part of the blue endobronchial cuff is visualized just below the tracheal carina in the left mainstem bronchus (**Fig. 2.1B**). If a right DLT is used, correct positioning is confirmed by visualization of the bronchial cuff in the right mainstem bronchus (**Fig. 2.1C**) and visualization of the right upper lobe orifice through a slot on the lateral surface of the DLT (**Fig. 2.1D**). For both left- and right-sided tubes, the bronchoscope should also be inserted in the bronchial lumen to evaluate the distance between the tip of the tube and the distal bifurcation of the bronchus. DLT position should be reconfirmed after the patient is positioned laterally, before inflating the blue cuff and isolating the lung.

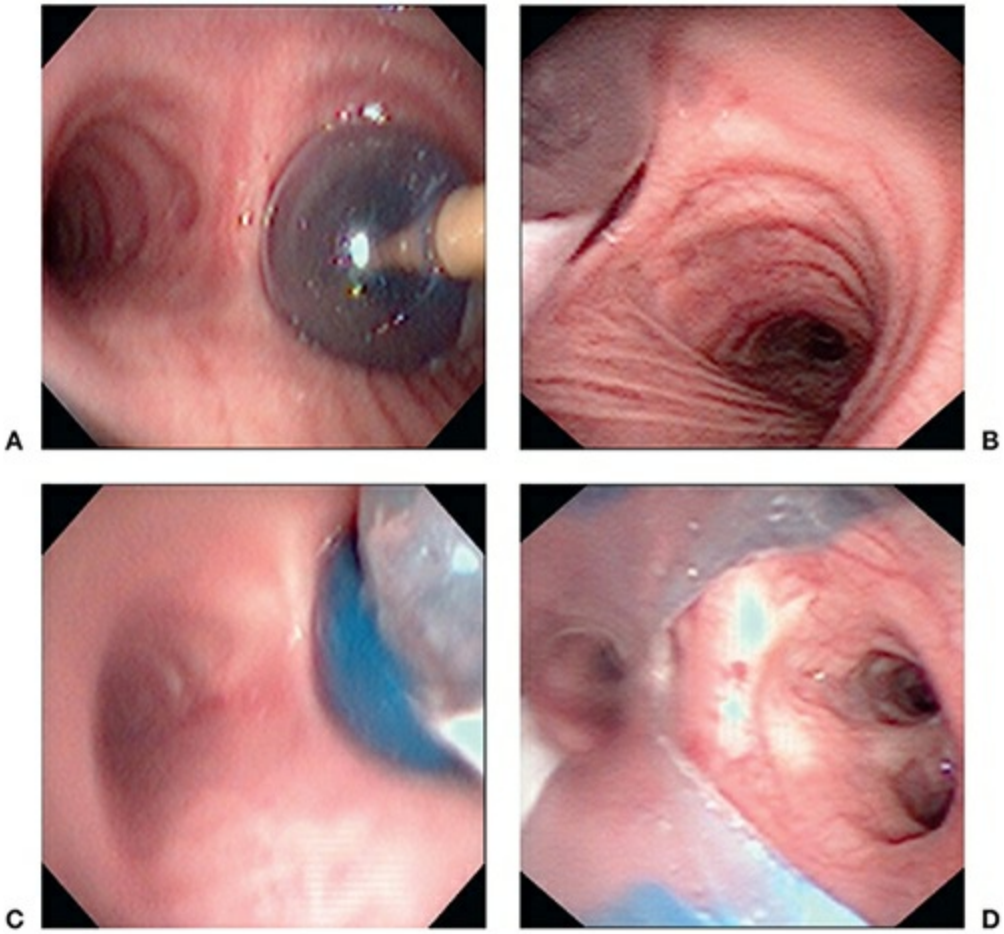

FIGURE 2.1. Representative bronchoscopic images of a bronchial blocker and DLT placement. **A.** Normal tracheal anatomy with cartilaginous rings anteriorly and membranous trachea posteriorly; this helps define left versus right. A bronchial blocking catheter is seen in the right mainstem bronchus. **B.** Placement of a left-sided DLT; the upper portion of the endobronchial cuff is evident as well as the orifice of the right upper lobe just below tracheal carina. **C.** Placement of a right-sided DLT; the upper portion of the endobronchial cuff is evident in the right mainstem bronchus. **D.** The orifice of the right upper lobe visualized through the slot on the lateral aspect of the bronchial side of a right-sided DLT.

When the **VivaSight**® (Ambu Inc, Columbia, MD) tube is used, placement and repositioning can be facilitated by the high-resolution built-in camera. The main advantage for its use is during robotic cases because of the difficult access to the patient being potentially far away from the anesthesiologist and the robotic arms very close to the patient head, making any adjustments to the DLT position a challenge. The main disadvantage is the fogging of the camera by secretions, especially during right-sided procedures, and the bigger outer

diameter, which may cause airway injury during the placement. The lack of a camera on the bronchial side still requires the use of a fiberoptic bronchoscope to assess secondary carina.

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Lee GK. Airway apparatus for thoracic surgery. *Anaesth Intensive Care Med*. 2014;15:499–504.

Licker M, Le Guen M, Diaper J, et al. Isolation of the lung: double-lumen tubes and endobronchial blockers. *Trends Anaesth Crit Care*. 2014;4:47–54.

Slinger P, ed. *Principles and Practice of Anesthesia for Thoracic Surgery*. Cham, Switzerland: Springer; 2019:283–309.

C.9. How many types of bronchial blockers are available? What are the advantages and disadvantages of bronchial blockers?

Several blockers are available, leaving ample preference of choice to the operator and the institution. Advantages and disadvantages of blockers are listed in **Table 2.3**.

TABLE 2.3 Advantages and Disadvantages of Bronchial Blockers

Advantages	Disadvantages
• Able to use in adults and children too small to fit a double-lumen tube • Difficult airway • If double-lumen tube contraindicated • Placed inside the ETT • No need to change ETT in the case of postoperative mechanical ventilation • Lobar isolation	• Unable to suction efficiently • Need to be positioned via fiberoptic bronchoscopy • Difficult for right mainstem position and RUL isolation, when the takeoff is too close to the carina • Tracheal occlusion if proximal dislodgment • Cross ventilation if the cuff is not completely inflated • Possible stapling in the stump if not retracted at the appropriate time

ETT, endotracheal tube; RUL, right upper lobe.

- **Fogarty embolectomy catheters** (Edwards Lifesciences, Irvine, CA) can be used to isolate the lung, although not specifically made for this purpose. No. 7 French (7F) Fogarty

catheters come with either a 12- or 20-mL high-pressure, low-volume balloon in both latex and nonlatex models. They have a metallic stylet that can be bent to facilitate endobronchial placement. In the case of dislodgment, the stylet can be reinserted and the blocker repositioned. Fogarty catheters have no communicating central channel; therefore, continuous positive airway pressure (CPAP) or suction cannot be applied intraoperatively. Lung collapse occurs by absorption of oxygen. Therefore, prior to inflating the balloon, it is recommended to both discontinue ventilation and depressurize the circuit of the ventilator if the patient tolerates it. The catheters are usually placed outside a single-lumen ETT and positioned via fiberoptic bronchoscopy (**Fig. 2.1A**). If placed inside the ETT, a connector such as a two-swivel adaptor is needed to facilitate insertion of both the catheter and a bronchoscope.

- **Arndt blockers** (Cook Medical Inc, Bloomington, IN) (wire-guided endobronchial blocker) are available in no. 5, 7, and 9 French with elliptical or spherical cuffs (low pressure, high volume), the latter particularly advantageous to isolate the right lung. They are usually inserted through the ETT via a three-way connector (catheter, bronchoscope, ventilation circuit). Their positioning is facilitated via Seldinger technique by an inner wire with a loop at the distal tip, where the flexible bronchoscope is placed. The wire is then removed once the blocker is in position, leaving an inner lumen that allows for suctioning or CPAP. Once the wire loop has been removed, it can be reinserted, allowing repositioning of the blocker in case of dislodgment.
- **Cohen blockers** (Cook Medical Inc, Bloomington, IN) are similar in shape to the Arndt blockers, but they use a positioning wheel to facilitate placement. By turning the wheel in a clockwise fashion, the distal portion of the blocker

deflects to the left. The main advantage of this blocker is its placement in the left mainstem because of its steep angle. Disadvantages include the cost, the fragility of the wheel, and the availability of only one size (no. 9 French).

- **EZ-blockers** (Teleflex Life Science Ltd, Morrisville, NC) are blockers with a Y-shaped bifurcation at the end fitted with two inflatable cuffs and a hollow channel in the center. The cuffs are high-pressure, low-volume, and color-coded. The blocker is placed inside the ETT, with the end on a horizontal plane to facilitate the placement of the Y across carina. Final position needs be confirmed via fiberoptic visualization because both cuffs may go in the right mainstem. The main advantage of this blocker is its stability, making it useful in cases where patient access is limited. The presence of the two cuffs makes sequential lung isolation feasible.
- **Univent tubes** (Teleflex, Triangle Park, NC) consist of an ETT with a built-in silicone bronchial blocking catheter. The main advantage is the ability of leaving the device in place in case of postoperative mechanical ventilation. However, this device is not commonly used in the United States because of its bulkiness. The outer diameter ranges from 9.7 to 13.7 mm (for a 6.0 to 8.0 inner diameter tube), with the potential to cause subglottic edema and stenosis in case of long-term use. The inner diameter is quite narrow, making suctioning or fiberoptic bronchoscopy difficult. The silicone blocker in the Univent is available as an isolated item (**Fuji blocker**). It is a high-volume, low-pressure system with a preformed “hockey stick” bend at the tip and a double stylet. It has a spherical cuff (ideally more suited to isolate the right mainstem bronchus) and two different sizes (no. 5 and 9 French). The **Coopdech** blocker (Daiken Medical Co Ltd, Izumi, Japan) is similar in shape to the Fuji blocker but offers the extra option of an auto-inflate balloon via an auto-inflate button, allowing

the use of one hand while maneuvering the fiberoptic bronchoscope.

Blockers can be used to rescue nonworking DLT, by placing the device inside the lumen of the nondependent lung. This may be needed in case of rupture of the bronchial cuff in a patient already positioned, or for lobar collapse in case of DLT dislodgment and inability to appropriately reposition in the mainstem bronchus. The DLT may be left in the original place or withdrawn and used as a single-lumen tube.

Campos JA. Lung isolation. In: Slinger P, ed. *Principle and Practice of Anesthesia for Thoracic Surgery*. Cham, Switzerland: Springer; 2019:283–309.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1663–1700.

Lee GK. Airway apparatus for thoracic surgery. *Anaesth Intensive Care Med*. 2014;15:499–504.

Licker M, Le Guen M, Diaper J, et al. Isolation of the lung: double-lumen tubes and endobronchial blockers. *Trends Anaesth Crit Care*. 2014;4:47–54.

C.10. How will systemic oxygenation be monitored during single-lung ventilation? What is the mechanism of pulse oximetry?

Pulse oximetry is still the hallmark for monitoring arterial oxygenation during lung resection, decreasing the need for repeated measurements of arterial blood gases. This technique uses spectrophotoelectric oximetric principles to determine oxygen saturation. Pulse oximeters are multiple-wavelength plethysmographs. The amplitude of the pulse is a function of arterial distention, hemoglobin oxygen saturation of the arterial blood inflow, and light wavelength. Hemoglobin saturation in the arterial blood is the result of the ratio between the pulse amplitude of red (660 nm = deoxyhemoglobin) and infrared (940 nm = oxyhemoglobin) light. Pulsatile waveform is a

characteristic of arterial blood flow, so there is no interference from surrounding venous blood, skin, connective tissue, or bone. Arterial pulsations cause changes in light absorption, which are used to calculate oxygen saturation. Adequate finger pulsation generally is lost with hypothermia of a few degrees, hypotension (mean blood pressure less than 50 mmHg), and infusion of vasoconstrictive drugs. Accuracy of the measurement is also lost for values below 70% and can be affected by dyshemoglobinemias (such as carboxyhemoglobin, methemoglobin, and sulfhemoglobin) as well as intravenous dye injection. The use of arterial oxygen saturation to monitor organ perfusion has been recently questioned by data of cerebral desaturation in the absence of arterial desaturation.

Cerebral oximetry has recently become a popular monitor of brain perfusion during thoracic and cardiac anesthesia. The technique uses near-infrared spectroscopy (NIRS) to integrate venous and arterial hemoglobin oxygen saturation signals in a ratio of 3:1. The presence of autoregulatory mechanisms guarantee that the brain is perfused and oxygenated at the expenses of other organs. Therefore, when significant cerebral desaturation occurs (<65%), it is likely that other organs have already been exposed to the same insult, with a higher risk for damage. Specifically, brain hypoperfusion seems to correlate with renal ischemia and subsequent acute renal failure (ARF). The magnitude and the duration of mean arterial pressure values below autoregulation limits appear to correlate with the incidence of postoperative ARF after cardiac surgery. ARF is also a known complication after anatomical lung resection. At the present time, there are no studies correlating its incidence with cerebral desaturation. Postoperative changes in mental status have been reported for prolonged periods of cerebral desaturation after thoracic procedures. Proposed physiologic mechanisms include hypoxemia during single-lung ventilation

and mediastinal shift with reduced cardiac output related to the lateral decubitus position.

Hofer CK, Rex S, Ganter MT. Update on minimally invasive hemodynamic monitoring in thoracic anesthesia. *Curr Opin Anesthesiol*. 2014;27:28–35.

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C.11. The patient was placed in the lateral decubitus position. Describe the effects of lateral positioning on pulmonary blood flow and respiration.

In both upright and supine positions, the right lung receives approximately 55% of the total blood flow, whereas the left lung receives the remaining 45%. In the lateral decubitus position, gravity causes a vertical gradient in blood flow distribution. Therefore, perfusion of the dependent lung is significantly greater than the nondependent counterpart. When the right lung is nondependent, it receives 45% of the total blood flow, whereas 55% perfuses the dependent left lung. When the left lung is nondependent, it receives 35% of the total blood flow, whereas right lung receives 65%. Therefore, the average blood flow of the nondependent lung is approximately 40% of the total blood flow with the dependent lung being perfused with the remaining 60% (**Fig. 2.2**).

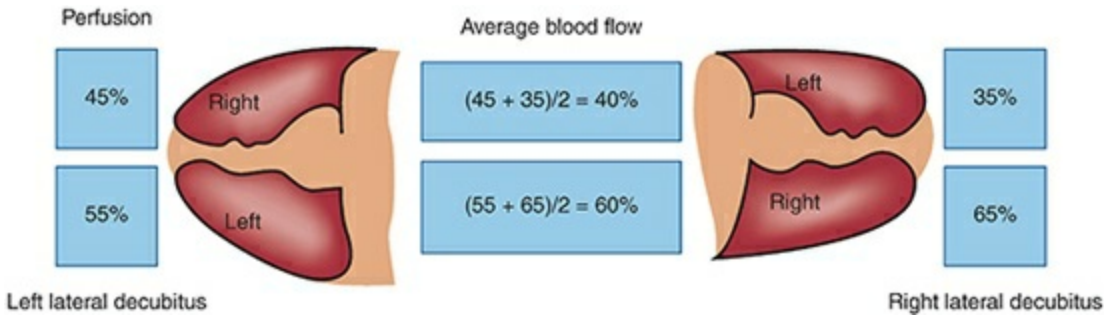

FIGURE 2.2. Changes in blood perfusion with the lateral decubitus position.

Respiratory Effects

The lateral decubitus position causes both mechanical interference with chest wall motion and a decrease in lung expansion. Specifically, the dependent chest wall is constricted by the operating room table, the lateral movements are limited by the bolsters or the "beanbag" used to hold the patient in position, whereas the upper expansion is reduced by the weight of the mediastinum. The flexion at the hips causes a theoretical improvement of the diaphragmatic motion, especially in morbidly obese patients. However, the caudad displacement of the abdominal organs is counteracted by the negative effects of general anesthesia and muscle relaxation. The final result is a gravity-induced mismatch of ventilation and perfusion while in the lateral position, with redistribution of blood flow toward the dependent lung, which is compressed by the mediastinal contents, resulting in an increase in atelectasis and hypoventilation. In the awake, spontaneously breathing subject, the lower (dependent) diaphragm is still able to contract more efficiently, maintaining ventilation in the dependent lung and matching the increased perfusion. In contrast, when the patient is anesthetized, with or without paralysis, most of the ventilation is preferentially switched to the more compliant upper lung, whereas perfusion increases in the lower lung. The result is an increased degree of ventilation/perfusion mismatch.

Liou DZ, Berry MF. Thoracic surgery considerations in obese patients. *Thorac*

Surg Clin. 2018;28(1):27–41.

Rehder K, Hatch DJ, Sessler AD, et al. The function of each lung of anesthetized and paralyzed man during mechanical ventilation. *Anesthesiology*. 1972;37:16.

Wulff KE, Aulin I. The regional lung function in the lateral decubitus position during anesthesia and operation. *Acta Anesthesiol Scand*. 1972;16:195–205.

Youngberg JA, Lake CL, Wilson RS, eds. *Cardiac, Vascular, and Thoracic Anesthesia*. New York: Churchill Livingstone; 2000:639–659.

C.12. What is hypoxic pulmonary vasoconstriction (HPV)?

HPV is an autoregulatory mechanism to prevent ventilation/perfusion mismatch and improve arterial oxygenation. Proposed mechanisms include an increase in reactive oxygen species in the pulmonary arterial smooth muscle, activation of redox-based oxygen sensors, and an increase in intracellular calcium. HPV is triggered by a decrease in Pa_{O_2} within the lung from low F_{IO_2}, hypoventilation, or atelectasis. The selective increase of vascular resistance in the hypoxic parenchyma diverts blood away to the better ventilated normoxic lung, decreasing the amount of shunt flow. This is a biphasic response that starts within 15 to 30 minutes from lung collapse, culminates at 120 minutes, and takes hours to reverse after normoxia is restored.

Increasing evidence indicates that significant systemic oxidative stress can be elicited by hyperoxic reperfusion of a lung in which HPV has been sustained for an extended period of time. Although the exact ramifications of this insult remain to be clarified, clinical data suggest an association between the magnitude of the oxidative stress and postoperative cardiopulmonary complications. Recommendations to decrease reexpansion injury include reinflating the collapsed lung with less than 100% F_{IO_2} as well as using protective lung strategies. The lowest F_{IO_2} possible is also recommended.

Brimioulle S, LeJeune P, Naeije R. Effects of hypoxic pulmonary

vasoconstriction on pulmonary gas exchange. *J Appl Physiol*. 1996;81:1535–1543.

Dunham-Snary KJ, Wu D, Sykes EA, et al. Hypoxic pulmonary vasoconstriction: from molecular mechanism to medicine. *Chest*. 2017;151(1):181–192.

Heerdt PM, Stowe DF. Single-lung ventilation and oxidative stress: a different perspective on a common practice. *Curr Opin Anesthesiol*. 2017;30(1):42–49.

Losher J, Slinger P. Lung injury after one-lung ventilation: a review of the pathophysiologic mechanisms affecting the ventilated and the collapsed lung. *Anesth Analg*. 2015;121(2):302–318.

Lumb AB, Slinger P. Hypoxic pulmonary vasoconstriction: physiology and anesthetic implications. *Anesthesiology*. 2015;122:932–946.

C.13. What are the effects of anesthetic agents on HPV and their clinical implications?

Any medication that causes vasodilation may inhibit hypoxic vasoconstriction. Several clinical studies have failed to demonstrate a decrease in HPV during single-lung ventilation and total intravenous anesthesia. Intravenous anesthetics, such as thiopental, ketamine, morphine, and fentanyl, have no direct effect on HPV. In contrast, inhalational anesthetics have been shown to inhibit HPV in a dose-related fashion but usually at concentrations much higher than clinically used. Other nonanesthetic drugs such as β-agonists and antagonists, calcium channel blockers, nitrovasodilators, and theophylline may influence the effects of inhalation anesthetics on shunting and arterial oxygenation during single-lung ventilation. There is no good evidence that neuraxial blockade affects HPV, unless causing a decrease in cardiac output or systemic vasodilation.

- The result of an increased shunt on Pa_{O_2} depends on the absolute level of the initial shunt and the inspired oxygen concentration used. Even when shunt is increased, Pa_{O_2} usually remains well above 100 mmHg, with minimal changes in oxygen saturation and content.
- Inhalational agents inhibit HPV, but they also decrease

cardiac output, oxygen consumption, and may cause a decrease in mixed oxygen venous tension (PvO_2). If cardiac output decreases and oxygen consumption does not change, there will be a decrease in PvO_2, which is a potent stimulus for HPV. A low cardiac output will result in a decreased perfusion of the collapsed lung (where there is an increase in pulmonary vascular resistance as a result of HPV). Nevertheless, the presence of chronic and irreversible vascular disease in the nondependent lung may impair HPV response.

- The presence of disease in the dependent lung will decrease the ability of accepting blood flow redistribution, thereby decreasing the local HPV effect.
- Direct surgical manipulation may cause the release of vasoactive substances, such as thromboxane and prostacyclin (PGI_2), promoting local vasodilatation and blunting HPV, with a subsequent increase in shunt.
- Metabolic or respiratory acidosis and hypothermia are also associated with an impairment in HPV.

Lumb AB, Slinger P. Hypoxic pulmonary vasoconstriction: physiology and anesthetic implications. *Anesthesiology*. 2015;122:932–946.

C.14. Discuss pulmonary blood flow distribution, shunt flow, and partial pressure of oxygen in the arterial blood (PaO_2) (fractional inspired O_2 concentration [FIO_2] = 1.0) during single-lung ventilation in the lateral position.

When the nondependent lung is collapsed, HPV will ultimately increase pulmonary vascular resistance and decrease lung blood flow in this area. If no complicating factors exist, HPV should decrease blood flow to that lung by approximately 50%, causing a total reduction from 40% to 20%. The resulting

nondependent/dependent lung blood flow ratio during OLV should be 20%:80%.

Once atelectatic, all the blood flowing into the nonventilated lung is shunt flow. Therefore, OLV creates an obligatory right-to-left transpulmonary shunt that was not present during double-lung ventilation. During single-lung ventilation, an ideal total shunt flow of 20% would be expected, if no shunt existed during double-lung ventilation (ignoring the normal 1% to 3% physiologic amount from the bronchial, pleural, and thebesian circulation). Pa_{O_2} with an F_{IO_2} equal to 1 should be approximately 280 mmHg if hemodynamic and metabolic states are normal. Clinically, Pa_{O_2} ($F_{IO_2} = 1$) ranges from 150 to 250 mmHg.

Lumb AB, Slinger P. Hypoxic pulmonary vasoconstriction: physiology and anesthetic implications. *Anesthesiology*. 2015;122:932–946.

Marshall BE, Marshall C. Continuity of response to hypoxic pulmonary vasoconstriction. *J Appl Physiol Respir Environ Exerc Physiol*. 1980;59:189–196.

C.15. How could you improve oxygenation during single-lung ventilation?

When hypoxia occurs during single-lung ventilation, the goal is to optimize the match between ventilation and perfusion on the dependent lung or increase the amount of oxygen in the shunted blood of the collapsed lung.

Ventilated Lung

a. *Optimize ventilation.*

- Use 100% oxygen.
- Check the position of the DLT with a fiberoptic bronchoscope.
- Ventilate manually to determine whether higher or lower tidal volumes or inspiratory pressures are beneficial.

- Set minute ventilation to maintain $Paco_2$ at 40 mmHg (hypocapnia may inhibit HPV in the nondependent lung, whereas hyperventilation may increase airway pressure and promote blood flow to the nonventilated lung).
- Apply 5 cm H_2O of PEEP. It may be beneficial if larger tidal volumes delivered manually improved arterial saturation (i.e., recruitable alveoli). Alternatively, if tidal volumes are too large, adding PEEP may overdistend alveoli that are already open and compress blood vessels, diverting blood to the nonventilated lung and worsening the shunt.
- Use two-lung ventilation intermittently.

b. *Increase perfusion.*

- Selective vasodilators (inhaled nitric oxide, inhaled PGI_2)

Collapsed Lung

a. *Oxygenate shunt blood:* A variety of approaches have been described but must be carefully considered for minimally invasive procedures because most involve some degree of lung reexpansion and therefore may affect surgical visualization.

- Insufflate oxygen continuously: A flow of about 3 L per minute allowed to freely circulate will often increase arterial oxygen saturation 3% to 4%.
- Intermittent single breath with oxygen
- Partially reexpand the nonventilated lung and then keep the lumen side closed.
- Apply continuous CPAP.
- Differential CPAP to the collapsed lung and PEEP to the ventilated lung has been described but is rarely necessary and generally impractical for minimally invasive procedures.
- High-frequency ventilation to the nonventilated lung

b. *Decrease the shunt.*

- Use medications to augment HPV (phenylephrine, norepinephrine, almitrine).
- Temporary clamp lobar vessels or the pulmonary artery of the nonventilated lung (rarely necessary).

Possible hypoventilation, in compliance with protective lung strategy and the ERAS guidelines will increase the need for the aforementioned maneuvers to maintain the saturation and the $Paco_2$ within acceptable ranges.

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Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1663–1700.

C.16. A right middle lobectomy was performed. Would you extubate the trachea at the end of the procedure?

After routine lung resection, the trachea can be extubated if the patient meets criteria and has adequate analgesia. If the patient cannot maintain adequate oxygenation and ventilation, postoperative mechanical support is indicated. If so, the DLT needs to be exchanged to a single lumen tube or a supraglottic device. Spontaneous ventilation avoids the potential hazards of positive pressure on the suture lines of the new bronchial stump or parenchymal air leaks. The combination of modest CPAP and pressure support ventilation is usually preferable to controlled intermittent mandatory ventilation.

Slinger PD, ed. *Principle and Practice of Anesthesia for Thoracic Surgery*. Cham, Switzerland: Springer; 2019:885–923.

D. Postoperative Management

D.1. What are the immediate life-threatening complications that follow lobectomy or pneumonectomy?

Serious complications after lobectomy include lobar collapse, massive hemorrhage caused by loosening of pulmonary vessels ligatures, bronchopleural fistula from disruption of a bronchial stump, and pulmonary torsion and infarction resulting from increased mobility of the remaining lobe. Mediastinal shift, pleural effusion, hemothorax, chylothorax, empyema, and pulmonary edema can also occur. Deep venous thrombosis can lead to pulmonary embolism.

Pneumonectomy can be complicated by supraventricular arrhythmias, acute respiratory insufficiency, nerve injuries (phrenic, vagus, or recurrent laryngeal) during radical hilar dissection or excision of mediastinal tumors, cardiac herniation (in the case of intrapericardial approach), acute right heart failure, and right-to-left shunting across a patent foramen ovale as a result of increased pulmonary vascular resistance and increased right ventricular pressure. *Postpneumonectomy syndrome* is a rare complication characterized by mediastinal shift ipsilateral to the side of surgery with herniation of the hyperinflated lung in the same direction.

Slinger PD, ed. *Principle and Practice of Anesthesia for Thoracic Surgery*. Cham, Switzerland: Springer; 2019:885–923.

D.2. Why is it important to control postoperative pain? How would you achieve this goal?

Adequate postoperative analgesia is important not only for patient comfort but also to minimize pulmonary complications, allowing the patient to breathe deeply, cough effectively, and ambulate. Several options are available, depending on the institution and surgical preferences.

Enhanced recovery pathways have been developed to decrease postoperative complications and expedite discharge. A multimodal analgesic approach is paramount for any surgical technique.

Epidural, Paravertebral, and Intrathecal Analgesia

Since the introduction of regional analgesia, there has been a trend towards reduced morbidity and mortality after open lung resection. **Thoracic epidural** analgesia is commonly achieved with a continuous infusion of a local anesthetic alone or in combination with an opiate. In order to reduce the volume required to produce an effect and lessen the chance of hypotension and motor weakness, the catheter is usually placed as close as possible to the dermatomes to be covered. A low concentration of local anesthetic such as 0.1% or 0.05% bupivacaine hydrochloride combined with an opiate (e.g., fentanyl 5 to 10 μg per mL, hydromorphone 8 μg per mL, or sufentanil 0.1 μg per mL) produces synergistic effects with a reduction of the sympathetic blockade associated with the use of a more concentrated local anesthetic alone. In addition, the presence of local anesthetics seems to increase the affinity of the narcotic for the opioid receptors. Potential complications of thoracic epidural technique can be related to the placement (inadvertent dural puncture, trauma to the spinal cord, hematoma) or drug administration (intravascular injection of local anesthetics with resultant cardiovascular and central nervous system toxicity). Long-acting antiplatelet medications discontinuation should follow the American Society of Regional Anesthesia and Pain Medicine guidelines to prevent neuraxial hematomas.

Paravertebral blocks and **catheters** can be used preoperatively or postoperatively, in combination with parenteral opiates and NSAIDs, as an alternative to thoracic

epidural analgesia. To be effective, multiple levels need to be blocked unless a catheter is placed. The failure rate for the blind technique is relatively high (6% to 10%) and can be decreased by locating the space via ultrasound guidance or under direct vision by the surgeon before closing the chest. Pneumothorax (especially if bilateral blocks are attempted), hypotension, local anesthetic toxicity due to the high vascularity of the area, and inadvertent total spinal are all potential risks. Advantages compared with epidural analgesia include less hypotension, less nausea or vomiting, and the ability to block just the surgical side.

Intrathecal injection of opiates can be used pre- or intraoperatively for an 18- to 24-hour postoperative pain relief. However, when compared to epidural injection, intrathecal opiates (i.e., morphine) are associated with an increased incidence of late respiratory depression (4% to 7% compared to less than 1% for epidural administration), pruritus, nausea and vomiting, which could increase length of stay (LOS) in the postoperative period.

The advantages of neuraxial techniques compared to systemic opiates include selective blockade of spinal pain receptors with minimal sympathetic blockade, no loss of motor function, and greater predictability of pain relief. Epidural opiates in combination with local anesthetics block the presynaptic and postsynaptic neuron cells of the substantia gelatinosa of the spinal cord by passive diffusion across the dura into the cerebrospinal fluid. The lipophilic narcotics, such as fentanyl 0.1 mg, methadone 5 mg, and meperidine 30 to 100 mg, have a relatively short onset of action (less than 12 minutes). They provide significant pain relief in 20 to 30 minutes, which can last for 6 to 7 hours. In contrast, a hydrophilic opiate such as morphine (5-mg dose) has a relatively slow onset of action (15 to 30 minutes), provides maximal pain relief in 40 to 60 minutes

with a duration of action of more than 12 hours. Other side effects include urinary retention, pruritus, nausea, and vomiting. The narcotic antagonist naloxone can reverse all the aforementioned side effects but will also reverse the analgesia, so it must be used cautiously. Overall, unlike epidural local anesthetic, epidural opioids have not been shown to decrease the incidence of postoperative respiratory complications.

Peripheral Nerve Blocks

Peripheral nerve blocks with long-acting local anesthetics can be used to control pain after thoracoscopy or thoracotomy. The duration of single injections is relatively short (6 to 8 hours when bupivacaine hydrochloride is used). Catheters can be left in place and dosed postoperatively. *Intercostal nerve blocks* can be done under direct vision by the surgeon before closing the chest cavity or percutaneously before awakening the patient. The intercostal nerves to be blocked are at the level of the incision and two or three interspaces above and below. Of the three main sensory divisions of the intercostal nerve (posterior, lateral, and anterior cutaneous nerve), the posterior branch cannot be blocked with this approach, limiting its usefulness in the case of a posterolateral incision. There is controversy on the quality of analgesia with this technique alone when compared with the epidural route. Intercostal catheters are indicated as part of a multimodality treatment when neuraxial blocks are contraindicated (e.g., patients on anticoagulation or tumor involvement of the epidural space) or for minimally invasive procedures. Recently, *serratus plane* and *erector spinae* block and catheters have been described as good analgesic options for minimally invasive lung resections. Ultrasound guidance makes these blocks relatively easy and with low risks of complications.

The use of extended-release formulation of liposomal bupivacaine (Exparel, Pacira Pharmaceuticals, Inc, Parsippany,

NJ) may increase the duration of the block, improving the quality of analgesia, especially when paired with other adjuvants. Because of the relatively high rate of systemic absorption of the local anesthetic from the intercostal space, there is an increased risk of systemic toxicity. Liposomal bupivacaine has been used off label for intercostal nerve blockade and other peripheral nerve blocks. The few case reports where the medication was used did not show permanent nerve damage or toxicity, whereas the degree of analgesia was reported comparable to thoracic epidural. Due to the concern of systemic toxicity, the use of liposomal bupivacaine in a peripheral nerve block precludes the use of local anesthetic via neuraxial blockade.

Systemic Opioids and Adjuvants

Systemic administration of **opioids** was the main analgesic modality in the past, alone or as part of a multimodal approach, especially for minimally invasive surgical procedures. With the advent of Enhanced Recovery after Thoracic Surgery (ERATS) protocols and the current opioid epidemic affecting the United States, there has been a shift in the analgesic paradigm in favor of a multimodal approach based on regional techniques and nonopioid medications, leaving opioids as a rescue. Sedation, potential respiratory depression, hypoventilation, inhibition of cough, and reduced sighing are the main side effects that can prolong LOS.

NSAIDs such as ketorolac, diclofenac, ketoprofen, and indomethacin can be used as adjuvants to parenteral opiates, particularly for the treatment of shoulder pain associated with chest tube placement. Potential side effects for NSAIDs include gastric bleeding, platelet dysfunction, and renal insufficiency in patients who are severely fluid restricted, especially the elderly. Intravenous acetaminophen is used in the US can be added to

potentiate analgesia if not contraindicated.

Low-dose intravenous **ketamine** infusion (0.25 mg/kg/hr) has been used as an adjuvant in the perioperative period, especially in patients with chronic pain. Psychomimetic side effects are a possibility but are rare at this dosage. Intravenous **dexmedetomidine** can be used intraoperatively to potentiate analgesia. The recommended dose is a continuous infusion of 0.2 to 0.7 (to a maximum of 1.5) μg/kg/hr without loading. Its central α_2-agonism potentiates analgesia, allowing a decrease in the dose of intravenous narcotics and decrease the minimal alveolar concentration (MAC) of general anesthesia. Hypotension and bradycardia are potential side effects as well as sedation. **Lidocaine infusion** (1.0 to 1.5 mg/kg/hr) can also be used as an adjuvant. Despite the concern of systemic toxicity, there has been no reports of such complication. Intravenous lidocaine infusion should be considered as an alternative when neuraxial blockade is contraindicated or for minimally invasive procedures.

Oral and Transdermal Agents

Gabapentin and **pregabalin** are analogues of γ-aminobutyric acid, usually used for neuropathic pain and given in the preoperative period as part of a multimodal analgesic approach. Sedation and dizziness are the main side effects, limiting their use in the elderly population. Their maximal plasma concentration occurs at 2 to 3 hours from ingestion. Pregabalin has a faster onset of action when compared with gabapentin, reaching faster peak of action. For both medications, it seems there is a better effect on analgesia if the drug is started days prior to surgery rather than one dose preoperatively. **Glucocorticoids** decrease postoperative pain, opioid requirements, and postoperative nausea and vomiting (PONV). Glucocorticoids mixed with local anesthetic prolong the

duration of the block more than when given intravenously in adjunct to the block. **Beta blockers** have antinociceptive properties. Esmolol infusion has been associated with a small decrease in intra- and postoperative pain scores in abdominal surgery, with a decrease in morphine equivalents and rescue doses. **Capsaicin** applied directly in the wound prior to closure deactivates C-fiber conduction due to depletion of substance P. Capsaicin has a long duration of action without any motor and autonomic activity, facilitating early rehabilitation in the postoperative period. Due to an intense burning on injection, the medication should be delivered during anesthesia. **Lidocaine patch** (5% concentration) has been used with some success as an adjuvant in chronic pain patients. Its efficacy is limited in the postoperative period, possibly because of an insufficient concentration in the wound and the inability of properly placing the patch on top of the incision, therefore with minimal absorption.

Intrapleural Regional Analgesia

Intrapleural analgesia utilizes the percutaneous introduction of a catheter between the parietal and visceral pleura for the injection of local anesthetic. Analgesia is thought to occur because of (1) diffusion of local anesthetic through the parietal pleura and the innermost intercostal muscle to the intercostal nerves (where the block occurs), (2) block of the intrathoracic sympathetic chain, and (3) direct action of local anesthetic on nerve endings within the pleura. Nevertheless, the quality of analgesia is extremely variable and unfavorable compared to that of other modalities. The local anesthetic can be lost through the thoracotomy drainage, it can be diluted by extravasated blood and tissue fluid in the pleural space, or it can be sequestered and channeled because of the decreased movements of the operated lung. Moreover, in the sitting position, the local anesthetic pools in the

costophrenic angle, limiting the quality of analgesia. The use of multiple or fenestrated catheters may achieve a more even distribution over the pleura and improve the quality of analgesia. However, this technique is rarely used today.

Cryoanalgesia

Long-lasting (3 to 4 weeks up to 6 months) intercostal nerve block can be obtained by cryoablation. Two 30- to 60-second freeze cycles (−60°C), separated by a 5-second thaw period, are applied to each of the nerves selected. Although cryoanalgesia was initially shown to effectively relieve pain and improve postoperative pulmonary function, more detailed studies have revealed a significant incidence of paresthesia and post thoracotomy pain syndrome.

Transcutaneous Electrical Nerve Stimulation

Transcutaneous electrical nerve stimulation (TENS) relies on the application of brief pulses of current via electrodes to the affected area. The advantages of TENS include low cost, ease of application, and lack of undesirable side effects. Nevertheless, TENS has a weak analgesic effect. It is generally reserved for adjunctive use to relieve mild-to-moderate postthoracotomy pain. It is ineffective if the pain is severe and is contraindicated in patients with pacemakers, defibrillators, and infusion pumps because the current could produce interference.

Shoulder Pain after Lung Resection

Independently from the analgesic technique used and the surgical approach, approximately 80% of patients who have undergone lung resection complain of ipsilateral shoulder pain that is unresponsive to epidural block or systemic opioid. Possible causes for shoulder pain include referred pain from diaphragmatic irritation, chest tube placement (too far at the apex of the hemithorax), the posterior end of a large

posterolateral incision, or surgical positioning in patients with arthritis. Shoulder pain usually responds to anti-inflammatory agents and often resolves on the second postoperative day. Phrenic nerve infiltration and brachial plexus block have been used but have the potential of causing diaphragmatic dysfunction.

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3 Aspiration and Postoperative Respiratory Failure

Kapil Rajwani, Edward J. Schenck, and David A. Berlin

A 62-year-old woman presents to the emergency department with a small bowel obstruction. She is vomiting and hypotensive and appears to aspirate. She is emergently intubated, fluid resuscitated, and brought to the operating room for emergency laparotomy.

A. Aspiration

1. What are the risk factors for perioperative aspiration?
2. How does large volume aspiration affect the respiratory system?
3. How should you manage the patient after an aspiration event?
4. How would you prevent aspiration during emergency surgery?

B. Postoperative Respiratory Failure

After successful lysis of abdominal adhesions, the patient recovers well and is extubated at the completion of surgery. Subsequently, she develops progressive hypoxemic respiratory failure while in the postanesthesia care unit.

1. How can you predict which patients will develop postoperative

respiratory failure?

2. How can intraoperative anesthesia management prevent respiratory failure?
3. What is the pathogenesis of postoperative respiratory failure?
4. What is the diagnostic approach to postoperative respiratory failure?

C. Indications for Ventilator Support

The patient has worsening hypoxemia and tachypnea despite treatment with high-flow supplemental oxygen.

1. What are the indications for noninvasive positive pressure ventilation (NIPPV)?
2. What are the indications for emergency endotracheal intubation?

D. The Acute Respiratory Distress Syndrome

The patient is intubated for respiratory failure. She has bilateral pulmonary infiltrates on chest x-ray and is severely hypoxemic.

1. What is the definition and etiology of the acute respiratory distress syndrome (ARDS)?
2. Explain the pathophysiology of ARDS.
3. What role does ventilator-induced lung injury (VILI) play in ARDS?

E. Management of Mechanical Ventilation

1. Which mode of mechanical ventilation will you choose? Describe the features of that mode.
2. How should you set the fraction of inspired oxygen (F_{IO_2})?
3. How should you set the positive end-expiratory pressure (PEEP)?
4. What tidal volume and inspiratory pressure target should you set?

F. Management of Refractory Respiratory Failure

The patient remains hypoxemic on F_{IO_2} of 0.8.

1. What else can promote additional lung recruitment?
2. What rescue strategies can you use for refractory ARDS?

G. Adjunctive Management of Respiratory Failure

Since intubation, the patient has become hypotensive.

1. What is the cause and treatment of the hemodynamic instability associated with mechanical ventilation?
2. What is the adjunctive medical therapy for ARDS?

H. Liberation of the Patient from Mechanical Ventilation

The patient slowly recovers over the next 3 days.

1. Explain the importance of the decision to extubate the patient or continue mechanical ventilation.
2. How will you prepare the patient for liberation from the ventilator?
3. How will you recognize when the patient is ready for extubation?

A. Aspiration

A.1. What are the risk factors for perioperative aspiration?

Clinically significant aspiration is a relatively rare complication of anesthesia. The reported incidence is 1 to 5 per 10,000 patients, although it is more common in certain situations, such as traumatic brain injury. About half of the cases of perioperative aspiration occur during induction of anesthesia. Although an emergency indication for surgery is a major risk factor for aspiration, the majority of cases occur during elective procedures. Increased gastric pressure, decreased lower esophageal sphincter tone, and blunted protective airway reflexes promote aspiration. Therefore, risk factors for aspiration

include full stomach, pregnancy, bowel obstruction, gastroesophageal reflux, obesity, gastrointestinal motility disorders, and neurologic conditions. Airway manipulation in an unfasted patient or an inadequate depth of anesthesia may increase the risk of aspiration. Many anesthetics reduce lower and upper esophageal sphincter tone and diminish protective airway reflexes. The appropriate use of laryngeal mask airways does not increase the risk of aspiration, although it may induce gastroesophageal reflux. Certain surgical procedures such as laparoscopic insufflation of the abdomen and bowel manipulation are associated with increased rates of aspiration.

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A.2. How does large volume aspiration affect the respiratory system?

Aspiration of gastric and oropharyngeal contents causes three overlapping syndromes. First, aspiration of large particulate matter may obstruct the airways and lead to atelectasis. Acute aspiration pneumonitis is more common and is a result of chemical burning of the tracheobronchial tree and pulmonary parenchyma by gastric and oral fluids. Finally, aspiration of bacteria from the oropharynx or a superinfection of the chemical pneumonitis may result in aspiration pneumonia.

Mendelson originally described aspiration pneumonitis in 66

obstetrical patients who aspirated gastric contents during anesthesia. Respiratory distress and cyanosis developed within 2 hours after the aspiration event. All of the patients (except two who had airway obstruction from solid food particles) recovered within 24 to 36 hours without antibiotics and had radiographic resolution. Signs and symptoms of aspiration pneumonitis include coughing, wheezing, dyspnea, hypoxia, fever, tachypnea, and crackles on lung auscultation. Radiography usually demonstrates diffuse bilateral infiltrates.

Aspiration pneumonitis may be mild and elude clinical detection. Rarely, aspiration is fulminant and rapidly fatal. Most patients rapidly improve after aspiration and have clearing of radiographic lung infiltrates. Occasionally, patients initially improve but then develop progressive lung infiltrates on chest radiograph. These infiltrates probably represent a secondary bacterial infection or ARDS. The volume and pH of the aspirated fluid are important factors affecting the degree of lung injury. In adults, approximately 25 mL of gastric acid with a pH <2.5 is considered a clinically relevant threat. Smaller volumes may produce a milder syndrome. Bile may elicit a potent inflammatory response and has been identified in patients' endotracheal tubes. Atelectasis, peribronchial hemorrhage, pulmonary edema, and degeneration of bronchial epithelial cells all develop within minutes of aspiration. By 4 hours, the alveoli fill with polymorphonuclear leukocytes and fibrin, and hyaline membranes form. The lung becomes grossly edematous and hemorrhagic with alveolar consolidation.

Aspiration pneumonia may result from a superimposed infection of the chemical injury or inhalation of microorganisms from the oropharynx. Poor dentition is a risk factor for aspiration pneumonia. Common bacteria include *Haemophilus influenzae*, streptococci, and other anaerobes. The oral flora changes in chronically ill patients and those in health care

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A.3. How should you manage the patient after an aspiration event?

Awake patients capable of airway protection should be placed in the upright or recovery position and encouraged to cough. However, clinicians may need to suction or rescue the airway if the patient has impaired protective airway reflexes. Supplemental oxygen should be administered for hypoxemia. Clinicians should avoid noninvasive ventilation because of the risk of gastric insufflation unless there is no further risk of additional vomiting. There is no evidence supporting lavage with saline or sodium bicarbonate. Gastric acid is rapidly neutralized by the physiologic response. When possible, the stomach should be emptied with a nasogastric tube. A chest radiograph should be ordered. In select circumstances, a bronchoscopy may be necessary for airway clearance and evaluation especially if airway obstruction is suspected. Bronchoscopy can provide quantitative lower respiratory tract

cultures from bronchoalveolar lavage or protected brushings. These techniques can distinguish aspiration pneumonitis from pneumonia.

Although some animal studies support the use of corticosteroids in aspiration pneumonitis, there is no evidence of benefit in human studies. Moreover, the literature does not support the routine use of antibiotics immediately after aspiration. A retrospective cohort study reviewing 200 patients divided into groups that received supportive care versus antimicrobials did not show any clinical benefit when looking at mortality or need for transfer to an intensive care unit. Patients, however, should be followed closely to identify the development of a secondary infection. If the clinicians diagnose aspiration pneumonia, they should choose antibiotics that provide coverage against oral flora including gram-negative coverage for patients with nosocomial colonization. This may include extended spectrum β lactamases inhibitors such as piperacillin-tazobactam.

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A.4. How would you prevent aspiration during emergency surgery?

Certain measures may help reduce the risk of perioperative aspiration. These include adequate fasting, prophylactic antiemetics, rapid sequence intubation (RSI), limited tidal volumes if bag ventilation is used, and extubation when the patient's laryngeal reflexes have returned. Anti-acid medications can increase gastric pH; however, their use is only supported by expert opinion.

RSI involves preoxygenation followed by intubation using an induction agent and neuromuscular blockade without face-mask ventilation. There are no prospective randomized controlled trials that show whether RSI reduces the incidence of aspiration. However, RSI has been shown to decrease the time to achieve successful intubation, which may be beneficial when the risk of aspiration is high. The value of cricoid pressure during intubation remains controversial. A recent randomized trial did not demonstrate a reduction in aspiration with cricoid pressure but did note an increased intubation time when cricoid pressure was applied.

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B. Postoperative Respiratory Failure

After successful lysis of abdominal adhesions, the patient recovers well and is extubated at the completion of surgery. Subsequently, she develops progressive hypoxemic respiratory failure while in the postanesthesia care unit.

B.1. How can you predict which patients will develop postoperative respiratory failure?

Respiratory failure commonly complicates the postoperative period and is strongly associated with an increased mortality. A number of clinical prediction rules exist to predict the risk of postoperative pulmonary complications. Predisposing factors include a high American Society of Anesthesiologists (ASA) Physical Status Classification, poor functional status, and hypoalbuminemia. Lung diseases such as obstructive airways dysfunction, extrapulmonary diseases such as liver cirrhosis, congestive heart failure, renal failure, and current or former smoking status also predispose patients to respiratory failure. Additional risk factors include emergency indications for surgery, prolonged procedural time, and the requirement for large volume fluid and blood product resuscitation. Because of their effects on respiratory mechanics, thoracoabdominal surgeries, especially aortic aneurysm repair, are particularly high-risk procedures.

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B.2. How can intraoperative anesthesia management prevent respiratory failure?

An extensive literature has evaluated the role of limiting tidal volumes to prevent VILI. Ventilation with tidal volumes greater than 8 mL per kg ideal body weight (IBW) is a risk factor for postoperative pulmonary complications in thoracic and abdominal surgery. Moreover, a randomized controlled trial in major abdominal surgery demonstrated that restricting tidal volumes from 6 to 8 mL per kg IBW decreased the incidence of postoperative respiratory failure. This intervention was part of a lung-protective strategy, which combined restricted tidal volumes with PEEP as compared to large tidal volumes without PEEP. Because the intervention also included PEEP, we cannot ascribe the full benefit to tidal volume restriction. A recent meta-analysis that included 19 studies comparing patients receiving tidal volumes of 6 to 8 mL per kg of IBW to those greater than 10 mL per kg of IBW showed a reduction in postoperative pneumonia and need for postoperative ventilatory support. In sum, the current data support targeting tidal volumes to less than 8 mL per kg IBW. However, there may be situations where these tidal volumes are inadequate. The optimum dose of intraoperative PEEP is less clear. A meta-analysis revealed that a no-PEEP approach was a risk factor for postoperative pulmonary complications in thoracic and abdominal surgery.

However, randomized trials during high-risk abdominal surgery did not demonstrate a benefit from high PEEP and recruitment maneuvers. Another observational study compared the effect of PEEP ≥5 cm H_2O on patients undergoing abdominal surgery and craniotomies. The beneficial effect of PEEP in reducing postoperative respiratory complications was observed in the abdominal surgery group but not in those undergoing craniotomies. As a whole, the current evidence supports the use of moderate PEEP (approximately 5 cm H_2O) during surgery in patients at risk of atelectasis, and higher PEEP and recruitment maneuvers when the patient's physiology suggests derecruitment.

Driving pressure is calculated as the plateau pressure minus the PEEP. The driving pressure is a factor of both the tidal volume and the set PEEP. A high driving pressure (>15 cm H_2O) is associated with an increased risk of postoperative pulmonary complications. Observing the effect of ventilator settings on driving pressure may be a useful strategy. However, this approach has not yet been fully evaluated in prospective studies.

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Serpa Neto A, Hemmes SN, Barbas CS, et al. Incidence of mortality and morbidity related to postoperative lung injury in patients who have undergone abdominal or thoracic surgery: a systematic review and meta-analysis. *Lancet Respir Med*. 2014;2(12):1007–1015.

B.3. What is the pathogenesis of postoperative respiratory failure?

Numerous mechanisms contribute to the pathogenesis of postoperative respiratory failure (**Fig. 3.1**). A combination of postoperative pain, recumbent position, anesthetics, and impaired secretion clearance leads to collapse of dependent lung regions. Atelectasis increases shunt fraction, diminishes respiratory system compliance, and commonly contributes to postoperative respiratory failure.

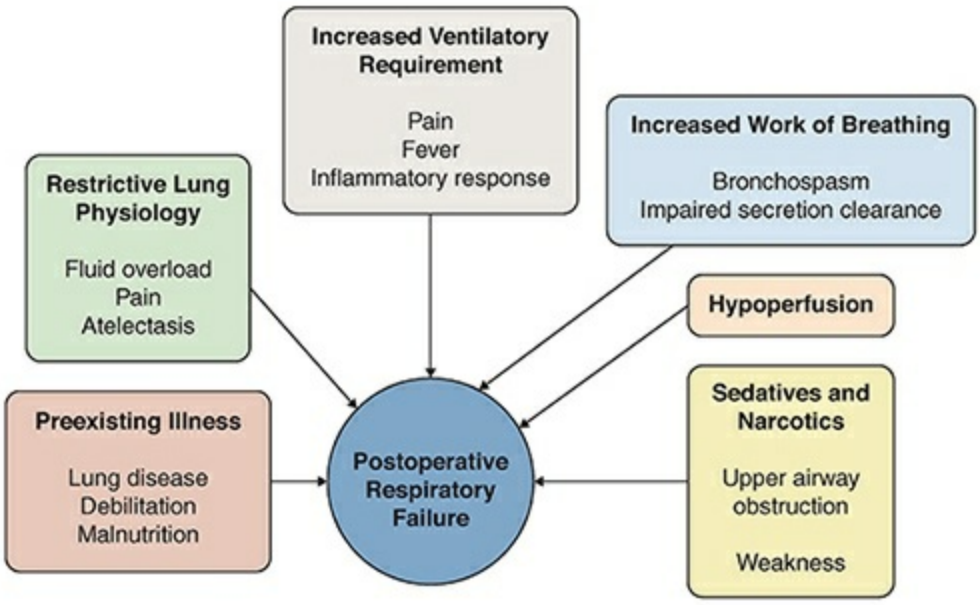

FIGURE 3.1. Pathogenesis of postoperative respiratory failure.

Treating postoperative patients with high concentrations of inspired oxygen can lead to absorption atelectasis. Normally, the consumption of oxygen by peripheral tissues creates a small gradient between the gas tensions in the alveoli and pulmonary capillary blood. The gradient is normally small compared to the total gas tensions because nitrogen is the most abundant gas in both compartments. Nitrogen acts as a pneumatic splint in the lung by limiting the magnitude of the gas tension gradient between the alveoli and pulmonary capillary. Breathing high F_{IO_2} denitrogenates the body and increases the partial pressure of oxygen in alveolar gas much more than in mixed venous blood. Without nitrogen, venous blood becomes very hypobaric relative to alveolar gas. Therefore, high F_{IO_2} increases the gas tension gradient, which drives gas from the alveoli to the pulmonary capillary blood. This promotes the collapse of poorly ventilated alveoli (**Fig. 3.2**).

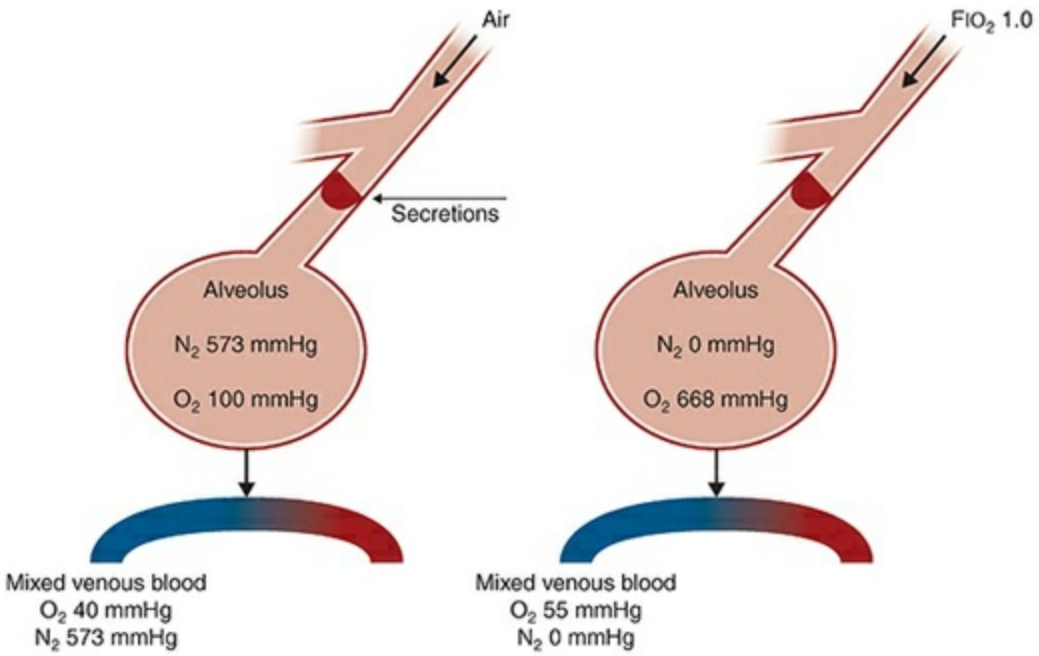

FIGURE 3.2. Nitrogen (N_2) content of inspired air prevents alveolar collapse. On the left, secretions obstruct the airway while the patient was breathing room air. There is a small oxygen (O_2) gradient between the alveolus and mixed venous blood. On the right, secretions obstruct the airway after denitrogenation. As a result, the mixed venous blood is very hypobaric compared with the alveolus. The alveolus will tend to collapse as O_2 rapidly flows down its pressure gradient. CO_2 and H_2O have been omitted for simplicity. (*Adapted with permission from West JB.* Respiratory Physiology. *4th ed. Baltimore, MD: Williams & Wilkins; 1990.*)

In the postoperative period, bronchospasm and impaired mucociliary clearance can decrease the rate of expiratory airflow and increase the work of breathing. Residual sedation and neuromuscular blockade may weaken respiratory muscles and diminish protective muscle tone in the upper airway. Shock causes acidosis and hypoperfusion of respiratory muscles leading to respiratory failure. In particular, clinicians should consider the diagnosis of occult hemorrhage in any postoperative patient who develops respiratory failure. However, the clinician must also consider the opposite problem of fluid overload. Fluid accumulation in the lungs, chest wall, pleura, and peritoneum is a common problem and may decrease respiratory compliance and worsen gas exchange.

The systemic inflammatory response to major surgery or an acute illness will increase rates of tissue oxygen consumption and carbon dioxide (CO_2) production. The increased ventilatory requirement may impose an unsustainable burden on a respiratory system impaired by the aforementioned factors. This is especially true in the setting of debility, malnutrition, and chronic lung disease.

Aubier M, Trippenbach T, Roussos C. Respiratory muscle fatigue during cardiogenic shock. *J Appl Physiol Respir Environ Exerc Physiol*. 1981;51(2):499–508.

West JB. *Respiratory Physiology—The Essentials*. 9th ed. Baltimore: Lippincott Williams & Wilkins; 2012.

B.4. What is the diagnostic approach to postoperative respiratory failure?

The history of the patient's illness provides key evidence for determining the cause of respiratory failure. The clinician should review the past medical history, anesthesia record, operative reports, and perform a careful physical examination. The integration of these data should generate a short list of diagnostic possibilities (**Table 3.1**). Laboratory testing can help exclude or confirm diagnoses.

TABLE 3.1 Differential Diagnosis of Postoperative Respiratory Failure

Aspiration pneumonitis Exacerbation of obstructive sleep apnea	Atelectasis Wound infections Abdominal compartment syndrome	Pneumonia Upper airway obstruction Diaphragmatic palsy from scalene nerve block	Bleeding and shock Neuromuscular weakness	Pleural effusions Exacerbation of underlying lung disorder Acute respiratory distress syndrome	Pulmonary embolism Pulmonary edema

Arterial blood gas analysis can help triage disease severity

and identify alveolar hypoventilation, increased alveolar–arterial oxygen gradient, and acid–base status. Additional labs including complete blood count, metabolic profile, and coagulation parameters are an important part of the early evaluation. Chest x-rays are an essential part of the diagnostic approach to respiratory failure. However, their interobserver variability is high and their diagnostic accuracy is limited in acute respiratory failure.

Point-of-care diagnostic ultrasound can aid the diagnosis of acute respiratory failure (**Table 3.2**). In critically ill patients, pulmonary ultrasound is superior to chest x-ray in identifying pneumothorax, consolidation, pleural effusion, and lung edema. The use of basic echocardiography to identify right or left heart dysfunction can improve diagnostic accuracy. This approach can help distinguish cardiogenic from noncardiogenic causes of pulmonary edema and raise the suspicion for pulmonary embolism. Ultrasonography, like all clinical skills, requires expert training.

TABLE 3.2 Pulmonary Ultrasound Findings

Sliding lung (rules out pneumothorax)	Consolidation	A lines (normal finding)
Lung point (rules in pneumothorax)	B lines (interstitial edema)	Pleural effusion
Diaphragm movement (rules out diaphragmatic palsy)		

Pulmonary emboli (PE) are common in the postoperative period. PE cause tachycardia, tachypnea, and mild hypoxemia. Large PE may cause shock. An abrupt increase in arterial to end-tidal P_{CO_2} gradient can be a sign of increased alveolar dead space from PE. If a clinician suspects PE, a computed tomography (CT) angiography is the best test. Ventilation-perfusion scintigraphy is an alternative if CT angiography cannot be performed. Given the high case fatality rate of untreated PE, therapeutic anticoagulation is indicated when PE is strongly suspected or confirmed. Clinicians must carefully

consider the risk of bleeding from surgery or neuraxial anesthesia sites.

Pneumonia is the most important postoperative infection. Surgery, hospitalization, and illness alter the host's bacterial flora and lead to pneumonia with antibiotic-resistant organisms. A chest x-ray, arterial blood gas, and blood cultures should be obtained in all patients suspected of having health care–associated pneumonia. In the case of ventilator-associated pneumonia, clinical diagnosis may be inaccurate. Quantitative cultures of the lower respiratory tract obtained from bronchoalveolar lavage or protected brushings can assist the diagnosis.

American Thoracic Society, Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med*. 2005;171(4):388–416.

Bataille B, Riu B, Ferre F, et al. Integrated use of bedside lung ultrasound and echocardiography in acute respiratory failure: a prospective observational study in ICU. *Chest*. 2014;146(6):1586–1593.

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Xirouchaki N, Magkanas E, Vaporidi K, et al. Lung ultrasound in critically ill patients: comparison with bedside chest radiography. *Intensive Care Med*. 2011;37(9):1488–1493.

C. Indications for Ventilator Support

The patient has worsening hypoxemia and tachypnea despite treatment with high-flow supplemental oxygen.

C.1. What are the indications for noninvasive positive pressure ventilation (NIPPV)?

NIPPV may be an alternative to endotracheal intubation in some situations. NIPPV can deliver high flow rates of oxygen, maintain PEEP, stent open the upper airway, and unload the work of breathing. Careful patient selection and recognition of contraindications to its use are essential. In this patient, the vomiting due to bowel obstruction is likely a contraindication to a trial of noninvasive ventilation (**Table 3.3**). Generally, the etiology of the respiratory failure and the type of mask interface are more important determinants of treatment success than the mode of NIPPV. The clinical indications with the best supporting evidence for NIPPV are acute cardiogenic pulmonary edema, obstructive sleep apnea, and exacerbations of chronic obstructive pulmonary disease (COPD). In cardiogenic pulmonary edema, the application of positive pressure can markedly reduce left ventricular preload and afterload. Bilevel and continuous positive airway pressure (CPAP) modes are both effective in cardiogenic pulmonary edema. Although there is little data from randomized controlled trials, there is a compelling physiologic rationale for the use of noninvasive ventilation for respiratory failure due to neuromuscular weakness and obesity–hypoventilation syndrome.

TABLE 3.3 Use of Noninvasive Positive Pressure Ventilation in Acute Respiratory Failure

Possible Indications	Contraindications
Increased dyspnea	Respiratory arrest
Tachypnea	Unable to fit/wear mask

Excessive work of breathing	Progressive shock
Hypoventilation	Multiorgan dysfunction
Obstructive sleep apnea	Poor airway protection
Hypercapnia	Recent upper airway or gastrointestinal surgery
Hypoxia	No patient cooperation
	Progressive and severe clinical instability
	Vomiting/hematemesis

Adapted from Nava S, Hill N. Non-invasive ventilation in acute respiratory failure. *Lancet*. 2009;374(9685):250–259. Copyright © 2009 Elsevier. With permission.

The clinical trial data for NIPPV in other causes of postoperative respiratory failure are mixed. A randomized trial compared the use of NIPPV to standard oxygen therapy in patients with hypoxemic respiratory failure within 7 days of abdominal surgery. The use of NIPPV reduced the need for tracheal intubation. However, clinicians must exercise caution when using NIPPV for acute hypoxemic respiratory failure. Although it can help avoid intubation in some situations, about half of the patients treated with NIPPV for ARDS or pneumonia ultimately require intubation. Patients with multiorgan dysfunction are more likely to require intubation. Unfortunately, the largest randomized trial of NIPPV for acute hypoxemic respiratory found no benefit. This trial used CPAP mode, which improved gas exchange. However, there was a markedly increased mortality rate among patients who failed NIPPV. There was also an alarmingly high rate of cardiac arrest during rescue intubation in this setting. This risk is likely due to the sudden derecruitment and loss ventilation during the intubation process.

Delivery of high flow rates of warmed and humidified O_2 via nasal cannulae (HFNC) is increasingly used for acute hypoxemic respiratory failure. The high flow rates limit entrainment of room air and therefore provide more consistent F_{IO_2} than traditional low flow oxygen systems. HFNC can theoretically help wash out the anatomic dead space and provide

a small amount of CPAP, which may decrease work of breathing and improve gas exchange. The exact role of HFNC in acute hypoxemic respiratory failure remains unclear. HFNC has similar contraindications to NIPPV, and there are concerns that its use may delay needed endotracheal intubation.

Antonelli M, Conti G, Moro ML, et al. Predictors of failure of noninvasive positive pressure ventilation in patients with acute hypoxemic respiratory failure: a multi-center study. *Intensive Care Med*. 2001;27(11):1718–1728.

Chiumello D, Chevallard G, Gregoretti C. Non-invasive ventilation in postoperative patients: a systematic review. *Intensive Care Med*. 2011;37(6):918–929.

Delclaux C, L'Her E, Alberti C, et al. Treatment of acute hypoxemic nonhypercapnic respiratory insufficiency with continuous positive airway pressure delivered by a face mask: a randomized controlled trial. *JAMA*. 2000;284(18):2352–2360.

Jaber S, Lescot T, Futier E, et al. Effect of noninvasive ventilation on tracheal reintubation among patients with hypoxemic respiratory failure following abdominal surgery: a randomized clinical trial. *JAMA*. 2016;315(13):1345–1353.

Monro-Somerville T, Sim M, Ruddy J, et al. The effect of high-flow nasal cannula oxygen therapy on mortality and intubation rate in acute respiratory failure: a systematic review and meta-analysis. *Crit Care Med*. 2017;45(4):e449–e456.

Nava S, Hill N. Non-invasive ventilation in acute respiratory failure. *Lancet*. 2009;374(9685):250–259.

C.2. What are the indications for emergency endotracheal intubation?

Endotracheal intubation is performed for impending or actual respiratory failure. The possible indications for emergency endotracheal intubation are shown in **Figure 3.3**. Often, a combination of problems drives the decision to intubate. In borderline situations, a need to transport the patient or a worsening trajectory of acute illness may tip the balance in favor of intubation.

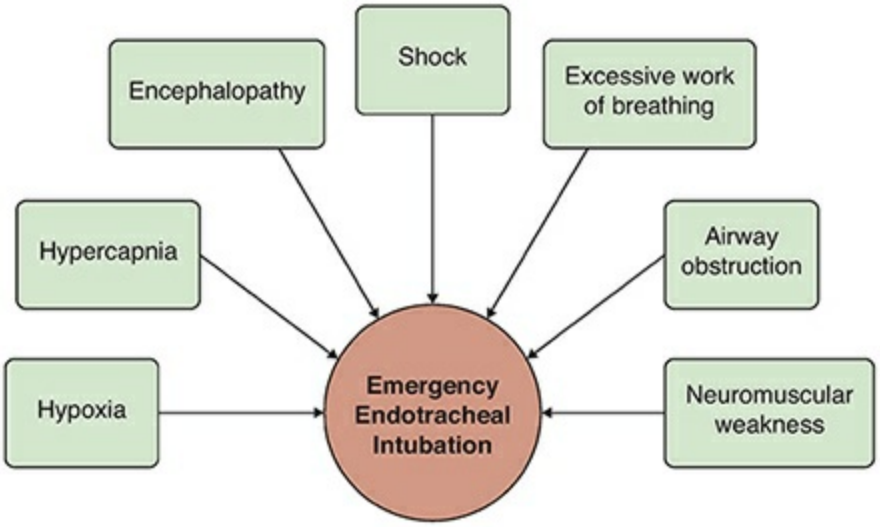

FIGURE 3.3. Possible indications for emergency endotracheal intubation.

Tobin MJ, ed. *Principles and Practice of Mechanical Ventilation*. 3rd ed. New York: McGraw-Hill; 2013:101–136.

D. The Acute Respiratory Distress Syndrome

The patient is intubated for respiratory failure. She has bilateral pulmonary infiltrates on chest x-ray and is severely hypoxemic.

D.1. What is the definition and etiology of the acute respiratory distress syndrome (ARDS)?

ARDS is a clinical syndrome of rapidly progressive respiratory failure characterized by severe hypoxemia and bilateral pulmonary infiltrates. ARDS occurs after or during an insult to the lungs or other organs and is not due to hydrostatic (cardiogenic) edema. The characteristic pathologic finding is diffuse alveolar damage (DAD).

The research definition of ARDS has evolved over time. A previous classification distinguished ARDS from acute lung injury (ALI) based on the severity of hypoxemia. The current consensus is called the Berlin (Germany) definition of ARDS (**Fig. 3.4**). This definition removed the distinction of ALI. This case definition encompasses a number of distinct disease

processes. A significant proportion of patients meeting the diagnostic criteria for ARDS do not have DAD on biopsy or autopsy.

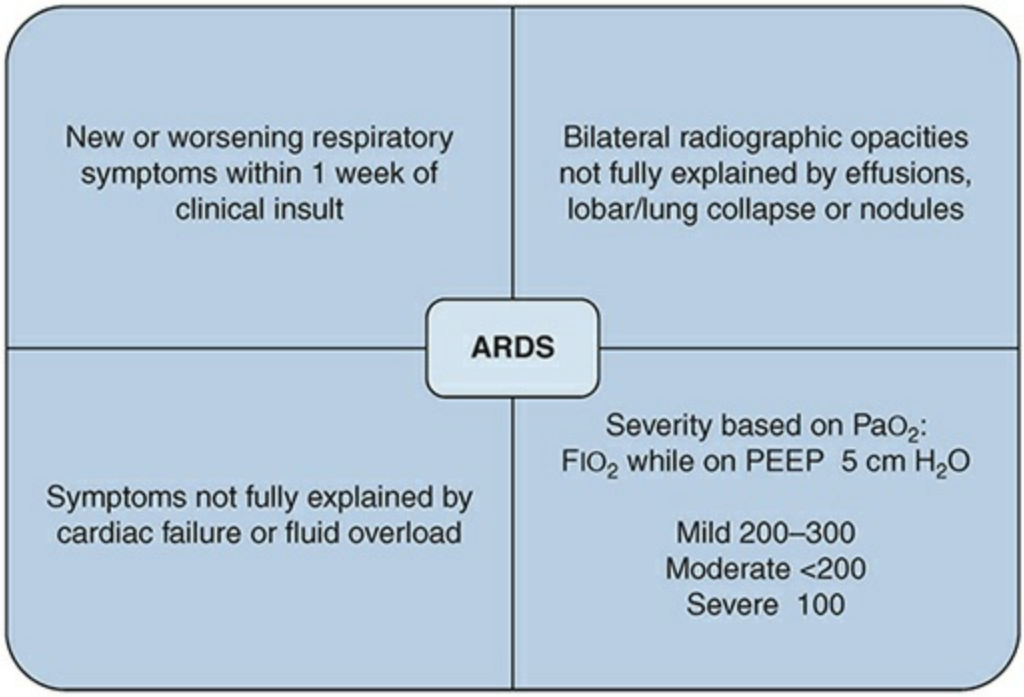

FIGURE 3.4. Definition of the acute respiratory distress syndrome (ARDS). FIO_2, fraction of inspired oxygen; PaO_2, partial pressure of oxygen; PEEP, positive end-expiratory pressure. (*Adapted from Ranieri VM, Rubenfeld GD, Thompson BT, et al. Acute respiratory distress syndrome: the Berlin definition.* JAMA. *2012;307[23]:2526–2533.*)

There are approximately 175,000 cases of ARDS each year in the United States, although the incidence has been decreasing. Worse outcomes are associated with severe hypoxemia, increased dead space, and the presence of concomitant organ failure. The case fatality rate of ARDS has decreased from approximately 40% in the late 1990s to approximately 25% in the mid-2000s; however, unadjusted mortality of those patients with severe ARDS may approach 50%. The most common etiologies of ARDS include pulmonary and nonpulmonary infections, large volume aspiration of gastric contents, trauma, acute pancreatitis, drug reactions, and transfusions of blood

products.

Bellani G, Laffey JG, Pham T, et al. Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. *JAMA*. 2016;315(8):788–800.

Ferguson ND, Fan E, Camporota L, et al. The Berlin definition of ARDS: an expanded rationale, justification, and supplementary material. *Intensive Care Med*. 2012;38(10):1573–1582.

Malhotra A. Low-tidal-volume ventilation in the acute respiratory distress syndrome. *N Engl J Med*. 2007;357(11):1113–1120.

Matthay MA, Ware LB, Zimmerman GA. The acute respiratory distress syndrome. *J Clin Invest*. 2012;122(8):2731–2740.

Ranieri VM, Rubenfeld GD, Thompson BT, et al. Acute respiratory distress syndrome: the Berlin definition. *JAMA*. 2012;307(23):2526–2533.

Rubenfeld GD, Caldwell E, Peabody E, et al. Incidence and outcomes of acute lung injury. *N Engl J Med*. 2005;353(16):1685–1693.

Thille AW, Esteban A, Fernández-Segoviano P, et al. Comparison of the Berlin definition for acute respiratory distress syndrome with autopsy. *Am J Respir Crit Care Med*. 2013;187(7):761–767.

Ware LB, Matthay MA. The acute respiratory distress syndrome. *N Engl J Med*. 2000;342(18):1334–1349.

D.2. Explain the pathophysiology of ARDS.

In ARDS, the alveoli are flooded with a neutrophilic protein-rich edema fluid (**Fig. 3.5**). Dysfunction of the alveolar epithelium and pulmonary capillary endothelium lead to noncardiogenic pulmonary edema. A depletion of functioning surfactant leads to alveolar collapse. The pathophysiologic cascade is incited at the molecular level. Pathogen microbial products (PAMPs) or endogenous damage-associated molecular pattern molecules (DAMPs) activate pattern recognition receptors such as the Toll-like receptors. This activation of innate immunity recruits inflammatory cells to the lung. The regulation of pulmonary inflammation plays a crucial role in both the control of pathogens and lung injury.

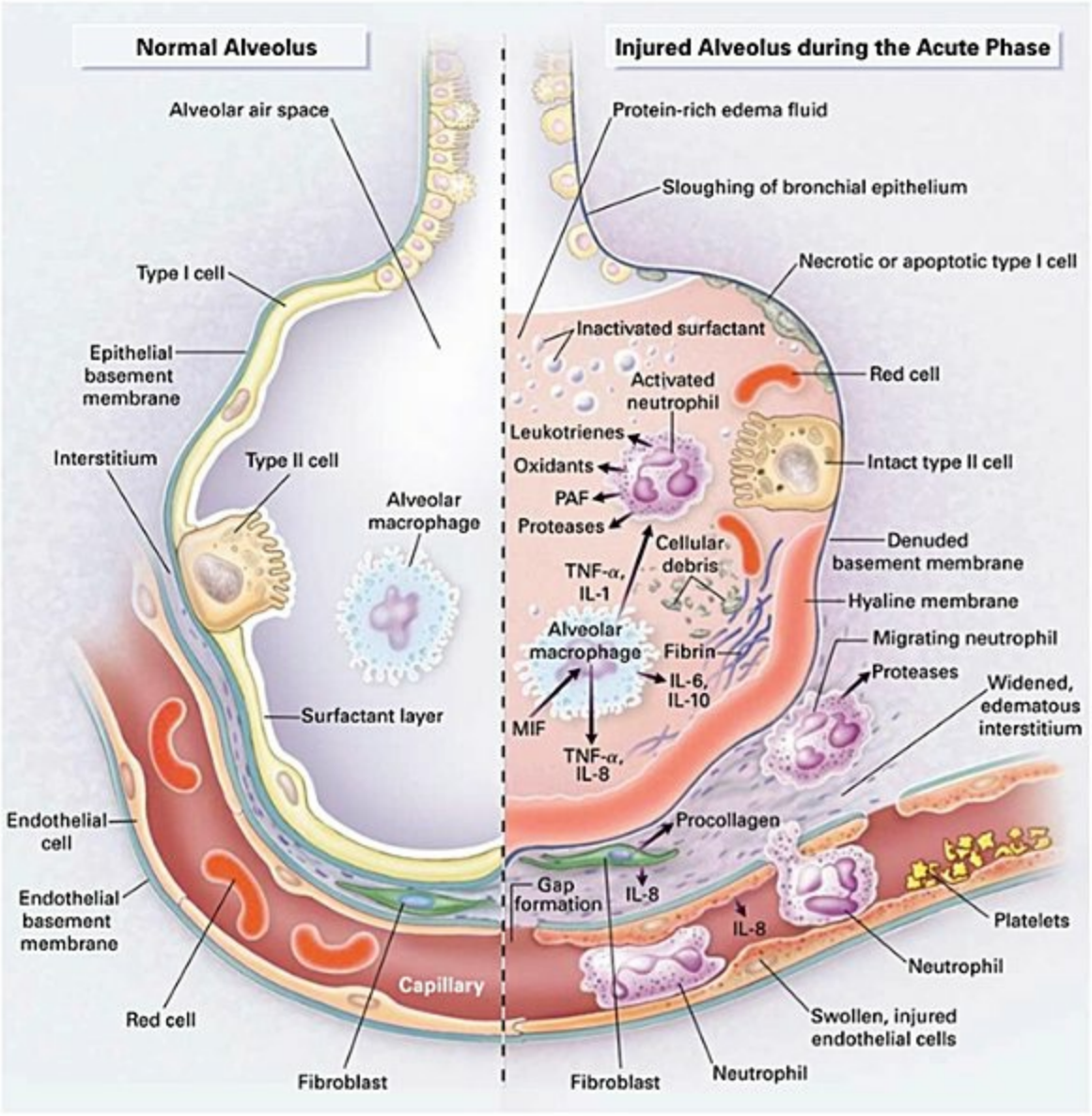

FIGURE 3.5. The pathogenesis of ARDS. IL, interleukin; MIF, macrophage inhibition factor; PAF, platelet-activating factor; TNF-α, tumor necrosis factor-α. (*From Ware LB, Matthay MA. The acute respiratory distress syndrome.* N Engl J Med. *2000;342[18]:1334–1349. Copyright © 2000 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.*)

ARDS progresses through distinct clinical, pathologic, and radiologic phases. The acute exudative phase of ARDS is characterized by severe hypoxemia that is refractory to supplemental oxygenation and often requires invasive mechanical ventilation. Hypoxemia in this early phase is due to

increased shunt fraction. Acute right-sided heart failure is common due to a marked elevation in pulmonary vascular resistance. Hypoxic and hypercapnic pulmonary vasoconstriction, regional atelectasis, and hyperinflation due to mechanical ventilation all contribute to the rise in pulmonary resistance. Radiologically, there are bilateral alveolar infiltrates. CT imaging demonstrates bilateral patchy opacities and dependent consolidation. Pleural effusions are common. ARDS caused by direct lung injury maybe more responsive to higher PEEP strategies. ARDS caused by systemic inflammatory states is associated with more pronounced shock and multisystem organ dysfunction.

The acute exudative phase of ARDS may progress to fibrosing alveolitis, which can appear as linear opacities on chest x-ray. The fibrosis reduces pulmonary compliance and increases dead space. Patients who recover from ARDS may have normal lung function or chronic fibrotic lung disease.

Calfee CS, Delucchi K, Parsons PE, et al. Subphenotypes in acute respiratory distress syndrome: latent class analysis of data from two randomised controlled trials. *Lancet Respir Med*. 2014;2(8):611–620.

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Wiener-Kronish JP, Matthay MA. Pleural effusions associated with hydrostatic and increased permeability pulmonary edema. *Chest*. 1988;93(4):852–858.

D.3. What role does ventilator-induced lung injury (VILI) play in ARDS?

Mechanical ventilation injures the lungs through complex pathophysiologic processes. A variety of illnesses, particularly

ARDS, increase the lung's susceptibility. Rarely, VILI leads to air leaks from the lung into the pleura or mediastinum. However, microscopic injury is a more common problem. The complications of VILI extend beyond the lungs. Excessive alveolar stretch in ARDS increases circulating inflammatory cytokines and injures small bowel and renal epithelial cells. These processes have been linked to progressive multisystem organ failure, which is the most common cause of death in ARDS.

VILI is due to excessive distention of some lung regions and repetitive collapse with shearing of others. "Volutrauma" is the name for the damage caused by excessive lung stretch with large amount of air. Despite its importance, it is difficult to measure the amount of air distending the lungs on mechanical ventilation. This is because ventilators only display the tidal volume—the amount of air delivered or exhaled. Ventilators do not measure the volume of air remaining in the lungs at end expiration (the functional residual capacity). The total lung volume that distends the lungs is the tidal volume plus the functional residual capacity. Because it is not possible to measure this volume, clinicians use the airway pressure at end inspiration as a surrogate marker for the lung's maximum distention by the ventilator. To measure this pressure, the clinician must pause the ventilator cycle momentarily at the end of inspiration to minimize the effect of resistance to airflow. This pause also allows time for the ventilator circuit to better equilibrate with the lungs. The plateau pressure is the pressure in the ventilator circuit during this pause.

The plateau pressure is an imperfect surrogate for the distending pressure of the lung. It is a composite of the force in the airway that distends the lung and the forces adjacent to the lung that may distend or oppose lung inflation. For example, a patient's inspiratory effort distends the lungs yet tends to lower

plateau pressure on volume-controlled ventilation. Conversely, positive pleural pressure from intra-abdominal hypertension and gravitational effects from obesity tend to raise plateau pressure without increasing lung distention. In sum, clinicians should consider both tidal volume and plateau pressure to evaluate the risk of overdistention.

Driving pressure is another way to evaluate the risk of VILI. Driving pressure reflects the relationship between the delivered tidal volume and lung compliance, and high driving pressure suggests a risk of overdistention. In an analysis of randomized trials in ARDS, higher driving pressure had a stronger correlation with mortality than tidal volume. Ventilator techniques that optimize lung compliance and driving pressure may offer some benefit, but this concept requires confirmation.

Amato MB, Meade MO, Slutsky AS, et al. Driving pressure and survival in the acute respiratory distress syndrome. *N Engl J Med*. 2015;372(8):747.

Dreyfuss D, Saumon G. Ventilator-induced lung injury: lessons from experimental studies. *Am J Respir Crit Care Med*. 1998;157(1):294–323.

Imai Y, Parodo J, Kajikawa O, et al. Injurious mechanical ventilation and end-organ epithelial cell apoptosis and organ dysfunction in an experimental model of acute respiratory distress syndrome. *JAMA*. 2003;289(16):2104–2112.

Meade MO, Cook DJ, Guyatt GH, et al. Ventilation strategy using low tidal volumes, recruitment maneuvers, and high positive end-expiratory pressure for acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. *JAMA*. 2008;299(6):637–645.

Schiller HJ, Steinberg J, Halter J, et al. Alveolar inflation during generation of a quasi-static pressure/volume curve in the acutely injured lung. *Crit Care Med*. 2003;31(4):1126–1133.

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E. Management of Mechanical Ventilation

E.1. Which mode of mechanical ventilation will you choose? Describe the features of that mode.

There is no proof that any mode of ventilation is superior in any clinical situation. Aside from avoiding purely assisted modes for passive patients, the choice of mode is largely dictated by physician preference. Choosing appropriate settings for a given mode of mechanical ventilation is more important than the choice of the mode. Therefore, it is essential for clinicians to have a detailed understanding of the settings for the mode they are using.

With traditional controlled mechanical ventilation, the patient had no control over any aspect of the respiratory cycle. Modern controlled ventilation modes can “assist” patients’ respiratory efforts. In assisted modes, the ventilator recognizes the patient’s inspiratory effort by a negative pressure deflection in the ventilator circuit. The ventilator then cycles to inspiration and forces gas into the circuit’s inspiratory limb. Gas is delivered until it reaches a set target of either pressure or volume.

Assist/control with volume targeting is the most commonly used mode in intensive care units worldwide. Inspiration begins when the ventilator recognizes the patient’s inspiratory effort or at a minimum frequency set by a clinician. The ventilator compresses the air sufficiently to deliver a set tidal volume. In general, assist/control volume targeting allows the best assessment of respiratory mechanics. The mode also guarantees the delivery of a minimum minute volume. It also limits tidal volume, which can help avoid alveolar overdistention. However, assist/control with volume targeting may provide insufficient support for a patient with a strong respiratory drive. The tidal volume, duration of inspiration, and inspiratory flow rate are all set by the clinician. The ventilator cannot meet the patient’s demand for an increased tidal volume or faster inspiratory gas flow. Patients with a strong respiratory drive may develop severe dyssynchrony and perform substantial work of breathing on this mode. Dyssynchrony is common with assist/control

volume targeting and is usually due to double or ineffective triggering of inspiration.

With assist/control pressure targeting, the ventilator delivers gas until the pressure reaches a specified target. The volume and rate of gas delivered varies with patient effort and respiratory mechanics. Clinicians must set some criteria of timing of the inspiratory and expiratory cycles (either the inspiratory time or the ratio of the duration of inspiration and exhalation). The usual time of inspiration to prevent dyssynchrony is 0.8 to 1.2 seconds. A virtue of assist/control pressure targeting is that the inspiratory pressure will not exceed the upper limit. Moreover, the patient with high ventilator demand can increase the volume and rate of gas delivery by making stronger inspiratory efforts. However, the ventilator does not guarantee a minimum tidal volume.

Assisted ventilation with pressure targeting is called pressure support. Patients have the most control with this mode because the rate and duration of inspiratory airflow depend on patient effort. This mode is inappropriate for passive apneic patients. Like all pressure-targeted modes, it provides increasing support to match increased patient inspiratory demand. In fact, oversupport is a common cause of dyssynchrony with this mode. In this situation, the patient's strong inspiratory drive causes the ventilator to deliver excessive airflow. This can lead to dynamic hyperinflation if the patient has insufficient time to exhale. Dynamic hyperinflation can lead to ineffective triggering and wasted ventilator effort. In this situation, dyssynchrony may improve with decreasing the inspiratory pressure target. Unlike assist/control pressure targeting, pressure support lacks a set ventilator rate. It also has different criteria for cycling from inspiration to exhalation. The inspiratory flow rate decreases as the patient's effort wanes during inspiration. The ventilator cycles to exhalation when inspiratory flow decreases below a set

threshold.

Synchronized intermittent mandatory ventilation (SIMV) is another popular mode. SIMV is a mixed mode; therefore, it shares the virtues and problems with its constituent modes. It is a combination of assist/control with spontaneous breaths. If the patient does make sufficient respiratory effort, the ventilator delivers controlled ventilation (either volume or pressure targeted). If the ventilator recognizes patient effort, it allows spontaneous ventilation. Spontaneous ventilation may provide improved distribution of gas flow compared with more supported breaths. Moreover, spontaneous breathing mitigates the hemodynamic effects of positive pressure. If there is PEEP, the breaths are CPAP. However, it is difficult for the patient to respond to alternating levels of support by modulating their effort on a breath-to-breath basis. Therefore, patient effort increases on controlled breaths. Many clinicians add pressure support to the spontaneous breaths. This will diminish the effects of spontaneous ventilation on SIMV.

A number of alternative modes are available. Many have refinements so that the ventilator adjusts flow during a breath or on subsequent breaths. Adaptive support ventilation, pressure-regulated volume control, and volume support are some of the options. Neurally adjusted ventilation assist (NAVA) uses a novel strategy; a tube placed from the nose/mouth into the esophagus provides electromyographic analysis of diaphragmatic effort. The ventilator synchronizes respiratory cycling and the magnitude of pressure support to the patient's diaphragmatic contraction. NAVA can improve ventilator patient synchrony because air leaks and dynamic hyperinflation do not obscure the patient's inspiratory efforts. High-frequency oscillating ventilation (HFOV) is an alternative mode that requires a special ventilator. The principle of HFOV is the maintenance of a high mean airway pressure with extremely

brief cycling above and below the mean. The ventilator targets pressure alternating between 70 and 0 cm H_2O at frequency around 4 to 12 Hz. Because the duration of the respiratory cycle is so brief, there is insufficient time for the lungs to equilibrate with the ventilator airway pressure. This results in 1 to 2 mL per kg breaths at a rate of 4 to 12 times per second. These breaths are smaller than the airway's dead space; therefore, HFOV exchanges gas via alternative mechanisms. The increased hemodynamic instability found in the HFOV trial is likely due to the continuously elevated airway pressure. In particular, right ventricular failure commonly complicates HFOV for ARDS. A well-designed randomized controlled trial found that HFOV increased mortality compared with a lung protective ventilation strategy when used as a treatment for adults with ARDS. It is possible that a different HFOV protocol (such as one that targets a lower mean airway pressure) would have a benefit.

There is increasing interest in airway pressure release ventilation (APRV) as a method to improve lung recruitment. This mode provides CPAP at a high level (called "PEEP high) coupled with very brief periods of exhalation. These brief releases incompletely empty the lung and lead to dynamic hyperinflation which raises mean airway pressures leading to lung recruitment. Importantly, APRV allows spontaneous pressure supported breaths during CPAP as well during the releases (called "PEEP low"). The freedom to initiate spontaneous breaths during all phases of the respiratory cycle may improve ventilator–patient synchrony.

At present, there is no proven benefit for any of these alternative modes. In general, pressure-targeted modes create less dyssynchrony than volume-targeted modes when the respiratory drive is strong. However, the settings on the mode affect dyssynchrony more than the choice of mode. For the patient in ARDS, unconventional modes are acceptable as long

as they are employed as part of a lung protective strategy described in the following text.

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E.2. How should you set the fraction of inspired oxygen (FIO_2)?

The FIO_2 is set to maintain sufficient arterial oxygenation. Given the poor solubility of oxygen, the oxygen saturation of hemoglobin rather than the PaO_2 is the more important determinant of arterial oxygen content. For example, a patient without anemia and hemoglobin that is 97% saturated with oxygen will carry 200 mL oxygen in every liter of blood (in

hemoglobin). The same patient will have a Pa_{O_2} 90 mmHg and just 2.7 mL oxygen dissolved in every liter of blood (in the plasma). In ARDS, it is acceptable to target an oxygen saturation of hemoglobin >88%. The F_{IO_2} should be limited as low as possible to avoid oxygen toxicity. The oxygen saturation target should be higher in situations such as intracranial hypertension, right ventricular failure, and systemic vasodilation.

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E.3. How should you set the positive end-expiratory pressure (PEEP)?

PEEP can recruit atelectatic alveoli, prevent cyclical alveolar closure, and decrease shunt fraction (**Fig. 3.6**). There is a theoretical benefit of higher levels of PEEP in severe ARDS. However, high levels of PEEP can decrease venous return and cardiac output. Excessive PEEP also overdistends alveoli leading to VILI and increased pulmonary vascular resistance. The ideal dose of PEEP would maximize respiratory system compliance, gas exchange, patient comfort, and hemodynamics. Unfortunately, the best method to select PEEP for individual patients remains controversial. The trial that established the current standard of care for ventilation in ARDS used a table to determine PEEP based on F_{IO_2} requirement. Multiple trials have failed to demonstrate a better method of PEEP determination than this table. Some clinicians use decremental PEEP trials by serially reducing PEEP after a recruitment maneuver. Other protocols set PEEP according to pressure–volume curves or measurement of transpulmonary gradients by esophageal probes. However, there is currently no evidence that physiologic methods effectively determine the PEEP that recruits lungs in

ARDS. Some protocols emphasize hemodynamic effects such as limiting PEEP based on Doppler analysis of pulmonary artery flow. The average PEEP used for ARDS in clinical settings is around 8 cm H_2O. It is unclear whether or not this is the ideal practice. A recent analysis of studies comparing high versus low PEEP settings showed no significant difference.

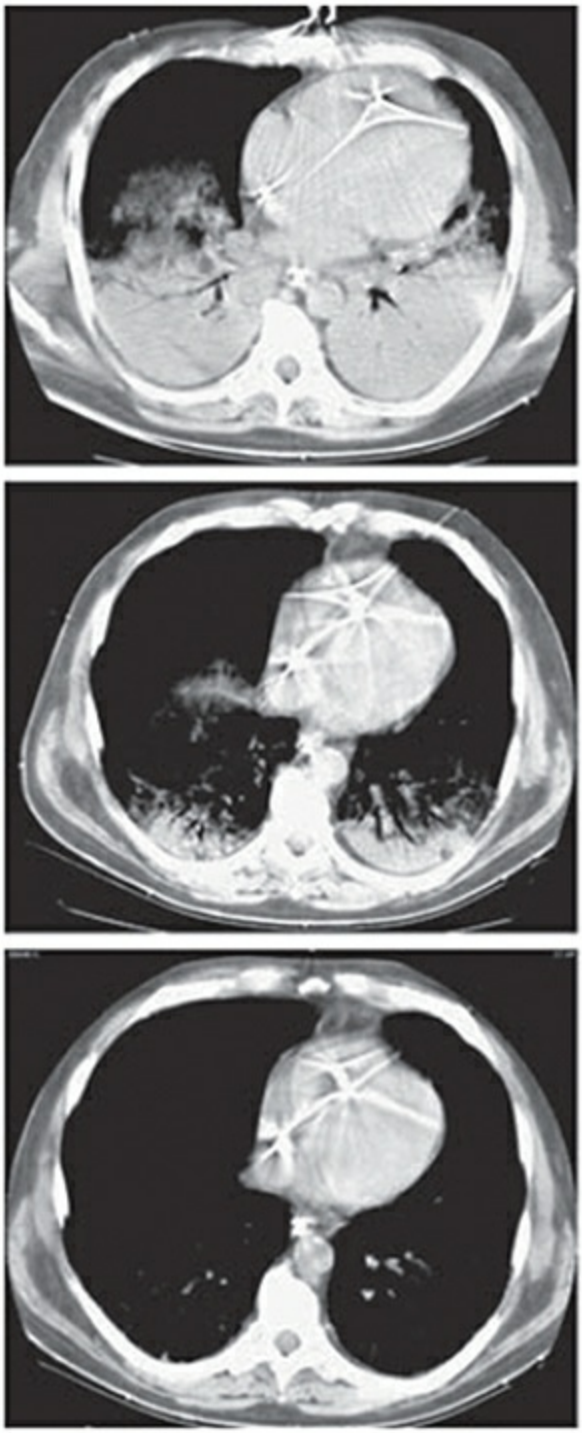

FIGURE 3.6. Lung recruitment in ARDS with progressive increase in PEEP. (*Reprinted with permission of the American Thoracic Society from Borges JB, Okamoto VN, Matos GF, et al. Reversibility of lung collapse and hypoxemia in early acute respiratory distress syndrome.* Am J Respir Crit Care Med*. 2006;174[3]:268–278. Copyright © 2019 American Thoracic Society.*)

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E.4. What tidal volume and inspiratory pressure target should you set?

The approach of limiting tidal volume and plateau pressure has been validated in a landmark randomized controlled trial in patients with ARDS. This technique, called low tidal volume ventilation, significantly reduced organ failure and mortality. Recent data has also looked at the driving pressure (plateau pressure—PEEP) and has demonstrated reduced mortality with decreases in driving pressure. Although low tidal volume ventilation initially worsens gas exchange, it ultimately limits lung and extrapulmonary injury. Therefore, the initial tidal volume or inspiratory pressure should be set to keep the tidal volume <8 mL/kg/IBW and the plateau pressure <30 cm H_2O. Tidal volume and pressure should be incrementally lowered to target 6 mL/kg/IBW and a plateau pressure <30 cm H_2O while monitoring the patient for dyssynchrony and worsening gas exchange (**Table 3.4**). Low tidal volume ventilation may reduce alveolar ventilation and worsen hypercapnia. Increasing

respiratory rate is often insufficient to maintain alveolar ventilation. In fact, the low tidal volume approach may necessitate permitting hypercapnia. Although it may be well tolerated, hypercapnia can constrict pulmonary arterioles and dilate systemic and cerebral arterioles. Tidal volume restriction and hypercapnia can worsen ventilator patient dyssynchrony and double triggering of the ventilator. In this setting, the delivered tidal volumes are much larger than the clinician sets on the ventilator. Moreover, a patient's strong inspiratory effort can overdistend the lungs. On pressure-controlled ventilation, the tidal volumes may be excessive, whereas on volume-controlled ventilation, the plateau pressure may underestimate the distending pressure.

TABLE 3.4 Low-Stretch Lung Protective Ventilator Strategy for Acute Respiratory Distress Syndrome

	Allowable Combinations of PEEP and F_{IO_2}			
	F_{IO_2}	PEEP cm H_2O	F_{IO_2}	PEEP cm H_2O
Ventilator mode: assist/control volume	0.3	5	0.7	14
Initial tidal volume 6 mL/kg predicted body weight	0.4	5	0.8	14
Plateau pressure ≤30 cm H_2O	0.4	8	0.9	14
Respiratory rate 6–35 breaths/min set to achieve pH 7.3–7.45	0.5	8	0.9	16
Ratio of inspiration to expiration 1:1–1:1.3	0.5	10	0.9	18
Oxygenation goal Pa_{O_2} 55–80 mmHg or Sp_{O_2} 88%–95%	0.6	10	1.0	18
	0.7	10	1.0	20
	0.7	12	1.0	22
	0.7	14	1.0	24

F_{IO_2}, fraction of inspired oxygen; Pa_{O_2}, partial pressure of oxygen; PEEP, positive end-expiratory pressure; Sp_{O_2}, peripheral capillary oxygen saturation.

From Brower RG, Matthay MA, Morris A, et al; for Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med*. 2000;342(18):1301–1308. Copyright © 2000 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

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F. Management of Refractory Respiratory Failure

The patient remains hypoxemic on F_{IO_2} of 0.8.

F.1. What else can promote additional lung recruitment?

Recruitment maneuvers rely on the principle that it requires more pressure to inflate an atelectatic lung to a given volume than it does to maintain that volume after exhaling from maximum inflation. To perform a recruitment maneuver, the clinician sets a high level of CPAP for a short time interval (e.g., 40 cm H_2O for 40 seconds). Alternatively, for passively ventilated patients, the extrinsic PEEP can be increased on the ventilator for a short duration. Recruitment maneuvers may prevent or treat derecruitment related to disconnection of the ventilator circuit for suctioning.

Ideally, lung recruitment will reduce the amount of atelectatic lung and decrease shunt fraction. The hallmark of success is an improvement in the ratio of Pa_{O_2} to F_{IO_2}. Recruitment maneuvers share the deleterious effects of all treatments that raise airway pressure. The high level of airway pressure may be sufficient to obstruct venous return and reduce cardiac output as well as cause barotrauma. The benefit of recruitment maneuvers for patients depends on the inherent recruitability of their lungs.

Recruitment maneuvers have been examined in various trials with conflicting results. This may be a result of the heterogeneity of the underlying disease processes as well as differing recruitment protocols. Given the physiologic rationale and benefits on gas exchange, clinicians may consider using recruitment maneuvers on a case-by-case basis especially in a setting of refractory hypoxemia.

Pronation is a recruitment strategy that avoids the deleterious effects of increased positive airway pressure. There are a number of mechanisms by which pronation may exert its benefit. Prone ventilation decreases the volume of lung that is compressed by the heart in the supine position. Pronation also displaces the diaphragm caudally and homogenizes the distribution of the pleural pressure. In ARDS, these mechanisms may recruit lung and decrease alveolar hyperinflation. Pronation may also have multiple effects on hemodynamics. By reducing the airway pressures clinicians set on mechanical ventilation, pronation may improve venous return and lower pulmonary vascular resistance. A large randomized trial demonstrated a survival advantage from prone positioning in severe ARDS. The patients had Pa_{O_2}:F_{IO_2} ratios <150 mmHg and were treated early in their illness for at least 16 hours per day. Other meta-analyses have also demonstrated a survival advantage in severe ARDS.

Providing mechanical ventilation to patients while they sit in a chair or walk is the ideal therapy to recruit lung. Exercise improves cardiac output, lowers pulmonary vascular resistance, and avoids sedation. Similarly, avoidance of deep sedation and neuromuscular blockade can improve recruitment.

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F.2. What rescue strategies can you use for refractory ARDS?

Inhaled nitric oxide (NO) can improve ventilation/perfusion matching in the heterogeneous lungs of ARDS. Inhaled NO distributes to better ventilated lung units where it relieves reflexive hypoxic and hypercapnic vasoconstriction. This effect can improve hypoxia and reduce pulmonary vascular resistance. NO has multiple other effects that may explain the absence of a demonstrable mortality benefit in ARDS. Therefore, the role of inhaled NO, if any, in ARDS should be restricted to refractory

hypoxemia. Similarly, inhaled prostacyclins have also been shown to improve oxygenation but evidence for any improvement in patient outcomes in lacking.

A number of ventilator strategies have been employed to rescue patients with refractory hypoxemia. A common feature is their use of high mean airway pressure to recruit lung. HFOV, APRV, and inverse ratio ventilation all employ a brief expiratory phase. This prevents exhalation and maintains high intrathoracic pressure throughout the respiratory cycle. With HFOV and APRV, the goal is to create auto-PEEP. It is unclear if any of these ventilator strategies offer any advantage over setting a high level of extrinsic PEEP on a conventional mode of ventilation. Recruitment maneuvers may also improve oxygenation. These are brief intervals (30 to 40 seconds) of high PEEP or CPAP (30 to 40 cm H_2O). Any of the strategies using high inflation pressures for lung recruitment may cause hemodynamic instability and barotrauma.

Extracorporeal gas exchange is also being evaluated as a rescue strategy for refractory ARDS. One approach is extracorporeal CO_2 removal, which requires relatively low blood flow rates. CO_2 removal can theoretically increase the gas tension available for oxygen in the alveoli and allow a reduction in tidal volume. A more aggressive strategy is venovenous extracorporeal membrane oxygenation (VV ECMO). It requires high blood flow rates and can reduce the CO_2 content and raise the oxygen content of mixed venous blood. VV ECMO can improve hemodynamics in ARDS by reducing hypoxic/hypercapnic pulmonary vasoconstriction and the magnitude of positive airway pressure required from mechanical ventilation. A randomized trial done at multiple centers in England demonstrated a survival advantage for patients with severe ARDS who were transferred to an ECMO center. There

was also better than expected survival for patients with severe ARDS due to influenza when treated with ECMO. Bleeding and vascular complications are its main side effects. A recent trial showed no statistically significant difference in mortality in patients with severe ARDS receiving ECMO versus conventional ventilation. However, there was a trend toward lower 60-day mortality in the ECMO group and the study was stopped early because of this benefit that in later analysis was not statistically significant. Patients receiving early ECMO had a higher survival as opposed to late (i.e., rescue) use of ECMO.

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G. Adjunctive Management of Respiratory Failure

Since intubation, the patient has become hypotensive.

G.1. What is the cause and treatment of the hemodynamic

instability associated with mechanical ventilation?

Hemodynamic instability is a common complication of emergency airway management and the institution of mechanical ventilation. Positive pressure ventilation can decrease the pressure gradient for venous return to the heart, thereby reducing cardiac output. Normally, circulatory reflexes will constrict the veins to restore venous return. However, sedatives and narcotics used to facilitate endotracheal intubation can blunt the autonomic response. Even low levels of positive pressure ventilation can reduce cardiac output in anesthetized postoperative patients, particularly if they have normal or reduced circulating blood volume. Fluid resuscitation and catecholamine vasopressors can raise the venous pressure and restore the pressure gradient for venous return and cardiac output. Many patients with ARDS require a positive fluid balance during the first 48 hours of mechanical ventilation to counteract the hemodynamic effects of PEEP and sedatives/narcotics.

Although diminished venous return is the most likely cause of hemodynamic instability, it is essential to consider acute cor pulmonale as an alternative explanation. The hypoxia, hypercarbia, and regional atelectasis associated with ARDS all raise pulmonary vascular resistance. Mechanical ventilation in ARDS may lead to areas of hyperinflation of the more normal lung regions. Hyperinflation raises pulmonary vascular resistance by compression of the capillaries in the alveolar septa. The severe rise of pulmonary vascular resistance can lead to right ventricular failure, particularly if the patient has had significant intravascular fluid resuscitation. The pressure rises in the right ventricle because it is unable to efficiently pump blood through the pulmonary vasculature. The incidence of acute cor pulmonale is as high as 50% in patients on mechanical ventilation for ARDS. The use of low-stretch ventilation and

limitation of PEEP can lower this risk. The presence of markedly elevated central venous pressure as well as echocardiographic evidence of dilated right ventricular size with flattening of the interventricular septum suggests the diagnosis of acute cor pulmonale. Respirophasic variation in pulse pressure or inferior vena cava diameter does not predict an increase in cardiac output with fluid resuscitation when right-sided heart failure is present. In acute cor pulmonale, vasopressors can raise the systemic blood pressure to maintain the coronary perfusion to the right ventricular myocardium. Diuresis can help optimize right ventricular preload. The ventilator should be adjusted to prevent extremes of lung hyperinflation and provide sufficient PEEP to recruit poorly ventilated lung regions. Pulmonary vasodilators may be needed.

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G.2. What is the adjunctive medical therapy for ARDS?

After the initial resuscitation phase, many patients with ARDS require a different approach to fluid balance. The Fluids and Catheters Treatment Trial (FACTT) evaluated two fluid strategies instituted after the first 48 hours. With the “restrictive fluid” approach, patients received diuretics if they had oliguria and adequate perfusion. The “restricted fluid” approach group had better gas exchange and a shorter duration of mechanical ventilation than the “liberal fluid” group. There was no increase in hemodynamic instability or renal failure with a restrictive fluid approach. FACTT had a two-by-two factorial design and simultaneously demonstrated that routine use of pulmonary artery catheterization did not improve outcomes in ARDS. Therefore, clinicians should target even or slightly negative net fluid balance once patients have achieved hemodynamic stability and to avoid routine use of pulmonary artery catheters.

Severe anemia can diminish oxygen delivery. However, red blood cell transfusions are linked to a wide range of complications including nosocomial pneumonia. Moreover, red blood cell transfusions have a limited capacity to improve oxygen consumption in critically ill patients. Although there is no specific randomized trial data in ARDS, it is reasonable to limit red blood cell transfusions in adequately perfused patients with isovolemic anemia unless the hemoglobin concentration is less than 7 g per dL.

Numerous trials have evaluated the ability of medications to modulate the natural history of ARDS. The support for systemic corticosteroids has waxed and waned for decades. The largest and highest quality randomized controlled trial found that corticosteroids offered no benefit and increased mortality if started after the first 2 weeks of ARDS. However, other analyses have shown improvement in mortality or time to resolution of ARDS. Currently, the evidence does not support the routine use of corticosteroids for ARDS. However, the Society of Critical Care Medicine (SCCM) and European Society of Intensive Care Medicine (ESICM) 2017 guideline does suggest the use of intravenous methylprednisolone 1 mg/kg/day in patients with early moderate-to-severe ARDS (Pa_{O_2}/F_{IO_2} <200 and within 14 days of onset).

A number of other disease-modifying agents have been studied in ARDS. Rosuvastatin, a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (statin), had no benefit in a much anticipated trial. Recombinant activated protein C and ω-3 fatty acids also had no benefit. Theoretically, inhaled β-agonists would decrease lung edema and lung inflammation. However, no randomized trial has shown a benefit. Their use should be restricted to treating bronchospasm. Mesenchymal stem cell therapy is currently the most promising therapy entering clinical trials.

Patients with severe respiratory failure often have a strong respiratory drive due to increased metabolic rates and dead space. This high demand for minute ventilation can lead to intolerance of low stretch ventilation. In these situations, deep sedation and neuromuscular blocking agents can blunt excessive respiratory effort and enforce low stretch ventilation. Moreover, neuromuscular blockade can reduce metabolic demand which may be helpful when oxygen delivery and carbon dioxide clearance are inadequate. However, neuromuscular blockade and

deep sedation may worsen delirium and muscular weakness. Surprisingly, a meta-analysis of three trials of neuromuscular blockade for ARDS did not find an increase in neuromuscular weakness. To help define the role of neuromuscular blockade, two high-quality randomized controlled trials of patients with early ARDS and severe hypoxemia have been performed. Both trials randomized patients to either cisatracurium besylate or placebo. Cisatracurium is useful in critical illness because it is cleared by a plasma esterase. The control group of the initial study received deep sedation, whereas the control group in the second was treated with lighter sedation targets. Rescue use of neuromuscular blockade was allowed in both studies to treat double triggering and overt ventilator dyssynchrony. The first study demonstrated that cisatracurium improved gas exchange, barotrauma, and mortality compared with placebo. The second study did not confirm this benefit. As a result, the exact role for neuromuscular blockade in ARDS remains unclear. One approach is to avoid the routine use of cisatracurium for ARDS and reserve it for patients with severe respiratory failure as well as strong respiratory efforts and dyssynchrony with mechanical ventilation.

A growing body of evidence supports limiting sedative use in patients on mechanical ventilation. In the absence of a compelling need for sedatives (e.g., status epilepticus), clinicians should interrupt continuous sedatives and neuromuscular blocking agents at least daily. This approach is associated with a marked reduction in duration of mechanical ventilation. Reassuringly, this approach is also associated with improved long-term neuropsychiatric function among survivors of respiratory failure. Another strategy uses a detailed sedation protocol to avoid oversedation. Sedatives can contribute to delirium and disuse muscle atrophy. Moreover, clinicians may fail to recognize that their deeply sedated patients may be able to

breathe without ventilator support. Sedation is not restorative sleep. Narcotics are still necessary for pain and dyspnea, and neuroleptics can be used for agitated delirium. Deeper sedation could be reserved for situations when severe agitation occurs or pronation is required. Treatment plans that limit sedative use require clinicians to provide calming, reassurance, repositioning, and ventilator adjustment to assure patient comfort. The study that validated the avoidance of routine sedatives for patients on mechanical ventilation used one-to-one bedside nursing and continuous presence of an intensivist in the intensive care unit.

Limiting sedation allows physical therapy. Patients may perform full physical therapy including walking while breathing through an endotracheal tube and a portable ventilator. The theoretical benefit of this approach is to decrease muscular atrophy, sedative requirements, and delirium.

The evolving treatment paradigm is to use deep sedation, narcotics, and neuromuscular blockade early in the course of severe ARDS in patients with excessive ventilator demands and ventilator dyssynchrony. Patients may require pronation during this phase. Clinicians should switch to the opposite approach of limited sedation as soon as there is stabilization. This includes limited or no sedation (aside from opiates for relief of pain or dyspnea) and physical therapy. This approach should also be used when the ARDS is less severe.

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H. Liberation of the Patient from Mechanical Ventilation

The patient slowly recovers over the next 3 days.

H.1. Explain the importance of the decision to extubate the patient or continue mechanical ventilation.

Unnecessarily, prolonged mechanical ventilation can lead to pneumonia, delirium, and neuromuscular weakness. Unfortunately, clinicians may not recognize that a substantial number of their mechanically ventilated patients are capable of breathing without ventilator support. Conversely, the mortality rate associated with reintubation is extremely high. Intensive care unit patients fail extubation at rates of 15% to 20%. The risk is substantially higher in patients with chronic illnesses. Patients who suffer extubation failure are 7 times more likely to die, and the survivors are much more likely to require long-term care. Reintubation is associated with nosocomial pneumonia, although it is unknown whether the pneumonia is the cause or effect of reintubation. Therefore, the decision of whether or not to extubate a patient is one of the most important challenges facing anesthesiologists. There is extensive literature and great

controversy surrounding the topic, and the strategies employed to liberate patients from mechanical ventilation vary widely.

Epstein SK, Ciubotaru RL, Wong JB. Effect of failed extubation on the outcome of mechanical ventilation. *Chest*. 1997;112(1):186–192.

Esteban A, Anzueto A, Alía I, et al. How is mechanical ventilation employed in the intensive care unit? An international utilization review. *Am J Respir Crit Care Med*. 2000;161(5):1450–1458.

Thille AW, Harrois A, Schortgen F, et al. Outcomes of extubation failure in medical intensive care unit patients. *Crit Care Med*. 2011;39(12):2612–2618.

H.2. How will you prepare the patient for liberation from the ventilator?

The most important aspect of liberation from mechanical ventilation is the general care of the patient and the reversal of the cause of the patient's respiratory failure. Early in the course of an acute illness, the patient must be resuscitated out of shock. Generally in later stages, volume overload and hypertension must be avoided. This is especially important during the switch to negative pressure ventilation, which increases cardiac preload and left ventricular wall tension. Adequate protection against the development of coronary ischemia should be ensured in patients with significant coronary artery disease. The neurologic status should be optimized with the goal of maintaining airway protection and patency as well as adequate respiratory drive and strength. Sedation should be limited and reversed at least daily. Delirium should be avoided and treated.

Clinicians should aggressively reduce the F_{IO_2} and PEEP to the minimum acceptable level. Derecruitment happens quickly after reducing PEEP, so lengthy weaning may be unnecessary.

Chiumello D, Coppola S, Froio S, et al. Time to reach a new steady state after changes of positive end expiratory pressure. *Intensive Care Med*. 2013;39(8):1377–1385.

H.3. How will you recognize when the patient is ready for

extubation?

Traditionally, once FIO_2 and PEEP were at minimal settings, clinicians would assess patients for their ability to undergo a weaning trial. Tests of weaning readiness were used to identify patients in whom it was safe to reduce ventilator support. These tests included objective measures such as the negative inspiratory force, vital capacity, and the rapid shallow breathing index (RSBI). The research literature makes a clear distinction between these tests of weaning readiness and tests of extubation readiness (such as a prolonged T-tube trial as discussed in the following text). The best validated test to predict readiness for weaning is the RSBI. This test was performed by switching patients from assist control ventilation to a T-tube. A spirometer attached to the end of the endotracheal tube measured the tidal volume, and the respiratory rate was counted. Patients with ratios of <105 could safely go on to a test of extubation readiness with a T-tube trial lasting up to 2 hours. However, there is no clear advantage to performing a test of weaning readiness (such as the RSBI calculation) prior to initiating a test of extubation readiness. Instead, clinicians can perform daily clinical screening of patients on mechanical ventilation to assess them for extubation readiness (**Table 3.5**).

TABLE 3.5 Clinical Screening Criteria for Extubation Readiness

Adequate level of alertness	Cause of respiratory failure improving
PaO_2/FIO_2 ≥150 or SpO_2 ≥90% on FIO_2 ≤0.4	Able to initiate an inspiratory effort
PEEP ≤5 cm H_2O	Hemodynamic stability
	Absence of refractory acidemia

FIO_2, fraction of inspired oxygen; PaO_2, partial pressure of oxygen; PEEP, positive end-expiratory pressure; SpO_2, peripheral capillary oxygen saturation.

The purpose of clinical screening is to determine a pretest probability of extubation success. The pretest probability of success will be extremely low in the presence of clinical signs

that clearly predict extubation failure. These signs include shock, severe intracranial hypertension, requirement of high F_{IO_2} or PEEP, and the absence of protective airway reflexes or spontaneous inspiratory efforts. If the pretest probability of extubation success is extremely low, there is no additional test that would be able to raise the posttest probability of success sufficiently to allow extubation. In these situations, the clinician should continue mechanical ventilation, treat the cause of the respiratory failure, and repeat the screening at least daily. Similarly, clinicians also should not perform tests of extubation readiness in situations where the pretest probability of extubation success is very high. These situations include patients who had been intubated for a brief and uncomplicated procedure as well as those intubated for a sedative overdose that has resolved. When clinicians calculate a very high pretest probability of extubation success, they can proceed directly to extubation without testing.

When there is an intermediate pretest probability for extubation success, clinicians should consider performing tests of extubation readiness. These tests simulate the conditions of spontaneous breathing after extubation. The most common tests are T-tube, CPAP, pressure support ventilation, and flow-by ventilation. The appearance of tachypnea, hemodynamic instability, diaphoresis, anxiety, or agitation signifies failure of the test. If the patient tolerates it, the trial continues for 30 to 120 minutes. Clinicians should consider extubation if the patient passes the trial. It is unclear there is a single best approach to test for extubation readiness. A recent trial fund that pressure support ventilation for 30 minutes was superior to 120 minutes of unassisted breathing via T-tube. Importantly, the vast majority of critically ill patients who undergo these tests are able to sustain spontaneous breathing after extubation. There are, however, important physiologic differences between the

methods. Given the varied causes of extubation failure, the utility of the different tests may vary in different situations. For example, in patients with significant heart disease, it is important to predict the consequences of switching from positive to negative pressure ventilation that occurs with extubation. Because positive pressure ventilation decreases cardiac preload and left ventricular afterload, extubation readiness testing performed with CPAP or minimal pressure support may not be predictive of success. Tests using T-tube or "flow-by" ventilation (with pressure support and PEEP set to 0 cm H_2O) better simulate the hemodynamic stressors of breathing after extubation (**Fig. 3.7**). There are concerns about T-tubes imposing an unfair resistive load due to its narrow diameter. In one series, T-tube trials failed to identify a number of patients capable of successfully breathing after extubation. However, T-piece trials using size 7 to 8.5 endotracheal tubes accurately predict the work of breathing after extubation in critically ill patients. T-tube trials add the expense of the humidification and tubing attachments to the oxygen source. Moreover, the T-piece trials do not benefit from ventilator alarms.

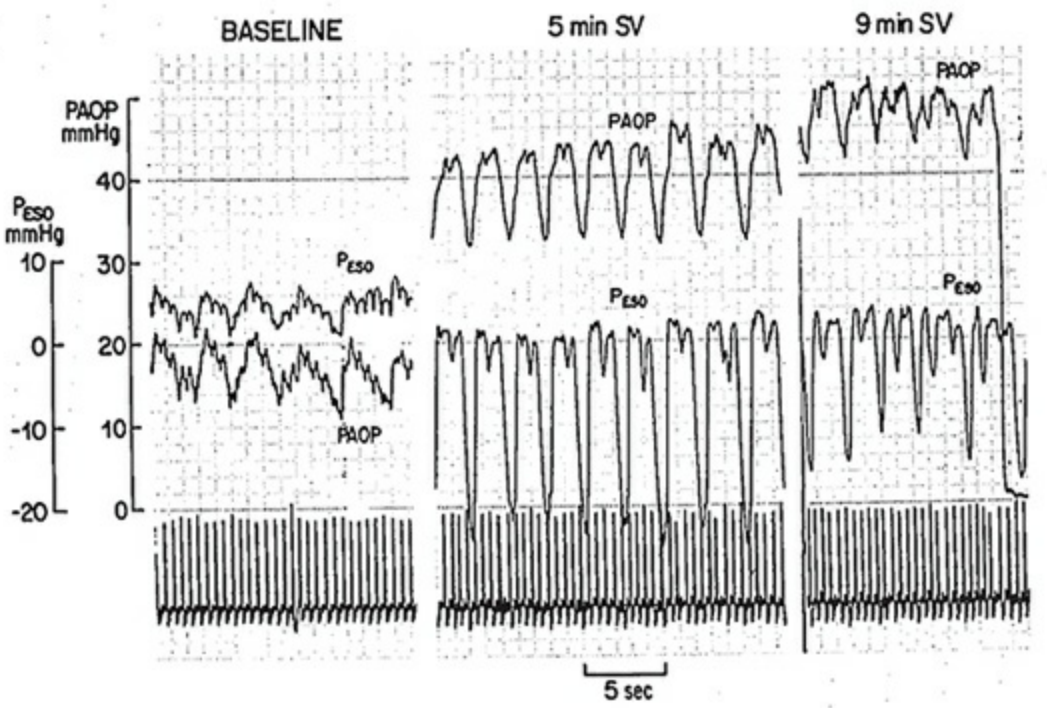

FIGURE 3.7. Ventricular failure and pulmonary edema precipitated by spontaneous ventilation. At baseline **(left)**, the patient is on positive pressure ventilation. During spontaneous ventilation (SV), the esophageal pressure (P_{ESO}) is negative during inspiration and the pulmonary artery occlusion pressure (PAOP) rises. By 9 minutes, the PAOP is catastrophically elevated and respiratory muscle fatigue decreases the amplitude of P_{ESO}. (*Reprinted with permission from Lemaire F, Teboul JL, Cinotti L, et al. Acute left ventricular dysfunction during unsuccessful weaning from mechanical ventilation.* Anesthesiology. *1988;69[2]:171–179.*)

Trials with pressure support theoretically overcome the resistance imposed by the ventilator circuit. However, the amount of pressure support required is unclear. These trials may underestimate the work of breathing after extubation. The opposite phenomenon is also important. Pressure support may create dyssynchrony on mechanical ventilation. In particular, oversupport may induce tachypnea. Clinicians may misinterpret tachypnea to mean that the patient cannot be extubated. This may lead to needlessly prolonged mechanical ventilation. Automatic tube compensation software is designed to improve the application of minimal pressure support during tests of extubation readiness. However, at present, there is no proof of advantage for this approach in clinical trials.

In place of tests of readiness for extubation, some clinicians prefer to gradually wean ventilator support. Pressure support can be incrementally reduced or the number of controlled breaths reduced on SIMV. However, there is no proof that any ventilator strategy or weaning process trains and strengthens respiratory muscles. Moreover, in clinical trials, these methods prolong the time to extubation. The importance of liberation as opposed to weaning from mechanical ventilation is illustrated by a clinical trial, which showed that pairing a once daily awakening from sedatives with a trial of spontaneous ventilation reduces mortality.

A final step prior to extubation is to consider the risk of postextubation stridor. The cuff leak test is an imperfect predictor. Clinicians should only consider using it when there are risk factors for laryngeal edema such as prolonged intubation, large endotracheal tube, asthma, traumatic intubation, and ventilator patient dyssynchrony.

In situations such as COPD or congestive heart failure, extubation directly to prophylactic NIPPV may reduce the need for reintubation. However, these patients must be carefully reevaluated to make sure they are not dependent on NIPPV for excessive periods of time, preventing effective nutrition and physical therapy.

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4 Lung Transplantation

Choy Lewis, Ryan Hood, and Charles W. Hogue

A 63-year-old woman with progressively worsening dyspnea on exertion and limited functional capacity despite maximal treatment with medication, pulmonary rehabilitation, and supplemental oxygen therapy is scheduled for bilateral sequential lung transplantation. Laboratory, radiographic, and spirometric data are consistent with severe obstructive pulmonary disease. Other significant medical findings include a 30 pack-year history of smoking (although none for 10 years), mild hypertension (145/86 mmHg), mild pulmonary hypertension (mean pulmonary arterial pressure, 32 mmHg), normal left and right ventricular function, and osteoarthritis.

A. Medical Disease and Differential Diagnosis

1. What are the expected manifestations of severe obstructive pulmonary disease in this patient, and why is she a transplant candidate?
2. What other end-stage lung diseases can also be treated with transplantation?
3. How many lung transplantations have been performed?
4. What are the selection criteria for recipients?
5. How is the decision made to transplant one or both lungs, and does this influence preoperative management?

6. How does a single-lung transplantation (SLT) differ technically from a bilateral-lung transplantation (BLT)?

B. Preoperative Evaluation and Preparation

1. What preoperative evaluation is desirable?
2. Would you premedicate this patient? If so, how?
3. What vascular access is appropriate?
4. Is preoperative epidural catheter placement advantageous?

C. Intraoperative Management

1. What special equipment is necessary?
2. How would you monitor this patient?
3. How would you induce anesthesia in this patient?
4. How would you ventilate this patient? What kind of endotracheal tube would you use?
5. How does the physiology of single-lung ventilation influence the procedure?
6. How does single-lung ventilation affect cardiopulmonary function? What are the problems of single-lung ventilation in this patient? How would you treat them?
7. What problems are associated with the lateral position?
8. Should volatile anesthetics be avoided during single-lung ventilation?
9. At what specific points in the procedure are problems anticipated?
10. How would you deal with problems related to clamping of the pulmonary artery (PA)?
11. What hemodynamic alterations would you expect during graft implantation and reperfusion? How would you correct them?
12. When is cardiopulmonary bypass (CPB) necessary for lung transplantation?
13. Should fluid administration be restricted, and are blood products commonly required?
14. Would you extubate the patient upon conclusion of the

procedure?

D. Postoperative Management

1. What are the major complications after lung transplantation?
2. How is postoperative ventilation managed, and for how long is it required?
3. What special precautions should be taken when a lung transplant recipient requires general anesthesia for subsequent nonpulmonary surgery?
4. What are the long-term outcomes of lung transplantation?
5. Are there surgical alternatives to lung transplantation?

A. Medical Disease and Differential Diagnosis

A.1. What are the expected manifestations of severe obstructive pulmonary disease in this patient, and why is she a transplant candidate?

Severe obstructive pulmonary disease results in increased airway resistance, reduced expiratory flow rates, and high residual lung volumes. There is a point at which the expiratory airway obstruction and lung hyperinflation become so severe that the chest wall cannot physically expand to accommodate a normal tidal volume, resulting in restrictive physiology superimposed on obstructive disease. This condition is usually refractory to medical management and substantially limits daily activity. This patient's age, the severity and progression of her disease despite maximal therapy, and the lack of contraindications support referral for lung transplant candidacy.

The International Society of Heart and Lung Transplantation (ISHLT) guidelines state that chronic obstructive pulmonary disease (COPD) patients can be recommended for lung transplantation if they demonstrate disease progression despite maximal medical therapy; hypoxemia (Pa_{O_2} <60 mmHg) or

hypercapnia ($PaCO_2$ >50 mmHg); forced expiratory volume in 1 second (FEV_1) <25% predicted; and body mass index, obstruction dyspnea, and exercise capacity (BODE) score 5 to 6 and are not candidates for lung volume reduction surgery (LVRS); simultaneous evaluation for lung transplant and LVRS is appropriate. The BODE index is a multivariate assessment that combines body mass index, FEV_1, the Modified Medical Research Council Dyspnea scale, and 6-minute walk test (6MWT) into a weighted 10-point score that is correlated to mortality in COPD. To be listed for transplant COPD, patients must meet one of more of the following criteria: (1) BODE index ≥7, (2) FEV_1 <15% predicted, (3) three or more severe exacerbations during the preceding year, (4) acute hypercapnic respiratory failure, or (5) concomitant moderate to severe pulmonary hypertension.

Historically, SLT has been used for patients with COPD and interstitial lung disease (ILD). There has been a progressive decline in the use of SLT for COPD due to concerns for the development of significant ventilation/perfusion mismatch from hyperinflation of the native lung and mediastinal displacement. In addition, there is a body of evidence showing a survival benefit and improved functional outcomes with double-lung transplantation (DLT) for COPD patients when compared to SLT in this patient population. Conversely, numerous studies have shown no difference in outcomes in COPD patients who had a single-lung transplanted versus those who had DLT or BLT. Clinical experience has also demonstrated that many patients with COPD can be successfully treated with SLT. With a severe shortage in organs for transplant, single-lung transplant has been advocated as a way to increase the number of recipients. The decision for SLT or BLT remains controversial and is based on the individual situation taking into account

regional organ allocation policies, individual center experience, and organ availability. Lung transplantation, when successful, significantly improves quality of life and survival for patients with severe COPD.

Martin AK, Renew JR, Jayaraman AL, et al. Analysis of outcomes in lung transplantation. *J Cardiothorac Vasc Anesth*. 2019;33(5):1455–1466.

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Weill D, Benden C, Corris PA, et al. A consensus document for the selection of lung transplant candidates: 2014—an update from the pulmonary transplantation council of the International Society for Heart and Lung Transplantation. *J Heart Lung Transplant*. 2015;34(1):1–15.

A.2. What other end-stage lung diseases can also be treated with transplantation?

The first successful (i.e., the patient left the hospital) SLTs were performed in 1983 for idiopathic pulmonary fibrosis. Since that time, the procedure has been applied to patients suffering from various end-stage pulmonary diseases (**Table 4.1**). In general, the underlying disease processes that produce lung dysfunction can be broadly characterized as obstructive, restrictive, infectious (e.g., cystic fibrosis and bronchiectasis), or vascular. As of 2008, most SLTs have been performed for obstructive lung disease, followed by idiopathic pulmonary fibrosis. The most common indications for BLT are cystic fibrosis and obstructive lung disease.

TABLE 4.1 Lung Transplants Categorized by Disease

End-Stage Lung Disease	Single-Lung Transplant (% of Total)	Bilateral-/Double-Lung Transplant (% of Total)
Cystic fibrosis	1.5	24.9

Retransplant	3.4	2.3
Idiopathic pulmonary arterial hypertension	0.6	4.4
α_1-Antitrypsin deficiency	5.0	5.9
Sarcoidosis	1.8	2.9
Interstitial lung disease	34.9	18.2
Emphysema/chronic obstructive pulmonary disease	43.0	26.6
Miscellaneous	4.5	5.9

Reflecting a loss of lung parenchymal elasticity and compliance, *end-stage restrictive disease* is characterized by profoundly reduced lung volumes and diffusing capacity but relative preservation of ventilatory flow rates. Comparisons of flow–volume loops representing obstructive and restrictive diseases are shown in **Figure 4.1**. The underlying disease process also tends to obliterate pulmonary microvasculature, thereby chronically increasing vascular resistance, producing pulmonary hypertension, and predisposing to cor pulmonale. Most patients with restrictive disease are good candidates for an SLT because the stiff, vasoconstricted native lung will receive relatively little ventilation and perfusion and can therefore usually be left without compromising the transplanted lung.

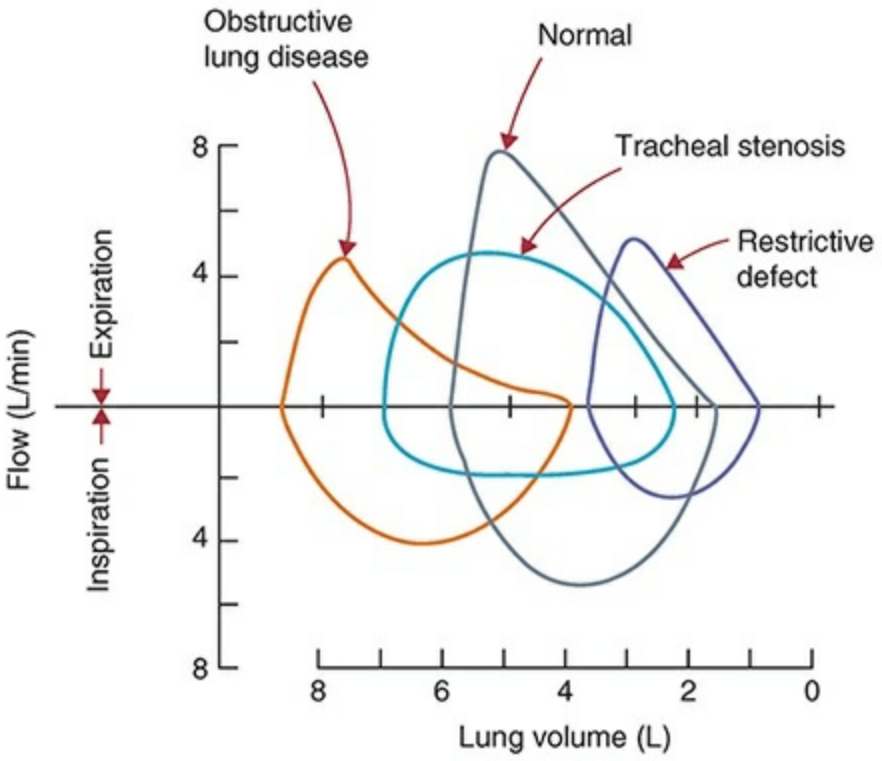

FIGURE 4.1. Representative tracings of flow–volume loops from a healthy individual, a patient with parenchymal obstructive disease, a patient with tracheal stenosis, and a patient with restrictive disease from parenchymal fibrosis. (*Modified with permission of McGraw-Hill Education, from Goudsouzian N, Karamanian A.* Physiology for the Anesthesiologist. *2nd ed. Norwalk, CT: Appleton-Century-Crofts; 1984:213; permission conveyed through Copyright Clearance Center, Inc.*)

Infectious lung disease, such as cystic fibrosis, is the most frequent indication for lung transplantation in patients younger than 18 years old. Characterized by chronic infection and the production of copious purulent secretions, patients with cystic fibrosis primarily exhibit obstructive functional abnormalities with increased airway reactivity. Under most circumstances, residual lung volumes and functional residual capacity are increased and bronchodilators have little effect on expiratory flow rates. Because of potential infectious cross-contamination of the transplanted lung, chronic infectious disease represents a contraindication to SLT. However, SLT with contralateral pneumonectomy has been performed as an alternative solution.

Pulmonary vascular disease with severe pulmonary hypertension and right ventricular dysfunction has also emerged

as an indication for transplantation. Pathologically, severe PA hypertension can result from idiopathic proximal vascular processes such as persistent pulmonary hypertension (PPH) or secondary to chronically increased pulmonary blood flow (e.g., left-to-right intracardiac shunt, leading to Eisenmenger's syndrome) or pulmonary venous hypertension from left-sided heart diseases. Pulmonary hypertension may precipitate chronic hypoxemia via an intracardiac defect that allows for development of a right-to-left shunt. Improved medical therapy for PPH, particularly with continuous long-term intravenous prostacyclin infusions or sildenafil, has affected the numbers of patients undergoing lung transplantation for this disease. Controversy exists with respect to choice of SLT versus BLT for patients with idiopathic pulmonary arterial hypertension (IPAH). Because a native lung can usually be left intact without compromising a transplanted lung (which will receive most of blood flow), some patients with pulmonary arterial vascular disease may be reasonable candidates for SLT, *with concurrent repair of any cardiac anomalies*. Early reports indicated poorer functional recovery and higher mortality after SLT versus BLT for PPH. Some reports suggest the earlier manifestation of bronchiolitis obliterans syndrome (BOS) in patients after SLT versus BLT, and although survival curves diverge 3 years after transplantation, controversy remains whether or not procedure type is the main cause. Some centers have adopted BLT as the mainstay of treatment for patients presenting with IPAH.

Christie JD, Edwards LB, Aurora P, et al. The registry of the International Society for Heart and Lung Transplantation: twenty-sixth official adult lung and heart-lung transplantation report—2009. *J Heart Lung Transplant*. 2009;28:1031–1049.

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pulmonary vascular disease. *Ann Thorac Surg*. 2002;73:209–219.

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A.3. How many lung transplantations have been performed?

Although the first human lung allograft was performed in 1963, transplantation of one or both lungs did not emerge as a viable therapeutic option for patients with end-stage lung disease until the 1980s. The ultimate emergence of this procedure can be largely attributed to advances in surgical technique, anesthetic management, organ harvest and preservation, infection prevention, and immunosuppressive therapy. Since initiation of the International Thoracic Organ Transplant registry in the mid-1980s, the number of procedures reported yearly has continue to rise. This is in part due to the use of extended criteria donors and ex-vivo lung perfusion systems. As of the end of June 2017, the registry contains data for 64,803 adult lung and 4,054 adult heart-lung transplants. There were 2,449 lung transplants and 29 heart-lung transplants done in the United States in 2017, based on Organ Procurement and Transplantation Network (OPTN) data as of January 9, 2019. These numbers do not include pediatric patients or patients who received both a lung and a liver or a lung and a kidney transplant. Despite this volume, the number of patients awaiting lung transplantation continues to exceed the limited donor supply.

Chambers DC, Cherikh WS, Goldfarb SB, et al. The International Thoracic Organ Transplant registry of the International Society for Heart and Lung Transplantation: thirty-fifth adult lung and heart-lung transplant report—2018; focus theme: multiorgan transplantation. *J Heart Lung Transplant*. 2018;37(10):1169–1183.

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A.4. What are the selection criteria for recipients?

In general, patients with severe end-stage lung disease are considered candidates for transplantation when their life expectancy is less than 2 to 3 years. They have minimal disease of other organ systems, and they are mentally and psychologically capable of following strict regimens for rehabilitation and immunosuppressive therapy. These criteria contribute to a high (>80%) likelihood of surviving the lung transplantation for at least 90 days and 5-year posttransplant survival from a general medical standpoint. Specific criteria, including age, are dependent on the type of lung disease and whether the planned procedure is SLT or BLT. Recent data reveal that the age of lung transplant recipients is increasing with approximately 35% now 60 years of age and older compared to 15% in 1998. The average age of the recipient is 35.5 years. In contrast to inclusion criteria formulated when lung transplantation was in its infancy, concomitant steroid therapy, previous intrathoracic surgery, mechanical ventilation, and right ventricular failure are no longer considered absolute contraindications.

Christie JD, Edwards LB, Aurora P, et al. The registry of the International Society for Heart and Lung Transplantation: twenty-sixth official adult lung and heart-lung transplantation report—2009. *J Heart Lung Transplant*. 2009;28:1031–1049.

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A.5. How is the decision made to transplant one or both lungs, and does this influence preoperative management?

Although BLTs are increasingly being performed for all etiologies of end-stage lung disease, bronchiectasis including cystic fibrosis and other infectious pathologies are the only *absolute* indication for BLT. The concern is that leaving an infective native lung can increase the risk of infection and decrease the long-term viability of the transplanted lung particularly in the setting of immunosuppression. However, SLT and BLT can be performed for all other etiologies of end-stage lung disease, including COPD, ILD, and primary pulmonary hypertension. With a perceived long-term mortality benefit with BLT, SLT is less frequently performed and BLT is more common for all etiologies of end-stage lung disease. In addition to greater distribution of limited donor organs and decreased wait times for recipients, SLT is technically less challenging with the potential for reduced cumulative periprocedural mortality. The data regarding short-term outcomes for SLT versus BLT is equivocal at best; there are some studies showing better outcomes with SLT. With BLT, there is increased functional lung parenchyma and greater reserve if there is a complication. With the exception of infectious etiologies, the decision to proceed with SLT versus DLT remains controversial. Patient (age, size, lung allocation scoring [LAS], etc.) as well as donor (age, size, comorbidities, state of the donor organ, etc.) specific factors must be taken into consideration and the benefits

must be weighed against the risk for both. Although SLT is technically easier and advocated for more difficult recipients, such as those with prior thoracic surgery or coexisting illnesses, functional improvements are often better with BLT. In addition, the status of the donor lungs further influences the decision of whether to perform a single or bilateral procedure. Finally, transplantation of two lobes from two living related donors for patients with inflammatory disease who are unlikely to survive the wait for a cadaver donor is gaining acceptance. The decision to proceed with SLT versus BLT may impact preoperative management of these patients. Although it is important to screen all patients for aspiration risk and to administer the appropriate premedications where necessary, it is especially important for potential SLT recipients. Aspiration can further damage the native lung and significantly impact outcome. Some people advocate that all SLT recipients should be treated as high aspiration risk and the appropriate premedications to safeguard against this should be administered. Also, with a lower chance for extracorporeal support and anticoagulation, SLT recipients are more likely to receive an epidural preoperatively than BLT recipients.

Chambers DC, Cherikh WS, Goldfarb SB, et al. The International Thoracic Organ Transplant registry of the International Society for Heart and Lung Transplantation: thirty-fifth adult lung and heart-lung transplant report—2018; focus theme: multiorgan transplantation. *J Heart Lung Transplant*. 2018;37(10):1169–1183.

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Subramanian MP, Meyers BF. Bilateral versus single lung transplantation: are two lungs better than one? *J Thorac Dis*. 2018;10(7):4588–4601.

Weill D. Lung transplantation: indications and contraindications. *J Thorac Dis*. 2018;10(7):4574–4587.

A.6. How does a single-lung transplantation (SLT) differ

technically from a bilateral-lung transplantation (BLT)?

It is extremely important that anesthesiologists be broadly familiar with the surgical methods because manipulation of the heart and lungs at specific points during the transplantation can produce marked cardiopulmonary disturbances. Ideally, the anesthesiologist should anticipate these changes and adapt the anesthetic management accordingly.

SLT is usually performed in the lateral decubitus position through a thoracotomy incision, often with the upper leg and pelvis angled to allow groin exposure for potential femoral cannulation and CPB. In contrast, bilateral sequential lung transplantation is usually performed with the patient supine through a "clamshell" incision (bilateral anterior thoracotomies with or without transverse sternotomy). For both SLT and BLT, intermittent single-lung ventilation is required during dissection of the native lung to be removed and implantation of the graft. Once stable single-lung ventilation is established, dissection of the lung to be transplanted is initiated with isolation of the PA. To assess the cardiopulmonary response to diverting the entire cardiac output through one lung, progressive temporary occlusion of the vessel is first performed manually; if well tolerated, the vessel is then clamped and stapled. After ligation of the PA, the pneumonectomy is completed. Implantation of the graft begins with anastomosis of the airway. In the past, the bronchial anastomosis was wrapped with an omental pedicle, mobilized through a small abdominal incision in an effort to improve blood supply to the airway and promote healing. However, the use of a "telescoping" bronchial anastomosis has now largely obviated the need for omental wrapping. The PA branch is then attached to the graft, followed by anastomosis of a cuff of the left atrium containing the pulmonary veins. The implanted lung is then partially inflated, the left atrial cuff and

pulmonary veins de-aired, and circulation to the organ restored. If the attempt to establish adequate hemodynamics and oxygenation after reperfusion of the transplanted lung is unsuccessful, this is the time to consider using extracorporeal membrane oxygenation (ECMO) or CPB. In a sequential BLT, the point in the case where the decision may be made to place the patient on extracorporeal support is prior to attempting to transplant the second lung. The use of extracorporeal support for BLT often varies by institutional and patient factors. If an en bloc technique for BLT is used, CPB is required. Additional surgical technique for BLT is described in the following text.

Patients presenting for SLT with chronic PPH of primary or secondary etiology often exhibit severe compromise of the right ventricular function. To avoid additional right ventricular compromise, many institutions choose to institute partial normothermic CPB during SLT for PPH or in patients with severe pulmonary hypertension and right ventricular dysfunction secondary to restrictive or obstructive disease. Cannulation is typically through the femoral artery and the right atrium unless simultaneous correction of an intracardiac defect is planned. In such patients, conventional aortic and single- or double-stage atrial cannulation are performed. Implantation of the lung is otherwise performed in the same manner as described earlier.

BLT was first described by the Toronto Lung Transplant Group in the mid-1980s as en bloc implantation of both lungs simultaneously. The procedure is performed through a median sternotomy using hypothermic CPB, cardioplegic cardiac arrest, and single tracheal (or double bronchial) anastomosis of the trachea and main PA. Although the procedure initially produced encouraging results, considerable limitations related to technical complexity, morbidity, mortality, and application to many patients with end-stage lung disease soon became apparent. Not surprisingly, use of the procedure declined sharply and has now

been largely replaced by the bilateral sequential implantation technique, which does not uniformly require hypothermic CPB. Introduced in 1990, bilateral sequential (or bilateral single) lung transplantation has become the surgical procedure of choice when replacement of both lungs is necessary. According to the 2014 international registry, approximately 75% of the transplants performed in 2012 were BLTs. As noted earlier, in contrast to SLT, bilateral sequential lung transplantation procedures are performed in the supine position. In general, the procedure can be regarded as having two phases. First, the most severely compromised lung (as determined by preoperative ventilation-perfusion lung scanning) is removed during ventilation of the "good" contralateral lung. Implantation is achieved through a bronchial anastomosis as with an SLT. The second lung is then removed and transplanted during ventilation of the new lung alone. As noted earlier, if there is hemodynamic or ventilatory instability during ventilation of the new lung alone, extracorporeal support may be instituted prior to implanting the second lung.

Aigner C, Klepetko W. Bilateral lung transplantation. *Operative Tech Thorac Cardiovasc Surg*. 2012;17(3):181–193.

Davis RD. Bilateral sequential lung transplantation. *Operative Tech Thorac Cardiovasc Surg*. 2007;12(1):57–72.

Flye MW, ed. *Atlas of Organ Transplantation*. Philadelphia, PA: WB Saunders; 1995:296–312.

Hayanga JW, D'Cunha J. The surgical technique of bilateral sequential lung transplantation. *J Thorac Dis*. 2014;6(8):1063–1069.

Nagendran M, Maruthappu M, Sugand K. Should double lung transplant be performed with or without cardiopulmonary bypass? *Interact Cardiovasc Thorac Surg*. 2011;12(5):799–804.

Pasque MK, Cooper JD, Kaiser LR, et al. Improved technique for bilateral lung transplantation: rationale and initial clinical experience. *Ann Thorac Surg*. 1990;49:785–791.

Yusen RD, Edwards LB, Kucheryavaya AY, et al. The registry of the International Society for Heart and Lung Transplantation: thirty-first adult

lung and heart-lung transplant report—2014; focus theme: retransplantation. *J Heart Lung Transplant*. 2014;33:1009–1024.

B. Preoperative Evaluation and Preparation

B.1. What preoperative evaluation is desirable?

At most centers, an extensive physical examination, psychological evaluation, and numerous tests of cardiopulmonary function are performed before acceptance into the transplant program. This facilitates the preanesthetic evaluation that ideally is performed when the patient is first accepted into the transplant program. Familiarity with pulmonary function tests, ventilation-perfusion lung scan results, heart catheterization, echocardiographic data (including evidence of intracardiac shunts), exercise tolerance, oxygen use, and dependence on continuous pulmonary vasodilator infusion (i.e., prostacyclin) are beneficial for formulating an anesthetic plan. Although many of these parameters are regularly reassessed, the interval between evaluation and transplantation necessitates that a careful history and physical examination be repeated before the procedure, focusing on signs of pulmonary hypertension and cardiac dysfunction.

Estafanous FG, Barash PG, Reves JG, eds. *Cardiac Anesthesia: Principles and Clinical Practice*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001:637–662.

Slinger P, Blank RS, Campos J, et al, eds. *Principles and Practice of Anesthesia for Thoracic Surgery*. 2nd ed. Basel, Switzerland: Springer; 2019:773–790.

B.2. Would you premedicate this patient? If so, how?

As with all critically ill patients, considerations regarding preoperative sedation are governed primarily by the functional limitations imposed by the underlying disease and the potential consequences of hypercarbia and hypoxemia as a result of the

sedation. Special consideration must also be given to the possibility that the donor lungs will be deemed unacceptable at final inspection, and therefore, the procedure is canceled. When indicated, parenteral sedation is usually chosen because of insufficient time to effectively administer oral anxiolytics. Midazolam alone or with diphenhydramine (potentially protecting the lung against drug-induced histamine release) is often sufficient. Clinically, most patients with end-stage restrictive, obstructive, or infectious lung disease are tachypneic while breathing room air and cannot tolerate aggressive sedation. Also, patients with pulmonary hypertension and significant right-to-left intracardiac shunting (i.e., Eisenmenger's physiology) are often cyanotic despite oxygen supplementation and may not tolerate sedation well. In contrast, patients with PPH and no intracardiac defect often appear reasonably normal and will benefit from sedation because of the potential for stress-related increases in pulmonary vascular resistance. In addition to sedative premedication, consideration needs to be given to immunosuppression protocols and in appropriate patients to supplemental bronchodilator therapy.

Hartigan PM, Pedoto A. Anesthetic considerations for lung volume reduction surgery and lung transplantation. *Thorac Surg Clin*. 2005;15(1):143–157.

Slinger P, Blank RS, Campos J, et al, eds. *Principles and Practice of Anesthesia for Thoracic Surgery*. 2nd ed. Basel, Switzerland: Springer; 2019:773–790.

B.3. What vascular access is appropriate?

Typically, a large-bore intravenous catheter and central venous access for PA catheter placement are secured before surgery. In many centers, additional central venous cannulation is performed with a multiple-lumen catheter to provide intraoperative and postoperative venous access. For patients with chronic infectious lung disease or a history of previous

intrathoracic procedures, a second large-bore intravenous catheter is often obtained because of the potential for brisk blood loss during dissection of pleural adhesions. Meticulous removal of air from venous infusion lines should be performed, particularly in patents with known or suspected right-to-left shunts. At many institutions, cannulation of a femoral artery, instead of the radial artery, is performed under local anesthesia in the operating room because radial arterial pressures may become damped during the procedure secondary to vasoactive medication infusion or positioning of the arms.

Flye MW, ed. *Atlas of Organ Transplantation*. Philadelphia, PA: WB Saunders; 1995:313–318.

Hartigan PM, Pedoto A. Anesthetic considerations for lung volume reduction surgery and lung transplantation. *Thorac Surg Clin*. 2005;15(1):143–157.

B.4. Is preoperative epidural catheter placement advantageous?

Pain control after lung transplantation can be critical in facilitating tracheal extubation and rehabilitation. Both lumbar and thoracic epidural catheters have been used for postoperative pain management. Epidural catheters may be placed immediately before the procedure or postoperatively prior to extubation. If placed before the procedure, there must be consideration that there is the possibility of anticoagulation and CPB during the transplantation procedure. The practice of placing preoperative epidurals is supported by data indicating no adverse sequelae to preoperatively placed epidural catheters, including those patients who required emergent heparinization and CPB. Obvious exceptions to this approach are patients who are anticoagulated preoperatively or those in whom CPB is planned. Delaying placement of the epidural catheter until the postoperative period may also be a possibility.

Feltracco P, Barbieri S, Milevoj M, et al. Thoracic epidural analgesia in lung

transplantation. *Transplant Proc*. 2010;42:1265–1269.

Hartigan PM, Pedoto A. Anesthetic considerations for lung volume reduction surgery and lung transplantation. *Thorac Surg Clin*. 2005;15(1):143–157.

C. Intraoperative Management

C.1. What special equipment is necessary?

Necessary items for lung transplantation include an anesthesia ventilator with options for several ventilatory modes and with good efficacy at higher airway pressures. In addition, the ventilator should be capable of delivering a wide range of inspiratory-to-expiratory ratios (I:E ratios) and varying inspired oxygen concentrations. A fiberoptic bronchoscope is necessary for airway assessment, guided airway suctioning, inspection of the bronchial anastomoses, and for confirmation of appropriate placement of the double-lumen endotracheal tube or bronchial blocker. An apparatus to deliver continuous positive airway pressure (CPAP) and a system for delivery of pulmonary arterial vasodilators, such as nitric oxide should be readily available. Transesophageal echocardiography (TEE) should be used. Lastly, a CPB machine and/or extracorporeal circuit should always be immediately accessible. Because multiple vasopressors and inotropes are often needed, infusion pumps that allow for the simultaneous administration of numerous drugs should be utilized.

C.2. How would you monitor this patient?

Intraoperatively, hemodynamic and respiratory changes are often acute and profound, so extensive monitoring is imperative. In addition to the electrocardiogram, arterial blood pressure, and peripheral arterial oxygen saturation, PA catheter placement is routine for lung transplantation at most institutions because of the profound changes in pulmonary and systemic hemodynamics that often occur. During SLT, PA catheters often migrate to the

operative side after the patient has been laterally positioned even when radiographically confirmed to be in the nonoperative lung. Therefore, the surgeon should be reminded to palpate the PA and withdraw the catheter if necessary before cross-clamping the vessel. PA catheters capable of measuring mixed venous oxygen saturation have become widely used. TEE is often employed during lung transplantation to evaluate vascular anastomoses and right ventricular function, particularly during clamping of the PA as well as to assess for intracardiac shunts and adequacy of de-airing maneuvers.

Estafanous FG, Barash PG, Reves JG, eds. *Cardiac Anesthesia: Principles and Clinical Practice*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001:637–662.

Miyaji K, Matsubara H, Nakamura K, et al. Equivalence of flow velocities through bilateral pulmonary vein anastomoses in bilateral living-donor lobar lung transplantation. *J Heart Lung Transplant*. 2005;24(7):860–864.

Schenk P, Globits S, Koller J, et al. Accuracy of echocardiographic right ventricular parameters in patients with different end-stage lung diseases prior to lung transplantation. *J Heart Lung Transplant*. 2000;19(2):145–154.

Slinger P, Blank RS, Campos J, et al, eds. *Principles and Practice of Anesthesia for Thoracic Surgery*. 2nd ed. Basel, Switzerland: Springer; 2019:773–790.

C.3. How would you induce anesthesia in this patient?

As with induction of anesthesia in any critically ill patient, multiple techniques have been safely used for patients undergoing lung transplantation. Effective alveolar ventilation and nitrogen washout are poor in the patient with severe obstructive lung disease and high residual volumes; therefore, prolonged (i.e., 15 to 20 minutes) preoxygenation is worthwhile. A slow, controlled induction is generally preferred; abrupt withdrawal of sympathetic tone in these patients with high sympathetic activity can lead to marked cardiovascular compromise, especially as you transition from spontaneous to mechanical ventilation. Rapid sequence induction should

therefore be reserved for patients deemed to be a high aspiration risk because large boluses of medication may cause profound hemodynamic instability. A rapid-acting induction agent to shorten the excitement stage, expedite airway management, and prevent opiate-induced truncal rigidity should be used. Propofol, etomidate, ketamine, and midazolam have all been used safely; the specific properties of each drug in the setting of the patient's underlying disease should be considered. For example, the sympathomimetic properties of ketamine may preclude use in the presence of pulmonary hypertension, whereas its bronchodilating effects may be beneficial in the setting of bronchospasm. Lidocaine, sufentanil or fentanyl, and succinylcholine or a nondepolarizing muscle relaxant are generally used to complete induction.

Because of the greater potential for hemodynamic and respiratory instability in this patient population, the surgeon and perfusionist must be present during induction to initiate ECMO or CPB if needed. In patients requiring high noninvasive respiratory support or with severe pulmonary hypertension, ECMO may be instituted prior to induction. Alternatively, the groin vessels may be accessed prior to induction to facilitate initiation of ECMO of CPB after induction.

Optimization of right ventricular preload, right ventricular support, and efforts to prevent increases in right ventricular afterload are keys to a safe anesthesia induction. Dysrhythmias, which may lead to decreased perfusion and ischemia of the right ventricle, should be avoided. Especially with positive pressure ventilation, suppression of the sympathetic system, myocardial depression, and vasodilation may lead to cardiovascular collapse. Conversely, acute increases in pulmonary arterial pressures and right heart failure may result from sympathetic stimulation (e.g., with intubation, acidemia, hypoxemia, hypercapnia) and should be avoided.

Kachulis B, Mitrev L, Jordan D. Intraoperative anesthetic management of lung transplantation patients. *Best Pract Res Clin Anaesthesiol*. 2017;31(2):261–272.

Nicoara A, Anderson-Dam J. Anesthesia for lung transplantation. *Anesthesiol Clin*. 2017;35(3):473–489.

Sellers D, Cassar-Demajo W, Keshavjee S, et al. The evolution of anesthesia for lung transplantation. *J Cardiothorac Vasc Anesth*. 2017;31(3):1071–1079.

C.4. How would you ventilate this patient? What kind of endotracheal tube would you use?

After induction, the trachea is usually intubated with a left endobronchial double-lumen tube for both SLT and BLT. Use of a single-lumen endotracheal tube with either an external or an internal bronchial blocking catheter has been described but does not appear to be clearly superior to the left double-lumen tube for most procedures. Furthermore, an endobronchial double-lumen tube allows for differential lung ventilation if required postoperatively. One exception to this approach has been in patients with cystic fibrosis who exhibit thick tenacious secretions that are difficult to suction through the small-lumen suction catheters necessary for double-lumen tubes. In these patients, it is often helpful to first place a large single-lumen tube and perform extensive bronchoscopic-directed bronchial lavage and suctioning before placement of the double-lumen tube.

The transition from spontaneous to mechanical ventilation invariably produces hemodynamic alterations resulting from acute changes in intrathoracic pressure and chest wall compliance. With obstructive lung disease, mechanical ventilation magnifies air trapping, leading to “pulmonary tamponade.” Varying degrees of this phenomenon should be expected during anesthesia induction. The treatment consists of intermittent apnea with an open ventilator circuit, adjustment of the ventilatory pattern to an I:E ratio of 1:5 or less with

moderate tidal volumes, and administration of bronchodilating drugs. Prompt restoration of blood pressure usually ensues. If hypotension persists, other causes of circulatory compromise must be excluded including pneumothorax. With restrictive disease, higher inflation pressures and positive end-expiratory pressure (PEEP) are often required. In both obstructive and restrictive disease, optimal balance of ventilation with hemodynamic stability often necessitates tolerating a degree of hypercapnia. In pulmonary hypertensive patients, mechanical ventilation usually produces less cardiovascular disturbance if caution is exercised to not increase pulmonary vascular resistance (e.g., from hypoxia, hypercarbia, or lung hyperinflation).

Hartigan PM, Pedoto A. Anesthetic considerations for lung volume reduction surgery and lung transplantation. *Thorac Surg Clin*. 2005;15(1):143–157.

Youngberg JA, Lake CL, Roizen MF, et al, eds. *Cardiac, Vascular, and Thoracic Anesthesia*. New York: Churchill Livingstone; 2000:703.

C.5. How does the physiology of single-lung ventilation influence the procedure?

In laterally positioned patients, gravity helps redistribute blood away from the nonventilated lung during single-lung ventilation and lessen the intrapulmonary shunt. In patients who are supine, this benefit is lost and single-lung ventilation may not be well tolerated. If appropriately preoxygenated prior to induction and ventilated prior to one-lung ventilation (OLV), patients with higher residual volumes, such as patients with severe obstructive pulmonary disease, may tolerate OLV better than patients with lower residual volumes. These patients have a higher reserve and may maintain oxygenation for the first 10 to 15 minutes of single-lung ventilation. Rapid arterial desaturation may then occur once a substantial portion of the residual volume is absorbed. Conversely, patients with restrictive lung disease and

a low functional residual capacity may become hypoxemic and hypercarbic rather rapidly if not ventilated. Multiple steps can be taken to improve oxygenation including insufflation of oxygen or CPAP to the nonventilated lung, bronchoscopic-guided suctioning of the ventilated lung, careful manipulation of the ventilatory pattern, and adding PEEP to the ventilated lung. Differential PEEP/CPAP should be done cautiously; however, because increased airway pressure in the ventilated lung can divert blood toward the nonventilated lung, thereby increasing the shunt and leading to a further decrease in Pa_{O_2}. Likewise, sustained hyperinflation of the ventilated lung may lead to an increase in right ventricular afterload and preload and have severe hemodynamic consequences. In some patients, intermittent ventilation of the operative lung may be necessary for appropriate oxygenation. In general, oxygenation improves after the clamping of the PA supplying the nonventilated lung. For desaturation not responding to the usual maneuvers, tourniquets can be placed around the PA by the surgeon as a temporizing step until dissection permits proper stapling of this vessel. Inhaled pulmonary arterial vasodilators may improve ventilation/perfusion matching by selective vasodilation of only the PAs that are being ventilated. ECMO or CPB should be initiated if the Pa_{O_2} continues to decrease, the Pa_{CO_2} continues to increase, and the patient is severely acidemic, despite all the previously stated interventions.

Kachulis B, Mitrev L, Jordan D. Intraoperative anesthetic management of lung transplantation patients. *Best Pract Res Clin Anaesthesiol*. 2017;31(2):261–272.

Nicoara A, Anderson-Dam J. Anesthesia for lung transplantation. *Anesthesiol Clin*. 2017;35(3):473–489.

Slinger P, Blank RS, Campos J, et al, eds. *Principles and Practice of Anesthesia for Thoracic Surgery*. 2nd ed. Basel, Switzerland: Springer; 2019:773–790.

C.6. How does single-lung ventilation affect cardiopulmonary function? What are the problems of single-lung ventilation in this patient? How would you treat them?

Isolated ventilation of the dependent lung is often accompanied by a marked acute increase in peak inspiratory pressure and a subsequent gradual progressive rise in PA pressure. As noted earlier, because of the beneficial effect of gravity on redistributing blood away from the nondependent nonventilated lung, single-lung ventilation is often tolerated better from a respiratory standpoint by patients undergoing SLT in the lateral position than those undergoing BLT in the supine position. Close monitoring of right ventricular performance during conversion to single-lung ventilation is extremely important because of the increase in afterload produced by hypoxic vasoconstriction and redistribution of blood flow. Although unusual, if the right ventricle becomes hypokinetic and distended (TEE imaging) or the central venous pressure (CVP) increases disproportionally to the raise in PA pressure and if the left ventricular ejection fraction decreases, ventilation may have to be altered to minimize the increase in PA pressure.

Triantafillou AN, Pasque MK, Huddleston CB, et al. Predictors, frequency, and indications for cardiopulmonary bypass during lung transplantation in adults. *Ann Thorac Surg*. 1994;57:1248–1251.

C.7. What problems are associated with the lateral position?

SLT is usually performed in the lateral decubitus position, often with the upper leg and pelvis angled to allow groin exposure for potential femoral cannulation and CPB. Not surprisingly, position-related changes in venous return, coupled with compression of the dependent lung by the mediastinum and diaphragm, may promote systemic hypotension and

ventilation/perfusion mismatch. Furthermore, PA pressure usually tends to rise after lateral positioning; this is likely secondary to gravity-induced shifts in pulmonary blood flow distribution, vascular congestion, and increased vascular resistance.

Youngberg JA, Lake CL, Roizen MF, et al, eds. *Cardiac, Vascular, and Thoracic Anesthesia*. New York: Churchill Livingstone; 2000:703.

C.8. Should volatile anesthetics be avoided during single-lung ventilation?

Because of experimental evidence demonstrating inhibition of hypoxic pulmonary vasoconstriction (HPV) by the volatile anesthetic agents, some authors have suggested that these drugs be avoided in the anesthetic management of patients with end-stage lung disease requiring single-lung ventilation. However, true clinical significance of these experimental observations remains somewhat controversial. From a clinical standpoint, commonly used doses of isoflurane (e.g., end-tidal concentrations of 1.0% or less) have not been empirically associated with worsening of intrapulmonary shunt and hypoxia. Therefore, isoflurane remains widely used in these patients and may actually benefit some lung recipients because of its bronchodilating properties (also see Chapter 2, section C.13).

Benumof JL. Anesthesia for one-lung ventilation [reply]. *Anesthesiology*. 1988;69:631.

Hartigan PM, Pedoto A. Anesthetic considerations for lung volume reduction surgery and lung transplantation. *Thorac Surg Clin*. 2005;15(1):143–157.

Lumb AB, Slinger P. Hypoxic pulmonary vasoconstriction: physiology and anesthetic implications. *Anesthesiology*. 2015;122:932–946.

C.9. At what specific points in the procedure are problems anticipated?

Challenges encountered during surgeries for lung transplantation

are usually related to the underlying disease process, anesthesia, the complexity of the surgery, physiologic changes associated with the different stages of the procedure, patient positioning, and immediate complications such as primary graft dysfunction (PGD). The procedure can be especially challenging at these particular points:

- Anesthesia induction
- Lateral positioning
- Single-lung ventilation
- Clamping of the PA
- Graft implantation
- Graft reperfusion

C.10. How would you deal with problems related to clamping of the pulmonary artery (PA)?

To assess the cardiopulmonary response to diverting the entire cardiac output through one lung, progressive occlusion of the vessel is first performed manually (**Fig. 4.2**). Careful assessment of right ventricular function is performed with the TEE looking for evidence of right ventricular distension or hypokinesis. If well tolerated, the vessel is then clamped and stapled. If occlusion is poorly tolerated, the vessel is unclamped and a pulmonary vasodilator, such as prostaglandin E_1 or inhaled nitric oxide (iNO), and/or a positive inotropic infusion are begun. If severe respiratory or cardiovascular derangement persists after reclamping of the vessel despite pharmacologic intervention, heparin is administered and CPB instituted to avoid profound hypoxia or right ventricular failure. However, for most patients undergoing SLT, hypoxemia during single-lung ventilation and after PA clamping is rarely a problem, and right ventricular performance is adequately maintained.

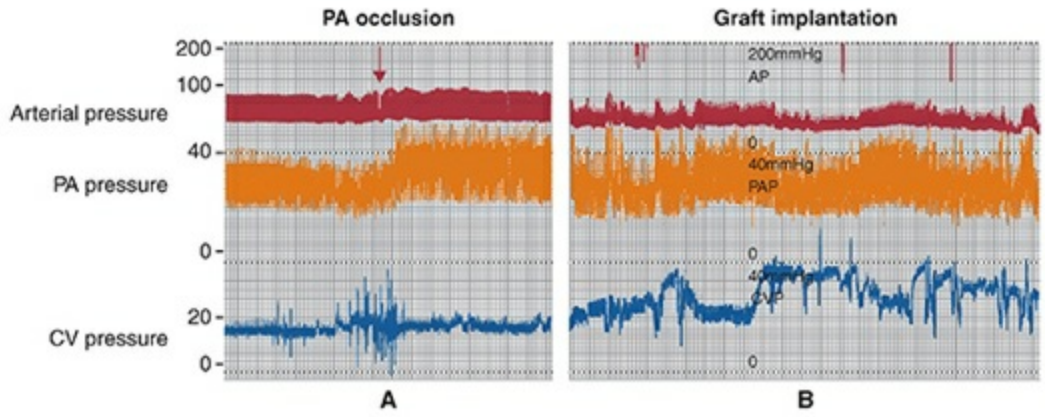

FIGURE 4.2. Tracings of femoral arterial blood pressure, along with pulmonary artery (PA) and central venous (CV) pressures, before and after occlusion of the left PA (A) and during implantation of a left lung graft (B). All pressures are in millimeters of mercury. AP, arterial pressure; CVP, central venous pressure; PAP, pulmonary artery pressure.

Youngberg JA, Lake CL, Roizen MF, et al, eds. *Cardiac, Vascular, and Thoracic Anesthesia*. New York: Churchill Livingstone; 2000:703.

C.11. What hemodynamic alterations would you expect during graft implantation and reperfusion? How would you correct them?

During the process of performing the vascular and bronchial anastomoses, major disturbances on cardiac filling and rhythm can be produced. Although often transient, systemic hypotension and pulmonary hypertension can ensue. Temporization with vasopressors, inotropes, or an inhaled pulmonary arterial vasodilator may be necessary. Electrical therapy should be used for sustained dysrhythmia causing hemodynamic instability. The final stages of graft implantation include attaching the pulmonary veins, via a left atrial cuff, to the left atrium. Bleeding of the pulmonary veins, prior to doing this, facilitates de-airing and removal of graft preservatives. Transient hypotension may follow the introduction of the preservative solution into the systemic circulation. Incomplete de-airing of the pulmonary veins can cause a coronary artery air embolism and lead to transient myocardial ischemia. The latter is manifested by ST-segment elevation and regional wall motion

abnormalities on TEE. These echocardiographic and electrocardiogram changes can be reversed by maintaining adequate perfusion pressure, with vasopressors. Rapid intravascular volume replacement may also be necessary during this time. After reperfusion and subsequent ventilation of the new lung, PA pressures and arterial blood gases should be closely followed. PA pressure usually falls after reperfusion of the transplanted allograft. If a substantial decrease is not observed, potential causes include anastomotic problems with the atrial cuff (pulmonary veins) or the PA. Such obstruction may lead to hemodynamic instability. Echocardiography is very useful in assessing for potential obstruction of the pulmonary vessels. Turbulent high-velocity flow and/or a diameter less than 75% of the proximal PA in the left or right PA are suggestive of obstruction. When pulmonary anastomotic problems are suspected, the surgeon should palpate to assess whether the PA catheter is located proximal or distal to the anastomosis. If a proximal location is confirmed, the PA pressure distal to the anastomosis should be directly measured by inserting a needle and connecting it to a pressure tubing handed off the operative field. A large difference in the two measurements is suggestive of obstruction to flow. Pulmonary vein obstruction from a thrombus or suture is possible and careful assessment must be done to assess for patency of these vessels. Pulmonary vein diameter greater than 0.5 cm and a velocity greater than 1 m per second are suggestive of obstruction. If significant obstruction of the pulmonary vasculature is detected, surgical revision/correction may be necessary because this may lead to early or late hemodynamic compromise. Anticoagulation may be necessary for obstruction secondary to thrombus. Ischemic metabolites may lead to severe vasodilation and hypotension with reperfusion. Vasopressors, inotropes, calcium chloride, and sodium bicarbonate may be needed. Other sources of

hypotension include pneumoplegia and leaks at the vascular anastomoses. Vasopressors, inotropes, and rapid intravascular replacement may be helpful in these situations.

Early graft dysfunction can manifest shortly after reperfusion of the first lung and may be the consequence of various insults. This may result in severe hypoxemia with hemodynamic compromise. Supportive measures with a lung protective ventilator strategy, iNO, and, if necessary, vasopressors/inotropes should be employed. ECMO should be considered for patients with refractory hypoxemia and/or hypotension despite these measures.

Batra K, Chamarthy M, Reddick M. Diagnosis and interventions of vascular complications in lung transplant. *Cardiovasc Diagn Ther*. 2018;8(3):378–386.

Kachulis B, Mitrev L, Jordan D. Intraoperative anesthetic management of lung transplantation patients. *Best Pract Res Clin Anaesthesiol*. 2017;31(2):261–272.

Nicoara A, Anderson-Dam J. Anesthesia for lung transplantation. *Anesthesiol Clin*. 2017;35(3):473–489.

C.12. When is cardiopulmonary bypass (CPB) necessary for lung transplantation?

CPB may be used electively for patients with severe PA hypertension, in whom double-lumen endobronchial tubes cannot be placed or when visualization of hilar structures is poor. However, in the absence of intraoperative complications, CPB is not always used because it may increase bleeding and blood product usage. It has also been suggested that CPB may aggravate postoperative lung dysfunction, although this has not been evident in cases where lung transplant was performed in conjunction with cardiac surgery. Nonetheless, the use of CPB has been associated with longer duration of mechanical ventilation and hospitalization, although it is difficult to differentiate whether the latter results directly from CPB or is the result of a complicated procedure that resulted in the need

for CPB. Indications for CPB include right ventricular dysfunction not responding to medical therapy, early graft dysfunction occurring during or prior to implantation of the second lung during bilateral procedures, and surgical misadventures. Unplanned CPB is reported to occur in 12% to 46% of lung transplantation procedures, but predicting which patients may require this intervention is extremely difficult. Some report that CPB is more likely to be necessary for restrictive lung diseases than obstructive diseases. Based on a 2010 review of published lung transplant articles regarding patient outcomes and the use of CPB, there was weak evidence to support using CPB electively. As noted in an earlier section, the use of CPB may vary based on institution and patient factors. In attempt to derive the benefits of CPB while reducing complications, some centers advocate the use of heparin-bound ECMO systems. This approach allows for pulmonary support both during and after the procedure with minimal systemic anticoagulation.

Dalibon N, Geffroy AN, Moutafis M, et al. Use of cardiopulmonary bypass for lung transplantation: a 10-year experience. *J Cardiothorac Vasc Anesth*. 2006;20:668–672.

Lau CL, Hoganson DM, Meyers BF, et al. Use of an apical heart suction device for exposure in lung transplantation. *Ann Thorac Surg*. 2006;81(4):1524–1525.

Nagendran M, Maruthappu M, Sugand K. Should double lung transplant be performed with or without cardiopulmonary bypass? *Interact Cardiovasc Thorac Surg*. 2011;12(5):799–804.

Parekh K, Meyers BF, Patterson GA, et al. Outcome of lung transplantation for patients requiring concomitant cardiac surgery. *J Thorac Cardiovasc Surg*. 2005;130(3):859–863.

Triantafillou AN, Pasque MK, Huddleston CB, et al. Predictors, frequency, and indications for cardiopulmonary bypass during lung transplantation in adults. *Ann Thorac Surg*. 1994;57:1248–1251.

C.13. Should fluid administration be restricted, and are

blood products commonly required?

The amount of crystalloid that can be safely administered intraoperatively without adversely affecting the graft appears to be widely variable. Although efforts should be made to minimize fluid infusion intraoperatively, many patients undergoing lung transplantation require large amounts to maintain hemodynamic stability. The transplanted lung is at risk for pulmonary edema due to lack of lymphatic drainage and inflammatory insults, direct pulmonary trauma, and inflammatory cytokine release associated with reperfusion and organ harvest.

PGD occurs in 10% to 30% of patients after lung transplantation and is thought to be in part due to decreased alveolar fluid clearance. Severe (grade 3) PGD is a risk factor for early mortality following lung transplantation and the development of BOS. With increasing evidence that large volume fluid administration is a modifiable risk factor for PGD, many providers advocate fluid restriction for lung transplantation. In a retrospective cohort study of 500 patients, Geube et al. showed that grade 3 PGD (PGD3) occurs in 25% of patients and that every liter of fluid increased the odds for grade 3 PGD by 22%. The patients who developed grade 3 PGD were transfused with more red blood cell concentrate than patients who did not develop grade 3 PGD. Interestingly, there was no association between the use of crystalloid or colloid (nonblood) and grade 3 PGD. Likewise, the Lung Transplant Outcomes Group published data showing that transfusing 1 L of red blood cell concentrate was associated with a twofold increase in the incidence of PGD.

Before the development of the BLT procedure without CPB, patients with a history of surgery involving the lung or pleura or chronic infectious lung diseases were not deemed acceptable candidates for lung transplantation because of the anticipated

excessive bleeding associated with dissecting a scarred lung after anticoagulation for CPB. Without the uniform requirement for heparinization (ECMO, bilateral sequential LT, etc.), such patients are now generally regarded as operative candidates. Even without the need for full heparinization, these patients are still at increased risk for excessive bleeding, albeit a lower risk. Other variables reported to increase the need for blood product usage include double-lung procedures (DLT/BLT) and patients with cystic fibrosis. The need for CPB is a confounding factor, however. Historically, BLT patients were more likely to get planned or rescue CPB. With the advent of ECMO, new circuit, new cannulas, and cannulation strategies, excessive bleeding occurs less frequently in all categories of patients. Strategies for blood conservation should be adopted. For example, some groups have found a reduction in intraoperative bleeding in patients with a history of cystic fibrosis or previous intrathoracic surgery when antifibrinolytics are given continuously. ECMO, especially with heparin-bonded circuits, is a reasonable alternative to CPB because full anticoagulation is not needed. In addition, use of ECMO for hemodynamic support also helps with reducing the amount of crystalloid and blood products being administered. Transfusion therapy should remain a team decision and warrants a discussion between members of the anesthesiology and surgical staff. If blood products are to be administered, the anesthesiologist must know whether the patient has antibodies to cytomegalovirus (CMV) and must closely check blood products to confirm they coincide with the patient's status.

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C.14. Would you extubate the patient upon conclusion of the procedure?

A few studies have shown with proper selection of patients after SLT or BLT that early or immediate tracheal extubation is possible and can be successful. However, because of the frequent use of CPB, the resulting insult often associated with the procedure, the large postoperative volume shifts, hypothermia, and the frequent need for postoperative bronchoscopy, the trachea of lung transplant recipients is not generally extubated immediately after the procedure. Accordingly, unless intraoperative events (e.g., hyperinflation of the remaining intact lung, functional issues such as profound oropharyngeal edema, or difficult intubation are present) suggest that postoperative differential lung ventilation will be required, the double-lumen endotracheal tube is exchanged for a single-lumen tube. In many patients, the endotracheal tube change can be facilitated by use of an exchange catheter. However, great care should be taken to not advance the catheter too far and damage the graft. It is often beneficial to perform fiberoptic bronchoscopy to examine bronchial anastomoses and aggressively suction secretions or blood after replacement of the double-lumen tube with a single-lumen endotracheal tube. As with many procedures, careful inspection of the upper airway for edema should be performed by laryngoscopy before the endotracheal tube is exchanged.

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D. Postoperative Management

D.1. What are the major complications after lung transplantation?

Complications from lung transplantation can occur in the immediate (<24 hours), early (24 hours to 1 week), intermediate (8 days to 2 months), or late (>2 months) postoperative period. Major immediate complications include hyperacute rejection, abnormalities due to malpositioning of tubes and lines (e.g., pneumothorax, hemothorax, and hemomediastinum), and issues related to size mismatch between the donor and recipient lung. Reperfusion injury and pleural complications (e.g., hemothorax, pneumothorax, and empyema) are the major early complications. Acute rejection, bronchial dehiscence, and *Candida pneumonia* are intermediate complications. Late complications include chronic rejection, infection (CMV, aspergillus, mycobacterium), and bronchial stenosis. Infection and graft failure are the leading causes of death in the first posttransplant year. In later years, BOS predominates, and there are fewer cases caused by graft failure, infection, and malignancy. BOS is perhaps the most important complication in the burden of subsequent mortality; it occurs in 10% of patients each year; the incidence is highest at 5 years posttransplant. Retransplant patients are at the highest risk for BOS, whereas patients with cystic fibrosis and those with multiorgan transplants seem to be protected.

Early graft dysfunction varies in severity from mild shunting and chest radiograph infiltrates to gross pulmonary edema with

reduced lung compliance and intrapulmonary shunting. Management includes fluid restriction, diuretics, PEEP, iNO, and ECMO for severe cases. Immunosuppression is usually initiated before surgery, and the induction phase of therapy is continued for 5 to 10 days. The exact regimen varies between institutions but typically includes azathioprine, steroids, cyclosporine, and polyclonal antilymphocyte/antithymocyte globulins or interleukin-2 receptor antagonists. Acute rejection episodes are usually treated with *intense* steroid therapy and optimization of other immunosuppressant dosages. A challenge arises in differentiating acute rejection from infection as a source of shunting and chest radiograph infiltrates. Transbronchial biopsy is often necessary to make the distinction from histologic specimens. Bacterial pneumonia is the most frequent infection in the first 2 weeks. Although unusual in the first 2 weeks after transplantation, CMV is the second most common source of infectious pneumonitis. Broad-spectrum antibiotics are given perioperatively, and the regimen is adjusted based on the results of donor and recipient cultures. Antibiotic therapy for patients with cystic fibrosis is challenging, and the drug chosen is dictated by the patient's cultures and prior history of the organisms colonizing his or her lungs. Prophylactic acyclovir appears to be effective in reducing infections caused by herpes simplex, and trimethoprim-sulfamethoxazole is given to prevent infections from *Pneumocystis carinii*.

Abelson D, Glanville AR. Controversies and emerging topics in lung transplantation. *Breathe (Sheff)*. 2018;14(4):278–287.

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Krishnam MS, Suh RD, Tomasian A, et al. Postoperative complications of lung transplantation: radiologic findings along a time continuum.

Radiographics. 2007;27(4):957–974.

D.2. How is postoperative ventilation managed, and for how long is it required?

After most procedures, the fraction of inspired oxygen (FIO_2) can be rapidly reduced, and weaning from the ventilator can be initiated as soon as the patient is warm and stable. An exception to this approach is the patient who has undergone SLT for pulmonary hypertension. Because of a propensity for episodes of cardiopulmonary instability during the first 24 to 48 hours postoperatively, it is advantageous to keep these patients mechanically ventilated during this period, although increasing experience is revealing the positive effects of rapid weaning protocols in those patients that tolerate it.

Lung protective strategies should be employed; patients should be ventilated with 4 to 5 mL per kg for single-lung ventilation and 6 to 7 mL per kg for double-lung ventilation with PEEP as well to protect against lung injury. When possible, a low FIO_2 (<40%) should be used for the same reason. Plateau pressures >30 cm H_2O should be avoided. The ventilator settings should be adjusted according to the patient's needs to achieve adequate ventilation with the lowest plateau pressure and optimal ventilation/perfusion matching.

Postoperatively, ventilation/perfusion mismatch and intrapulmonary shunt are often more pronounced after SLT than BLT. Not surprisingly, patients with restrictive disease usually display the best pulmonary function after SLT because the graft receives the majority of both ventilation and perfusion. After SLT in emphysemic patients, the remaining native lung often receives a substantial portion of the tidal volume. The opposite is true in patients with pulmonary hypertension; the native lung continues to be ventilated but with limited blood flow. On rare occasions where there is a high difference in compliance

between the graft and recipient lung, lung isolation and differential ventilation of the transplanted and native lung is needed after SLT for obstructive lung disease (e.g., emphysematous lung disease). In these situations, the double-lumen endobronchial tube is left in place and two ventilators are employed. The native lung is ventilated with a low tidal volume (2 to 3 mL per kg) and rate, or even just connected to CPAP without intermittent mandatory ventilation. Nonetheless, the condition usually resolves rapidly with the return of spontaneous ventilation. Postural changes in arterial oxygen saturation are often prominent in SLT recipients. In general, patients who received a single lung for pulmonary hypertension or emphysema display better postoperative pulmonary function with the "transplant side up," whereas the opposite may be true in certain patients with restrictive lung disease. The precise etiology of this response is unclear but probably reflects positional variation in ventilation/perfusion matching.

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Nicoara A, Anderson-Dam J. Anesthesia for lung transplantation. *Anesthesiol Clin*. 2017;35(3):473–489.

D.3. What special precautions should be taken when a lung transplant recipient requires general anesthesia for subsequent nonpulmonary surgery?

Both the utilization of "extended criteria" donors and ex vivo lung perfusion systems have allowed for an increase in the number of recovered donor organs. Despite transplanting more complex patients and a greater acceptance of donor organs, survival has not changed over the past 5 years. The increased

number of transplants along with stable survival resulted in more lung transplant recipients being alive than ever before. After lung transplantation, patients may present to the operating room for surgeries not related to their pulmonary disease. With careful consideration and vigilance of the implications of lung transplantation, successful anesthetics can be carried out with minimal issues. Aspiration precautions should be implemented, and patients should be assessed for gastritis, peptic ulcer disease, or a history of gastrointestinal bleed especially in situations where anticoagulation is necessary. They should be evaluated for renal dysfunction, which may be caused by immunosuppressive therapy as well as hepatobiliary and/or pancreatic dysfunction. In addition to perioperative antibiotics, stress dose steroids, and bronchodilators, such as β_2-agonists, should be considered; lung transplant patients usually take steroids long term and are more apt to bronchoconstriction.

Not surprisingly, differences in the compliance and expiratory flow rates of a native and transplanted lung after SLT for emphysema can result in alterations in intraoperative capnography. This phenomenon has been described as producing a biphasic pattern of carbon dioxide exhalation, with the first peak reflecting exhalation from the transplanted lung and the second peak exhalation from the native lung. In addition, the transplanted lung is denervated so the cough reflex is present only in the proximal native airway and mucociliary function is impaired. In contrast, HPV is intact after lung transplantation and central respiratory control is unaffected. However, a blunted response to carbon dioxide may persist for patients with preoperative hypercapnia. The major factor limiting long-term survival from lung transplantation is BOS. This progressive condition characterized by progressive narrowing of small airways must be considered in patients with prior lung transplantation presenting for surgery and anesthesia after the

initial recovery phase. Other perioperative considerations for the patient with a prior lung transplant undergoing subsequent surgery are based on whether the patient was the recipient of one versus two lungs. In the former case, ventilation and perfusion of the remaining "diseased" native lung is influenced by the functional status of the transplanted lung. For patients with obstructive lung disease, overinflation of the native lung and resultant mediastinal shift with associated ventilation and hemodynamic consequences, although rare, must be considered when employing positive pressure ventilation.

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D.4. What are the long-term outcomes of lung transplantation?

Increased experience, improved techniques, and an increase in the number of donor organs facilitated by extended criteria donor and ex vivo perfusion systems have made lung transplantation a realistic option for many patients. The LAS system was introduced in 2005 to shift the method of distributing organs from a time-based seniority system to one where severity of disease is prioritized. Since then, more complex patients have been receiving lung transplantation. The procedure, however, is not without substantial risk, and a favorable outcome is by no means ensured. Although survival has not changed over the last 5 years (84.6% 1-year, 67.8% 3-year, and 55.5% 5-year survival), the absolute number of patients living after lung transplantation has increased because more procedures are being done. From June 2009 to 2016, the median survival was 6.5 years after primary lung

transplantation. For adult recipients who survived for 1-year posttransplantation, the median survival is 8.7 years. Graft failure is the leading cause of death in the first posttransplant year and BOS predominates in later years, with lower rates of death due to graft failure, infection, and malignancies. Gender, underlying cause for lung transplantation, and type of procedure (SLT vs. BLT) are a few of the factors influencing outcomes for these patients. SLT recipients seem to do better in the first year posttransplantation, whereas BLT recipients have a survival benefit starting the first year after transplantation. Likewise, patients with cystic fibrosis have better survival than patients with all other indications for lung transplantation. Female gender also confers a survival benefit.

A history of hypertension for donors is independently associated with higher 1-year survival while donor smoking, CMV mismatch, nonidentical blood type, history of diabetes, and other donor comorbidities as well as poor functional status for the donor are independently associated with lower survival at 1 year. Other factors associated with 1-year mortality include recipient age, donor age, recipient serum creatinine and bilirubin, recipient lung functional vital capacity (percent predicted), allograft ischemic time, and transplant center volume. Risk factors that are independently associated with 5-year mortality are similar to those of 1-year mortality with a few differences. Patients with lymphangioleiomyomatosis have better survival than those with an increasing number of human leukocyte antigen mismatches who have lower 5-year survival. Likewise, extremes of recipient age, older donor age, lower transplant center volume, and higher panel reactive antibody percentage are associated with higher mortality.

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Thabut G, Mal H. Outcomes after lung transplantation. *J Thorac Dis*. 2017;9(8):2684–2691.

D.5. Are there surgical alternatives to lung transplantation?

Some patients with severe emphysema who are not deemed transplant candidates may benefit from LVRS or "reduction pneumoplasty." Performed either through a median sternotomy, through a bilateral thoracoscopy, or via bronchoscopy, LVRS is thought to be most beneficial in patients with upper lobe emphysematous disease with the goal being to remover up to 30% of the patient's most severely compromised lung tissue. Postoperatively, this allows the previously hyperexpanded chest and depressed diaphragm to resume a more normal shape, improving chest wall mechanics, and eventually pulmonary function. There is a body of data demonstrating improved functional capacity in patients after LVRS. However, the beneficial effects of the procedure are not immediately evident and usually require 1 to 2 months to appear. Furthermore, whether the improvement in pulmonary function is sufficient to warrant the risk of the procedure remains controversial. Bronchoscopic LVRS techniques are relatively new and may be beneficial in this regard because they are less invasive. The data for endoscopic lung volume reduction is limited to small case series and case reports; more extensive studies are warranted. The evidence suggests that for carefully selected patients, LVRS represents a viable alternative to transplantation. In addition, LVRS may be used as a bridge to transplant. There are concerns that prior LVRS increases the risk during lung transplantation because of tissue scarring. Several studies have addressed this

and found no difference between outcomes in patients with end-stage COPD who had and those who did not have LVRS prior to transplantation. For patients with hyperinflation of the native lung after SLT for COPD/emphysema, LVRS of the native lung can be considered instead of a second SLT.

Fishman A, Martinez F, Naunheim K, et al. A randomized trial comparing lung-volume-reduction surgery with medical therapy for severe emphysema. *N Engl J Med*. 2003;348:2059–2073.

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SECTION 2 The Cardiovascular System

5 Ischemic Heart Disease and Coronary Artery Bypass Grafting

Yasdet Maldonado, Nikolaos J. Skubas, and Fun-Sun F. Yao

A 57-year-old man with triple-vessel coronary artery disease (CAD), hypertension, and type-II diabetes is scheduled for coronary artery bypass grafting (CABG). He had a myocardial infarction (MI) 7 months ago. He is taking metoprolol, metformin, and lisinopril. His blood pressure (BP) is 130/80 mmHg, and his heart rate (HR) is 55 beats per minute.

A. Medical Disease and Differential Diagnosis

1. What is triple-vessel CAD? Name the branches of the coronary arteries.
2. What are the indications for CABG?

3. What is percutaneous coronary intervention (PCI)? Discuss its indications, contraindications, and results.
4. What are the expected results of CABG?

B. Preoperative Evaluation and Preparation

1. Which preoperative tests would you order?
2. How would you evaluate the patient's left ventricular function?
3. Which factors determine myocardial oxygen supply?
4. What are the three major determinants of myocardial oxygen consumption? How are they measured clinically?
5. Would you continue the β-blocker (metoprolol) on the day of surgery? Why/why not? What is its half-life? What is the role of β-adrenergic blockers in treating congestive heart failure (CHF)?
6. Would you continue the angiotensin-converting enzyme (ACE) inhibitor on the day of surgery? Why/why not?
7. If the patient who is on lisinopril develops hypotension intraoperatively, how would you manage it?

C. Intraoperative Management

C.I. *Before Cardiopulmonary Bypass*

1. What is your plan to monitor the patient?
2. What is the Allen test?
3. How would you monitor electrocardiogram (ECG)? Why lead V_5? If you do not have precordial leads in your ECG machine, how can you monitor the left ventricle (LV)?
4. Should you monitor temperature from multiple sites?
5. Is it necessary to monitor pulmonary artery (PA) pressure for coronary artery operations?
6. What are the possible complications of PA catheterization?
7. What is normal pulmonary artery occlusion pressure (PAOP)?
8. What are the hemodynamic consequences of myocardial

ischemia? How can you detect myocardial ischemia? Is PAOP a sensitive indicator of myocardial ischemia?

9. Discuss the principles and clinical applications of intraoperative transesophageal two-dimensional echocardiography.
10. How would you induce anesthesia? Is there any advantage/disadvantage to using propofol versus etomidate as the main induction agent? What kind of neuromuscular blocker (NMB) would you use? Why?
11. How would you maintain anesthesia? Volatile anesthetics or total intravenous anesthesia (TIVA)?
12. What are the cardiovascular effects of volatile anesthetics, morphine, and fentanyl?
13. What should you do during sternotomy?
14. Would you use prophylactic nitroglycerin during CABG to prevent intraoperative myocardial ischemia or perioperative MI?
15. If ST-segment depression is seen during surgery, how would you treat it? What is the relation between perioperative myocardial ischemia and postoperative MI?
16. Discuss autologous transfusion and blood conservation for cardiac surgery.
17. What antifibrinolytic will you use to reduce blood transfusions?
18. How do you know that the tip of the PA catheter is in the right ventricle (RV) or the PA?

C.II. *During Cardiopulmonary Bypass*

1. What anticoagulant would you give before cardiopulmonary bypass (CPB)? How much would you give? What is its mechanism?
2. What is the half-life of heparin? How is it eliminated?
3. How do you monitor heparin dosage? What is the activated

coagulation time (ACT) test?
4. What is total CPB? What is partial bypass?
5. What kinds of pumps are used in CPB? Are they pulsatile or not?
6. What is the purpose of venting the LV? How can it be done?
7. How many types of oxygenators are there? What are the advantages of each type?
8. What kind of priming solution would you use? How much priming solution would you use? When would you prime with blood? Why?
9. What are the advantages and disadvantages of hemodilution?
10. How do you monitor the patient during CPB?
11. What should your target BP be during CPB?
12. How would you treat hypotension during CPB?
13. How would you treat hypertension (a mean arterial pressure [MAP] of over 100 mmHg)?
14. How do you prepare an IV infusion of sodium nitroprusside, nicardipine, and nitroglycerin? What are the usual doses? Which do you prefer to use?
15. How much pump flow would you maintain during CPB? During hemodilution? During hypothermia?
16. How does blood viscosity change during hemodilution and hypothermia?
17. How is anesthesia provided during CPB?
18. Would you give muscle relaxants during CPB? How is the action of muscle relaxants affected during CPB?
19. How do you know the patient is well perfused during CPB?
20. How much gas flow would you use for the oxygenator? What kind of gas would you use? Why?
21. What are the disadvantages of hypocapnia during CPB?
22. How would you preserve the myocardium during CPB?
23. What is cardioplegia? How much would you use?
24. The arterial blood gases and electrolytes during CPB are as

follows: pH, 7.36; $Paco_2$, 42 mmHg; Pao_2, 449 mmHg; CO_2 content, 24 mEq per L; sodium (Na), 128 mEq per L; potassium (K), 5.8 mEq per L; glucose, 180 mg/dL; and hematocrit, 20%. The patient's temperature is 27°C (80.6°F). At what temperature are blood gases measured? How would you correct the blood gases according to patient's body temperature? Would you treat the arterial blood gases at 37°C (98.6°F) or at patient's body temperature?

25. How does the blood sugar level change during CPB? Why? What is optimal glucose control intraoperatively? Does hyperglycemia increase neurologic complications during CPB?
26. What are the effects of CPB on platelet and coagulation factors?
27. If the blood level of the venous reservoir is low, what would you replace it with? Blood or balanced salt solution?
28. How do you estimate the fluid balance during CPB?
29. For how long a period can the aorta be cross-clamped?
30. Why does the urine turn pink in some cases of CPB? What is the renal threshold for plasma hemoglobin?
31. Why does it take longer to rewarm than to cool the patient via the pump oxygenator?
32. At what temperature can the patient be weaned from CPB?
33. How would you defibrillate the heart internally during CPB?
34. If the HR is 40 beats per minute, what should you do?
35. How would you prepare for termination of CPB?
36. How would you decide the need for inotropic support?

C.III. *After Cardiopulmonary Bypass*

1. How would you reverse heparin? How much protamine would you use? What are the other drugs used to neutralize heparin?
2. What is the action mechanism of protamine?
3. What are the complications of too much protamine?
4. What is a protamine reaction? How can you prevent this

condition? How do you treat it?

5. What are the indications for intra-aortic balloon pump (IABP)?
6. What are the principles of IABP?
7. What are the complications of IABP?

D. Postoperative Management

1. Would you reverse the muscle relaxants? Why?
2. When will you wean the patient from the ventilator?
3. What criteria would you use in deciding when to wean the patient from the ventilator?
4. What are potential postoperative complications?

A. Medical Disease and Differential Diagnosis

A.1. What is triple-vessel CAD? Name the branches of the coronary arteries.

Triple-vessel CAD involves progressive atherosclerosis of the major branches of the coronary arteries with eventual luminal obstruction and myocardial injury. The intimal disease is typically segmental but can be diffuse in severe cases. The coronary arteries are the following:

- The right coronary artery (RCA)
- The left anterior descending (LAD) branch of the left main coronary artery (LMCA)
- The left circumflex (CX) branch of the LMCA

The branches of coronary arteries are shown in **Figure 5.1**. The LAD and CX arise from the LMCA. The sinus node is supplied by the RCA in approximately 50% to 60% of people and by the CX artery in the remaining 40% to 50%. Cardiac dominance is determined by which coronary artery branch supplies the posterior descending artery (PDA). It could be the RCA (right dominant circulation, 70% to 80%), left CX artery (left dominant), or both (codominant). Small branches from the

PDA perfuse the atrioventricular (AV) node.

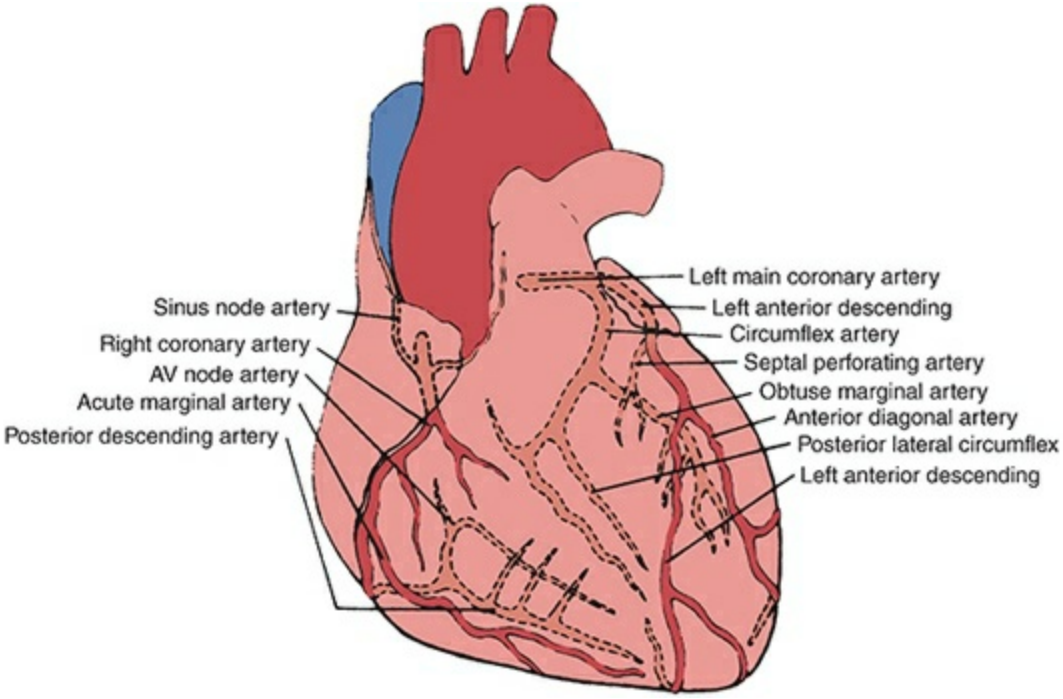

FIGURE 5.1. Branches of the coronary arteries. AV, atrioventricular.

The most common "targets" for coronary bypass grafting are the LAD, obtuse marginal (branch of CX), and posterior descending (branch of RCA) arteries. A suitable distal target site, beyond the level of the proximal stenosis, is determined by the surgeon after review of angiographic images and direct external inspection and palpation.

Villa ADM, Sammut E, Nair A, et al. Coronary artery anomalies overview: the normal and the abnormal. *World J Radiol*. 2016;8(6):537–555.

Zipes DP, Libby P, Bonow RO, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 11th ed. Philadelphia, PA: Elsevier; 2019:1301.

A.2. What are the indications for CABG?

Patients whose angina is not controlled by medical treatment or who have unacceptable side effects with such management should be considered for coronary revascularization. The indications for CABG are as follows:

- Acute MI if a nonsurgical intervention failed or there is ischemia at rest or hemodynamic instability/cardiogenic shock or complications, such as ventricular septal defect or ruptured papillary muscle and mitral regurgitation
- Life-threatening ventricular arrhythmia in the presence of significant left main (>50%) or coronary artery (>70%) obstruction
- At the same time with other cardiac surgical procedures

The SYNTAX (Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery) trial provided a good comparison of PCI versus CABG. A SYNTAX score is a derivative of this trial, with a score >22 being associated with favorable outcomes after CABG. The score reflects factors that increase complexity of PCI.

Patel MR, Calhoon JH, Dhemer GJ, et al. ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS 2017 appropriate use for coronary revascularization in patients with stable ischemic heart disease: a report of the American College of Cardiology Appropriate Use Criteria Task Force, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society of Thoracic Surgeons. *J Am Coll Cardiol*. 2017;69(17):2212–2241.

Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med*. 2009;360:961–972.

Zipes DP, Libby P, Bonow RO, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 11th ed. Philadelphia, PA: Elsevier; 2019:1301.

A.3. What is percutaneous coronary intervention (PCI)? Discuss its indications, contraindications, and results.

PCI has developed rapidly since its introduction in 1977. It is now an acceptable method of treating selected patients who have angina pectoris. This technique involves the passage of a small (3 French) catheter into the involved coronary artery and

through the stenosis. With the balloon portion of the catheter straddling the stenosis, inflations are performed that result in enlargement of the stenotic lumen and a controlled injury involving, to a varying degree, plaque compression, intimal fissures, and medial stretching. Following the dilation, coronary stents are introduced to maintain long-term patency. The stents are either bare-metal (cobalt–chromium alloy) or drug-eluting stents (DES).

PCI has redefined who is candidate for elective surgical myocardial revascularization. With the current available technology, PCI is considered a therapeutic option in any individual with disabling ischemic symptoms despite good medical therapy and focal obstructive coronary disease regardless of cause. The indications for PCI are as follows:

- Isolated discrete proximal single- or double-vessel disease
- Post-CABG with new stenotic lesions or stenosis at distal anastomosis
- Restenosis following PCI
- Contraindications to CABG
- Coronary stenosis following cardiac transplantation
- Occluded vessels within the last 6 months and less than 15 mm in length
- Post-streptokinase therapy for revascularization

PCI is contraindicated in the following:

- Left main CAD in which the distal coronary vessels are not protected by at least one completely patent large collateral vessel
- Multivessel severe diffuse disease
- Absence of a discrete obstructing lesion

The primary success rate of PCI is approximately 90%, but restenosis occurs at a rate of approximately 30%, 6 months postprocedure. Dilatation can be repeated with a 90% success rate. The artery tends to remain patent after the second

angioplasty. With the introduction of coronary stents, which act as a metal scaffold, the restenosis rate after PCI has been decreasing, and fewer patients require subsequent revascularization: 10% to 15% after stenting versus 25% to 35% after PCI alone. The decrease in luminal diameter following stent placement is evident within the first 6 to 9 months after stent placement and is the result of proliferative neointimal tissue growth in response to the associated injury and inflammation. The stent scaffold is coupled with polymers that elute or slowly release pharmacologic agents (sirolimus, an immunosuppressant, and paclitaxel, an antineoplastic), which inhibit the neointimal growth. The DES have reduced the need for repeat revascularization to an even lower rate, 4% to 6%.

However, PCI is a different therapeutic approach other than CABG. PCI is targeting the area of lesion only, whereas CABG bypasses these lesion areas. This may be the reason that, at least in the intermediate term, CABG is considered to be superior for patients with multivessel disease.

Diegeler et al. showed that, for isolated high-grade lesions of the LAD, CABG through a left anterior thoracotomy is as effective as PCI with stent placement. Although stenting provided excellent short-term results with fewer periprocedural adverse events, CABG was superior with regard to the need for repeated intervention in the target vessel and freedom from angina at 6 months of follow-up. Further, Serruys et al. compared outcomes between PCI with stent and CABG surgery and found that at 5 years, there was no difference in mortality between stenting and surgery for multivessel disease. Importantly, the incidence of stroke or MI was not significantly different between the two groups. However, the rate of major adverse cardiac and cerebrovascular events was higher in the stent group, driven by the increased need for repeat revascularization. A recent report on 10-year outcomes also

showed that for the treatment of unprotected LMCA disease, PCI with stent implantation showed similar long-term mortality and rates of death, Q-wave MI, or stroke. However, stenting, even with DES, was associated with higher rates of repeat revascularization than was CABG. Lastly, a recent comparison between stenting and CABG in patients with previously untreated three-vessel disease or LMCA disease concluded that CABG remains the standard of care for patients with three-vessel or LMCA disease because the use of CABG, as compared with PCI, resulted in lower rates of the combined end point of major adverse cardiac or cerebrovascular events at 1 year.

Diegeler A, Thiele H, Falk V, et al. Comparison of stenting with minimally invasive bypass surgery for stenosis of the left anterior descending coronary artery. *N Engl J Med*. 2002;347:561–566.

Hillis LD, Smith PK, Anderson JL, et al. 2011 ACCF/AHA guideline for coronary artery bypass graft surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2011;124:e652–e735.

Moliterno DJ. Healing Achilles—sirolimus versus paclitaxel. *N Engl J Med*. 2005;353:724–727.

Park DW, Kim YH, Yun SC, et al. Long-term outcomes after stenting versus coronary artery bypass grafting for unprotected LMCA disease: 10-year results of bare-metal stents and 5-year results of drug-eluting stents from the ASAN-MAIN (ASAN Medical Center-Left MAIN Revascularization) Registry. *J Am Coll Cardiol*. 2010;56(17):1366–1375.

Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med*. 2009;360:961–972.

Zipes DP, Libby P, Bonow RO, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 11th ed. Philadelphia, PA: Elsevier; 2019:1301.

A.4. What are the expected results of CABG?

CABG has been demonstrated to provide a survival benefit over medical therapy alone in the following three randomized, controlled trials from the 1970s and 1980s: the Veterans

Administration Cooperative Study, the European Coronary Surgery Study, and the Coronary Artery Surgery Study. A 1994 meta-analysis confirmed that CABG resulted in lower mortality when compared to medical management at 5 years (10% vs. 16%, $P < .01$) and 10 years (26% vs. 31%, $P = .03$). Survival is greatest for those with extensive disease and/or left ventricular dysfunction. Patients in the SYNTAX trial with triple-vessel disease also had a survival benefit with CABG when compared to PCI (mortality, 9.2% vs. 14.6%; $P = .006$).

Bypass conduits can be either arterial or venous, with arterial grafts considered superior conduits over venous grafts. The success of CABG depends on the long-term patency of the graft. The internal thoracic (mammary) artery (ITA) is the most commonly used bypass graft. Use of the ITA graft is considered a quality indicator by the Society of Thoracic Surgeons (STS). The saphenous vein is the most commonly used venous graft. Failure rates of venous grafts are related to variable size and quality.

Passamani ER, Frommer PL, Mullin S, et al. Coronary Artery Surgery Study (CASS): a randomized trial of coronary bypass surgery: survival data. *Circulation*. 1983;68:989–950.

Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med*. 2009;360:961–972.

The Society of Thoracic Surgeons. Performance measure descriptions. https://www.sts.org/quality-safety/performance-measures/descriptions. Accessed December 20, 2019.

Varnauskas E; and European Coronary Surgery Study Group. Twelve-year follow-up of survival in the randomized European coronary surgery study. *N Engl J Med*. 1988;319:332–327.

Veterans Administration Coronary Artery Bypass Surgery Cooperative Study Group. Eleven-year survival in the Veterans Administration randomized trial of coronary bypass surgery for stable angina. *N Engl J Med*. 1984;311:1333–1339.

Yusuf S, Zucker D, Peduzzi P, et al. Effect of coronary artery bypass graft

surgery on survival: overview of 10-year results from randomised trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. *Lancet*. 1994;344:563–570.

B. Preoperative Evaluation and Preparation

B.1. Which preoperative tests would you order?

In addition to the routine systemic examinations of all organ systems, special attention should be paid to the cardiovascular status.

- Renal function—urinalysis, blood urea nitrogen, creatinine
- The routine evaluation of hepatic function is not standard. Patients who should have testing to evaluate hepatic function include those with a previous history of hepatitis, jaundice, or a history of drug abuse.
- Pulmonary function—chest x-ray film, baseline arterial blood gases, and spirometry if indicated
- Hematologic function—complete blood count, prothrombin time, partial thromboplastin time, platelets (platelet function if available and/or indicated; namely, for those patients previously receiving antiplatelet therapy)
- Metabolism—electrolytes and blood sugar
- Cardiovascular function—computed tomography (CT) scan absolutely indicated in redo sternotomy to investigate the proximity of the sternum to the anterior surface of the heart, resting and exercise ECG (if a stress test was performed preoperatively), cardiac catheterization and coronary angiography, location and severity of coronary occlusion, echocardiography, and left ventricular function (from catheterization, magnetic resonance imaging, enhanced multidetector CT, and/or echocardiography)

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA:

Elsevier; 2017:3–19.

B.2. How would you evaluate the patient's left ventricular function?

- Medical history: history of MI and presence or absence of angina
- Symptoms and clinical signs of left ventricular failure (dyspnea at rest or exercise, nocturnal orthopnea) and/or right heart failure (ascites, pitting edema, jugular vein distention)
- Cardiac catheterization, angiography, and echocardiography
- Ejection fraction (normally approximately 65%)
- Left ventricular end-diastolic pressure (LVEDP) or PAOP: normal 6 to 15 mmHg
- Left ventricular wall motion (by echocardiography)—normal (wall thickening of >30%), hypokinesis (wall thickening of 10% to 30%), akinesia (wall thickening of <10%), or dyskinesia (outward motion during systole) (**Fig. 5.2**)

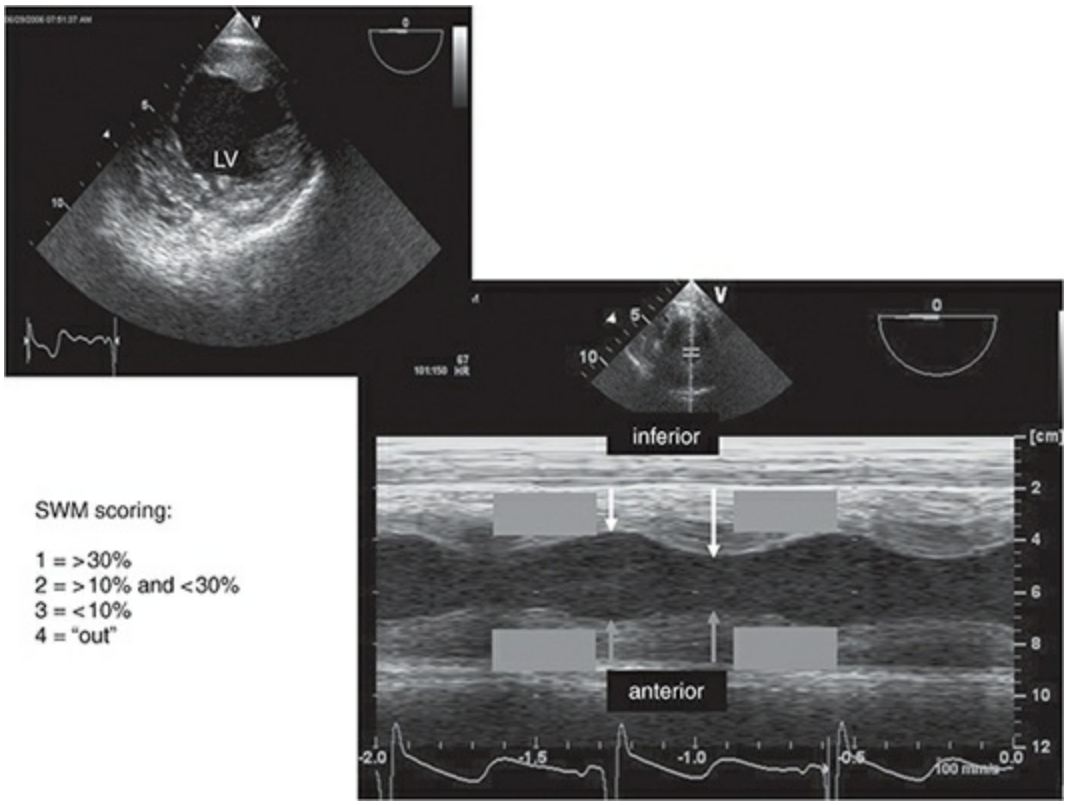

FIGURE 5.2. Echocardiographic evaluation of the left ventricle (LV). The transgastric midpapillary

short-axis view of the LV is shown in left. By placing a cursor line across the middle of the inferior **(top of the image)** and anterior **(bottom of the image)** segments of the left ventricular myocardium, the motion of the segments over time is shown in the right image. The percentage of wall thickening can be either visually estimated or measured between diastole and systole. SWM, segmental wall motion.

- Cardiac index (normal >2.2 L/min/m^2)
- Myocardial viability studies (contrast echocardiography or positron emission tomography study)

Segmental wall motion abnormality (SWMA) is the result of CAD. The interruption of perfusion results in abnormal motion in the related myocardial segments. There is a gradation of wall motion abnormality that consists progressively of hypokinesis, akinesis, and, subsequently, dyskinesis in which a wall moves away from the center of the ventricle. Wall thickening and endocardial motion are intrinsically tied, and all SWMAs are expected initially to be associated with abnormalities of thickening as well as endocardial motion.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:179–205, 390–426.

Schuleri KH, Centola M, George RT, et al. Characterization of peri-infarct zone heterogeneity by contrast-enhanced multidetector computed tomography: a comparison with magnetic resonance imaging. *J Am Coll Cardiol*. 2009;53(18):1699–1707.

B.3. Which factors determine myocardial oxygen supply?

Myocardial oxygen (O_2) supply = coronary blood flow × arterial O_2 content

The coronary blood flow depends on the following:

- Diastolic aortic pressure (DAP)
- LVEDP
- Patency of coronary arteries
- Coronary vascular tone

And it can be determined by the formula:

Coronary blood flow = coronary perfusion pressure ÷ myocardial vascular resistance, or, Coronary blood flow = (DAP − LVEDP) ÷ myocardial vascular resistance

The arterial O_2 content (CaO_2) is determined by the following equation:

$$CaO_2 = 1.34\ (mL/g) \times \text{hemoglobin concentration}\ (g/dL) \times O_2\ \text{saturation}\ (\%) + (0.0031 \times PaO_2)$$

O'Brien ERM, Nathan HJ. Coronary physiology and atherosclerosis. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:132–156.

B.4. What are the three major determinants of myocardial oxygen consumption? How are they measured clinically?

The three major determinants of myocardial oxygen consumption are myocardial wall tension, contractility, and HR.

Myocardial wall tension of the LV is estimated by the following:

- The Laplace equation states that the myocardial wall tension (T) is analogous to the diameter of the ventricle (R, radius) and the intracavitary pressure (P) and inversely proportional to the myocardial wall thickness (Th): $T = P \times R \div 2Th$
- Diastolic wall tension is related to the diastolic radius (R) of the ventricle, which is considered a surrogate of preload or left ventricular end-diastolic volume (LVEDV); the latter is estimated by the PAOP (because neither LVEDP nor left atrial pressure can be directly measured).
- Afterload is approximated via the systolic BP, which equals systolic ventricular pressure if there is no aortic stenosis.

Contractility is evaluated by:

- *Invasive techniques*. Maximal velocity of contraction (Vmax), dP/dt (pressure time indices of ventricle: how fast [dt] the

intraventricular pressure [dP] rises), or left ventricular end-systolic pressure/volume ratio

- *Noninvasive technique*. Pre-ejection period/left ventricular ejection time, and global and regional ventricular wall motion by echocardiography (**Fig. 5.3**)

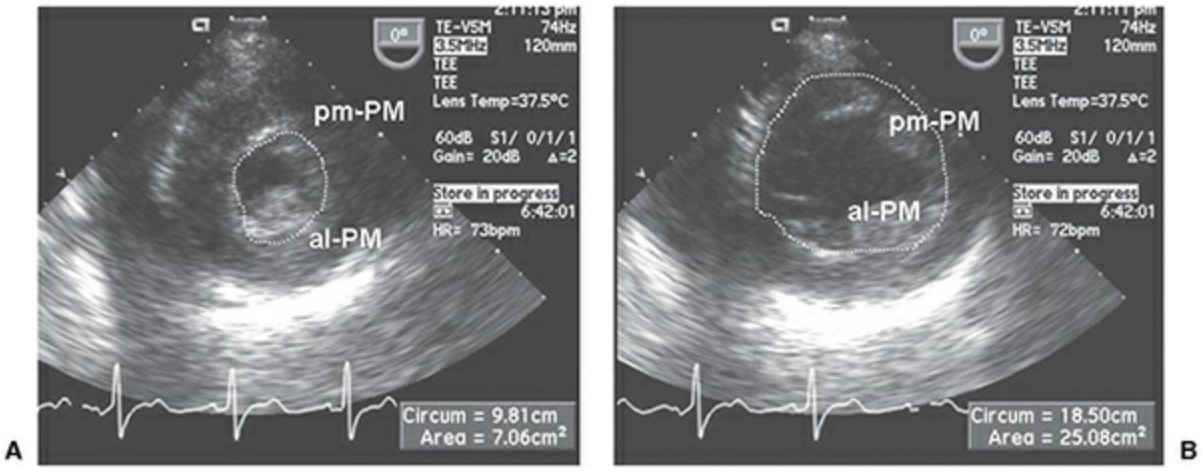

FIGURE 5.3. Echocardiographic evaluation of the systolic function of the LV. The transgastric midpapillary short-axis view of the LV is shown in systole **(A)** and diastole **(B)**. The endocardial border is traced (without including the endocardium of the two papillary muscles), and the end-systolic area (ESA) and end-diastolic area (EDA) are calculated. The percentage area change (fractional area change [FAC]) is calculated as: FAC = (EDA − ESA) / EDA. The FAC correlates with but does not substitute the percentage ejection fraction. al-PM, anterolateral papillary muscle; pm-PM, posteromedial papillary muscle.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:179–205.

B.5. Would you continue the β-blocker (metoprolol) on the day of surgery? Why/why not? What is its half-life? What is the role of β-adrenergic blockers in treating congestive heart failure (CHF)?

The β-blocker (metoprolol) should be continued not only up until surgery but also throughout the perioperative period. In patients with unstable angina, sudden withdrawal of β-blocker may produce an exacerbation of symptoms and may precipitate an acute MI. The dose of β-blocker does not need to be reduced

before surgery for fear of bradycardia, hypotension, or difficulty in weaning from CPB. The half-life of oral metoprolol is 3 hours. It is metabolized in the liver.

Reductions in HR with a β-blocker occur at lower serum levels than depression of myocardial contractility. Accordingly, as drug levels decrease after discontinuation of therapy, reductions in chronotropic response last longer than reductions in inotropy. This is an important concept in treating tachycardias in patients with significant ventricular dysfunction and CHF—a small dose is appropriate and indicated, whereas a large dose may suppress even further the inotropic state.

Numerous studies have confirmed improvements in cardiac function, exercise capacity, and long-term survival in patients with heart failure resulting from MI, hypertrophic cardiomyopathy, or idiopathic dilated cardiomyopathy with β-blockers. β-Blockers may also be of benefit in patients with diastolic dysfunction, secondary to hypertension.

Potential benefits of β-adrenergic blockade in heart failure include decreased HR and normalization of β-receptor function. A slower HR improves diastolic function by increasing the diastolic filling time and myocardial perfusion and by decreasing the myocardial oxygen consumption. β-Adrenergic receptors are downregulated in heart failure, but their response is normalized by long-term β-blockade.

Hillis LD, Smith PK, Anderson JL, et al. 2011 ACCF/AHA guideline for coronary artery bypass graft surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2011;124:e652–e735.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:292–356.

B.6. Would you continue the angiotensin-converting enzyme (ACE) inhibitor on the day of surgery?

Why/why not?

Major medical societies such as the American College of Cardiology and American Heart Association recommend continuation of ACE inhibitors in the perioperative period. There is no difference in the amount of vasopressor or inotrope requirements during cardiac surgery in those patients who continue ACE inhibitors preoperatively. In fact, ACE inhibitors may help control post-CPB hypertension. Diabetic patients may specifically benefit from receiving ACE inhibitors preoperatively. Patients at risk for vasoplegia or impaired left ventricular function may, however, suffer from intraoperative hypotension.

Bhatia M, Arora H, Kumar P. Pro: ACE inhibitors should be continued perioperatively and prior to cardiac surgery. *J Cardiothorac Vasc Anesth*. 2016;30(3):816–819.

Disque A, Neelankavil J. Con: ACE inhibitors should be stopped prior to cardiac surgery. *J Cardiothorac Vasc Anesth*. 2016;30(3):820–822.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130(2):2215–2245.

Kristensen SD, Knuuti J. New ESC/ESA guidelines on noncardiac surgery: cardiovascular assessment and management. *Eur Heart J*. 2014;35:2344–2345.

B.7. If the patient who is on lisinopril develops hypotension intraoperatively, how would you manage it?

The more common causes of intraoperative hypotension, such as hypovolemia, deep anesthesia, and surgical manipulation, should be corrected first. Vasoplegic syndrome is most commonly observed in cardiac surgery. It is characterized by severe refractory hypotension in the absence of other identifiable causes of hypotension. Persistent hypotension increases

perioperative mortality.

BP is maintained by three systems: the sympathetic system, the renin–angiotensin system (RAS), and the vasopressinergic system. Most anesthetic medications reduced the influence of the sympathetic system, and, as a result, the body relies more on the RAS and vasopressinergic systems. ACE inhibitors and angiotensin receptor blockers are RAS antagonists. ACE inhibitors specifically prevent the conversion of angiotensin I to angiotensin II. This results in a lower arterial resistance and increased vascular capacitance.

There is no specific antagonist for ACE-inhibitors. Treatment may be challenging. Conventional therapies such as volume expansion and vasopressors may be tried. When these conventional therapies are not effective, exogenous vasopressin may improve hypotension. Refractory hypotension may be treated with methylene blue, which interferes with the nitric oxide-cyclic guanylate monophosphate (cGMP) pathway. Methylene blue is contraindicated in patients with renal impairment because it is primarily eliminated by the kidneys.

Ertmer C, Rehberg S, Westphal M. Vasopressin analogues in the treatment of shock states: potential pitfalls. *Best Pract Res Clin Anaesthesiol*. 2008;22:393–406.

Fischer GW, Levin MA. Vasoplegia during cardiac surgery: current concepts and management. *Semin Thorac Cardiovasc Surg*. 2010;22:140–144.

Gomes WJ, Carvalho AC, Palma JH, et al. Vasoplegic syndrome after open heart surgery. *J Cardiovasc Surg (Torino)*. 1998;39:619–623.

Lange M, Aken HV, Westphal M, et al. Role of vasopressinergic V1 receptor agonists in the treatment of perioperative catecholamine-refractory arterial hypotension. *Best Pract Res Clin Anaesthesiol*. 2008;22:369–381.

Turan A, You J, Shiba A, et al. Angiotensin converting enzyme inhibitors are not associated with respiratory complications or mortality after noncardiac surgery. *Anesth Analg*. 2012;114(3):552–660.

C. Intraoperative Management

C.I. Before Cardiopulmonary Bypass

C.I-1. *What is your plan to monitor the patient?*

- Standard American Society of Anesthesiologists (ASA) monitors
- ECG—simultaneous leads V_5 and II, multiple-lead ST-segment analysis
- Arterial line for BP and arterial blood gases. The site of arterial line placement will vary per institution. Brachial artery catheters provide a good balance of estimating aortic pressures and rarely cause complications. Arterial cannulation is performed on the upper extremity not intended to be used for harvesting of an arterial conduit.
- PA catheter—pulmonary and central venous pressures (CVPs), hemodynamic parameters (cardiac output, stroke volume, systemic and pulmonary vascular resistance)
- CVP line only—if the patient has good left ventricular function and no problems are expected
- Urine output
- Temperature—esophageal (or PA) and bladder (or rectal, tympanic, or nasopharyngeal)
- Laboratory—arterial blood gases, electrolytes, hematocrit, ACT, and oxygen saturation of the mixed venous blood (SVO_2)
- Transesophageal echocardiography (TEE) if not contraindicated. Absolute contraindications are esophagectomy or esophagogastrectomy, active upper gastroesophageal bleeding, or recent surgery, oropharyngeal trauma, and presence of esophageal pathology (tracheoesophageal fistula, stricture, trauma, tumor, scleroderma, Mallory-Weiss tear, and diverticulum). The anticipated benefits should be weighed, however, against potential risks in every patient prior to

deciding whether to insert a TEE probe.

- Cerebral oximetry, especially for patients with high risk of postoperative neurologic outcomes, such as those undergoing hypothermic circulatory arrest
- Bispectral index to ensure adequate level of unconsciousness and eliminate the risk of intraoperative awareness

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Singh A, Bahadorani B, Wakefield B, et al. Brachial artery pressure monitoring during cardiac surgery rarely causes complications. *Anesthesiology*. 2017;126(6):1065–1076.

C.I-2. *What is the Allen test?*

The Allen test is used to detect the presence of adequate collateral ulnar arterial circulation. The radial and ulnar arteries are occluded by the examiner's fingers, and the patient is then asked to make a tight fist repeatedly until the palmar skin is blanched (to empty the blood from the hand). If the patient is under anesthesia, the blood in the hand may be drained by a third person squeezing the hand. The hand is held above the heart level to help venous drainage. Then, the fist is opened slowly and put down to the heart level. Only the ulnar compression is released, and the flush of the palmar skin is watched. The Allen test is:

- Normal—if the flush appears in less than 7 seconds (presence of adequate collateral connections between the superficial [ulnar] and deep [radial] palmar arches)
- Borderline—7 to 15 seconds
- Abnormal—greater than 15 seconds

A modified Allen test may be done with a Doppler detector or a pulse oximeter. The results of Allen test are abnormal in approximately 3% of young healthy individuals. However, Slogoff et al. studied the complications following radial artery cannulation in 1,699 cardiovascular surgical

patients. They concluded that in the absence of peripheral vascular disease, Allen test is not a predictor of ischemia of the hand during or after radial artery cannulation, and that radial artery cannulation is a low-risk, high-benefit monitoring technique that deserves wide clinical use. However, in the current litigious setting and in the face of some evidence to the contrary, it is probably prudent to continue to perform Allen test and document the results. Some authorities still consider the use of Allen test as the standard of care.

Alastruey J, Parker KH, Peiró J, et al. Can the modified Allen's test always detect sufficient collateral flow in the hand? A computational study. *Comput Methods Biomech Biomed Engin*. 2006;9(6):353–361.

Brzezinski M, Luisetti T, London MJ. Radial artery cannulation: a comprehensive review of recent anatomic and physiologic investigations. *Anesth Analg*. 2009;109(6):1763–1781.

Cederholm I, Sørensen J, Carlsson C. Thrombosis following percutaneous radial artery cannulation. *Acta Anaesthesiol Scand*. 1986;30:227–230.

Hildick-Smith D. Use of the Allen's test and transradial catheterization. *J Am Coll Cardiol*. 2006;48(6):1287.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:390–426.

Slogoff S, Keats AS, Arlund C. On the safety of radial artery cannulation. *Anesthesiology*. 1983;59:42–47.

C.I-3. *How would you monitor electrocardiogram (ECG)? Why lead V_5? If you do not have precordial leads in your ECG machine, how can you monitor the left ventricle (LV)?*

Multiple-lead ECG monitoring provides the best clinically available method of detecting perioperative ischemia. Based primarily on results obtained from exercise treadmill testing, 96% of ischemic events can be detected by combining ECG

leads II and V_5; therefore, leads II and V_5 are the optimal leads for intraoperative myocardial ischemia. However, London et al. found that the standard combination of leads II and V_5 was only 80% sensitive, whereas combining leads V_4 and V_5 increased sensitivity to 90% in patients with known or suspected CAD undergoing noncardiac surgery with general anesthesia. The sensitivity increased to 96% by combining leads II, V_4, and V_5. If only one lead can be displayed, lead V_5 should be used because it has the greatest sensitivity: 75% intraoperatively and 89% during exercise treadmill testing (see also Chapter 14, section C.3).

London MJ, Hollenberg M, Wong MG, et al. Intraoperative myocardial ischemia: localization by continuous 12-lead electrocardiography. *Anesthesiology*. 1988;69:232–241.

C.I-4. *Should you monitor temperature from multiple sites?*

In many cardiac surgery centers, temperature may be measured from two or more sites in order to estimate the accurate core temperature and achieve even distribution of body heat during cooling and rewarming by extracorporeal circulation (ECC). Esophageal, nasopharyngeal, bladder, or tympanic sites measure core temperature; the axillary and rectal sites measure peripheral temperature. Urinary bladder temperature monitoring through a urinary catheter is quite convenient and popular and reflects a body temperature between core and periphery. During cooling and rewarming by ECC, the core temperature changes rapidly, whereas the peripheral temperature changes slowly. The opposite changes are witnessed during surface cooling or warming. Nowadays, single-site core temperature monitoring is the prevailing practice when ECC is conducted at near normal body temperature.

Temperatures are measured during cooling on ECC to ensure that the organs most susceptible to potential hypoperfusion, such as the brain, actually receive the protective effect of the desired hypothermia. In this regard, nasopharyngeal or tympanic membrane temperatures are the monitoring sites, although they, at times, overestimate or underestimate the actual brain temperature. During rewarming, cerebral hyperthermia should be avoided (by maintaining a gradient of 5°C between the arterial blood and brain, with the brain having the lower temperature) and should be corrected immediately because hyperthermia increases the cerebral oxygen consumption and may exacerbate postoperative neuropsychological dysfunction.

Bar-Yosef S, Mathew JP, Newman MF, et al. Prevention of cerebral hyperthermia during cardiac surgery by limiting on-bypass rewarming in combination with post-bypass body surface warming: a feasibility study. *Anesth Analg*. 2004;99:641–646.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1248–1290.

Sessler D. Temperature monitoring and perioperative thermoregulation. *Anesthesiology*. 2008;109(2):318–338.

C.I-5. *Is it necessary to monitor pulmonary artery (PA) pressure for coronary artery operations?*

The indication to monitor PA pressure includes the following:

Diagnostic

- Diagnosis of shock states
- Differentiation of high- versus low-pressure pulmonary edema
- Diagnosis of primary pulmonary hypertension
- Diagnosis of valvular disease, intracardiac shunts, cardiac tamponade, and pulmonary embolus

- Monitoring and management of complicated acute MI
- Assessing hemodynamic response to therapies
- Management of multiorgan system failure and/or severe burns
- Management of hemodynamic instability after cardiac surgery
- Assessment of response to treatment in patients with primary pulmonary hypertension

Therapeutic: Aspiration of Air Emboli

The indication to monitor PA pressure depends on the ventricular function. For patients who have good left ventricular function (ejection fraction >50% and normal ventricular wall motion), the CVP is considered to correlate well with the PAOP; therefore, PA pressure monitoring may not be necessary for this group of patients. On the other hand, for patients with poor left ventricular function (ejection fractions <40% or prominent wall motion abnormalities), PA pressure monitoring is indicated. Other indications for monitoring PA pressure include the presence of pulmonary hypertension, combined coronary stenosis and valvular disease, and complex cardiac lesions.

However, results of several studies in recent past involving critically ill patients have consistently demonstrated that use of PA catheter was either associated with increased mortality and morbidity or no difference in fatal and nonfatal outcomes as compared to use of CVP alone or other noninvasive monitoring. Much debate exists regarding this topic, and it is unlikely that there ever will be a resolution. Nevertheless, there has been substantive reduction in the use of the PA catheter both in surgical and medical settings.

Djaiani G, Karski J, Yudin M, et al. Clinical outcomes in patients

undergoing elective coronary artery bypass graft surgery with and without utilization of pulmonary artery catheter-generated data. *J Cardiothorac Vasc Anesth*. 2006;20(3):307–310.

Hessel EA, Apostolidou I. Pulmonary artery catheter for coronary artery bypass graft: does it harm our patients? Primum non nocere. *Anesth Analg*. 2011;113:987–989.

Sandham JD, Hull RD, Brant RF, et al. A randomized, controlled trial of the use of pulmonary-artery catheters in high-risk surgical patients. *N Engl J Med*. 2003;348(1):5–14.

Schwann NM, Hillel Z, Hoeft A, et al. Lack of effectiveness of the pulmonary artery catheter in cardiac surgery. *Anesth Analg*. 2011;113:994–1002.

Vender JS. Pulmonary artery catheter utilization: the use, misuse, or abuse. *J Cardiothorac Vasc Anesth*. 2006;20:295–299.

C.I-6. *What are the possible complications of PA catheterization?*

Similar to Central Venous Catheter Insertion

Common Complications

- Infection—sepsis
- Hematoma
- Air embolism
- Thrombosis
- Catheter shearing and embolization

Subclavian Approach

- Pneumothorax
- Hemothorax
- Hydrothorax

Internal Jugular Approach

- Pneumothorax
- Neck hematoma from puncture of carotid artery
- Possible vagus nerve injury and brachial plexus injury
- Thoracic duct perforation from left-side approach

The basilar or cephalic vein approach has fewer

complications, but the failure rate is higher.

From Pulmonary Artery Catheter

- Arrhythmias 1.5% to 11%
- Complete heart block
- Thromboembolism
- Pulmonary infarction from continuous wedging
- Massive hemorrhage from perforation of PA or right atrium (RA)
- Failure to wedge
- Hemoptysis
- Intracardiac knotting
- Balloon rupture
- Endocardial thrombi
- Tricuspid valve injury

The incidence of PA catheter complications is more related to operator experience.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:390–426.

Murphy GS, Vender JS. Monitoring the anesthetized patient. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:707–708.

C.I-7. *What is normal pulmonary artery occlusion pressure (PAOP)?*

- Normal—4 to 12 mmHg
- Borderline—13 to 17 mmHg
- Heart failure—over 18 mmHg

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:390–426.

C.I-8. *What are the hemodynamic consequences of myocardial ischemia? How can you detect*

myocardial ischemia? Is PAOP a sensitive indicator of myocardial ischemia?

Acute myocardial ischemia affects systolic and diastolic cardiac function. Diastolic dysfunction usually manifests before alterations in systolic function. The immediate impact on ventricular compliance is related to the etiology of the ischemic event. Decreased myocardial oxygen supply is initially accompanied by an increase in compliance. In contrast, increased myocardial oxygen demand is associated with an immediate loss of ventricular compliance (e.g., the ventricle becomes stiffer). Therefore, the ventricle requires a higher filling pressure (end-diastolic pressure) to maintain a given stroke volume. A cascade of events occurs, which may include SWMA, dysrhythmias, and conduction blocks. An 80% reduction of coronary blood flow causes akinesis (<10% of radial systolic thickening), whereas a 95% decrease causes dyskinesis (thinning, instead of thickening, during systole). If the ischemia becomes severe, the continuously elevated LVEDP will lead to pulmonary edema (**Fig. 5.4**).

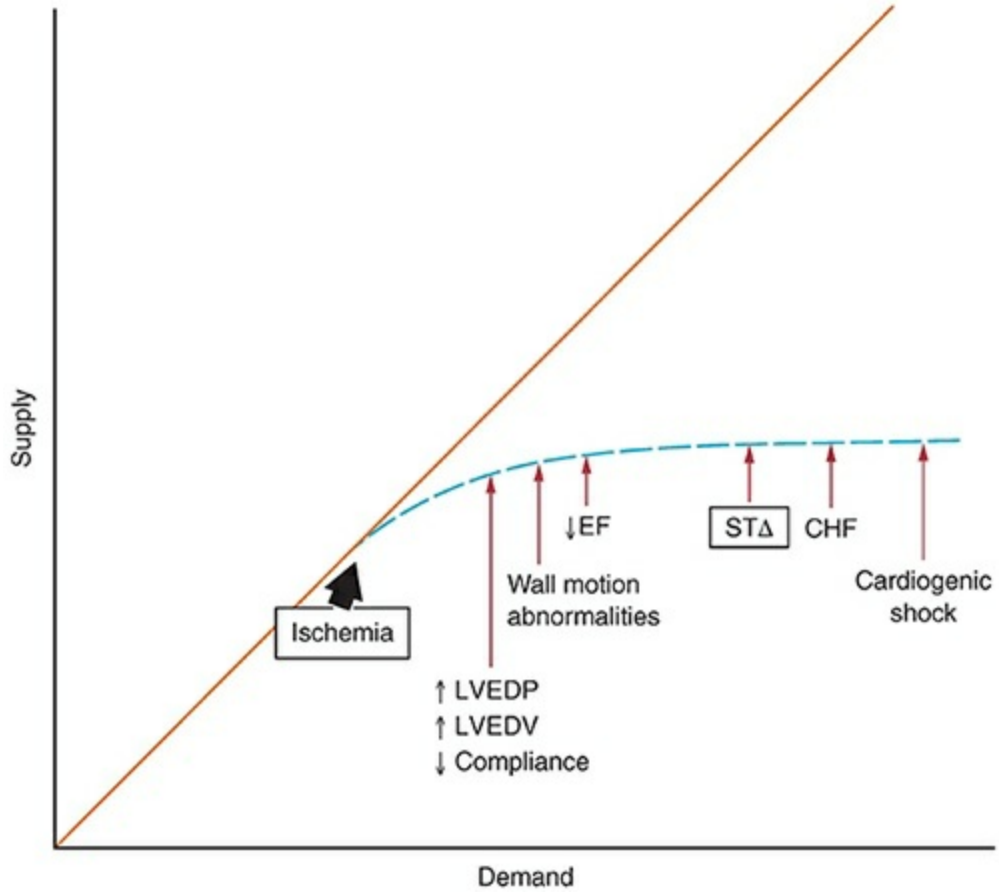

FIGURE 5.4. Hemodynamic consequences of myocardial ischemia. Ischemia occurs when demand exceeds supply. CHF, congestive heart failure; EF, ejection fraction; LVEDP, left ventricular end-diastolic pressure; LVEDV, left ventricular end-diastolic volume; STΔ, ST-segment changes. (*Reprinted with permission from Barash PG. Monitoring myocardial oxygen balance: physiologic basis and clinical application.* ASA Refresher Courses in Anesthesiology. *1985;13:24.*)

The most popularly recognized sign of ischemia is ECG ST-segment changes. The ECG criteria for ischemia are horizontal or down-sloping ST-segment depression at least 0.1 mV at 0.06 second from the J-point, up-sloping ST-segment depression at least 0.2 mV at 0.08 second from the J-point, and ST-segment elevation at least 0.15 mV (1 mV = 10 mm). Other ECG signs of ischemia include inverted T waves and a new onset of arrhythmias or conduction abnormalities.

SWMA, detected with two-dimensional echocardiography, have been shown to be the earliest and most sensitive sign of

myocardial ischemia. SWMA appear with just 25% decrease in coronary blood flow in the absence of ECG changes, whereas ECG signs of ischemia are apparent with a 50% decrease in coronary blood flow. SWMA is 4 times more sensitive than ECG ST-segment change in detecting intraoperative ischemia. Moreover, ST-segment changes cannot be analyzed if the patient has conduction disturbances, such as bundle branch block or ventricular-paced rhythms. Worsening wall motion after CABG surgery should be considered a prognostic indicator of adverse cardiovascular outcome.

Measurement of PAOP has been suggested as an early and sensitive indicator of ischemia to be used when the ECG is not diagnostic. Although acute increases in PAOP or development of V waves may reflect ischemia, the absence of a change in PAOP does not ensure the absence of ischemia. Häggmark et al. reported that the sensitivity, specificity, and predictive value (positive and negative) of PAOP abnormalities for ischemia ranged between 40% and 60%. Leung et al. found that 61% of TEE wall motion abnormalities in CABG patients occurred without significant changes in HR, systolic arterial pressure, or PA pressure. Only 10% of episodes were accompanied by 5 mmHg or greater changes in PA pressure. These studies question the value of PA catheterization and monitoring for detection of intraoperative ischemia.

Häggmark S, Hohner P, Ostman M, et al. Comparison of hemodynamic, electrocardiographic, mechanical, and metabolic indicators of intraoperative myocardial ischemia in vascular surgical patients with coronary artery disease. *Anesthesiology*. 1989;70:19–25.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:731–769.

Leung JM, O'Kelly B, Browner WS, et al. Prognostic importance of

postbypass regional wall-motion abnormalities in patients undergoing coronary artery bypass graft surgery. SPI Research Group. *Anesthesiology*. 1989;71:16–25.

Swaminathan M, Morris RW, De Meyts DD, et al. Deterioration of regional wall motion immediately after coronary artery bypass graft surgery is associated with long-term major adverse cardiac events. *Anesthesiology*. 2007;107:739–745.

C.I-9. *Discuss the principles and clinical applications of intraoperative transesophageal two-dimensional echocardiography.*

TEE is a well-established technique to visualize cardiac anatomy and function. Echocardiography is based on fundamental ultrasonic principles. Ultrasound is defined as sound above the upper threshold of human hearing (20,000 Hz). The ultrasound waves (1 to 7 MHz) are created by applying an alternating electric current of 500 to 1,500 pulses per second on a piezoelectric crystal. A short burst (pulse) of high-frequency, low-intensity sound is then emitted and directed through the human body to detect boundaries between structures of different acoustic impedance. The ultrasound wave is partially reflected at the boundary of media with different acoustic impedance, a property that is primarily determined by the slight difference in density between different tissues. The transmission of ultrasound through the heart, with detection of the returning echoes detailing the position and movement of cardiac structures, is termed *cardiac ultrasound* or *echocardiography*. Two-dimensional ultrasound reconstructs cardiac anatomy in shades of gray, from the time delay and decreased intensity of the reflected ultrasound. The ultrasound beam sweeps in an arc to give a panoramic view of the heart that results in cross-sectional images that are anatomically recognizable (see also Chapter 7, section A.6).

Doppler echocardiography blood flow is measured by

applying Doppler frequency shift analysis to echoes reflected by a moving target (red blood cells or cardiac tissue). According to the Doppler principle, the frequency of the reflected ultrasound is different from the frequency of the emitted ultrasound. This change in frequency is proportional to the speed of the moving target. Color-coded Doppler flow imaging (color flow Doppler) simultaneously presents real-time images of intracardiac blood flow and moving cardiac structures in two dimensions. Color flow Doppler permits the evaluation of valvular function and intracardiac shunts.

The clinical applications of intraoperative echocardiography are as follows:

- Monitoring ventricular volume and function. When left ventricular short-axis cross section is monitored at the level of the midpapillary muscles, TEE provides the anesthesiologist with a direct, semiquantitative method to assess left ventricular preload (left ventricular cross-sectional area at end-diastole) and ejection (difference of left ventricular cross-sectional area between end-diastole and end-systole) in real time and guide the administration of fluids, inotropes, or pressors.
- *Monitoring diastolic filling patterns*. Both Doppler assessment of transmitral and transpulmonary vein flow patterns can provide important information about diastolic dysfunction that may be prevalent in as many as 50% of patients presenting for open heart surgery, namely, those with history of hypertension, aortic stenosis, and hypertrophic cardiomyopathy. It is important to note that in patients with valvular disease, a component of left ventricular dysfunction arises from abnormal diastolic function.
- *Ischemic heart disease*. SWMAs, such as hypokinesia, akinesia, and dyskinesia, are the earliest signs of

myocardial ischemia (**Figs. 5.2** and **5.3**), as discussed in section C.I-9. Measurements of systolic wall thickening, a sensitive sign of myocardial ischemia, are not reproducible because of a difficulty in delineating the epicardial border accurately in two-dimensional echocardiography. The impairment of the diastolic function can be qualitatively estimated, and the filling pressures can be estimated using a combination of spectral Doppler measurements of the blood flow through the transmitral and transpulmonary vein flows.

- *Air embolism*. In the left atrium, LV, and aorta, air embolism can be detected by TEE during open heart surgery. Therefore, TEE can be used to help the surgeon evacuate air bubbles from the left heart before the heart ejects blood and air into the systemic circulation. This is more important when cardiac cavities are opened during surgery (aortic or valve surgery, etc.).
- *Valvular regurgitation*. Valvular regurgitation can be determined intraoperatively by color Doppler echocardiography before and immediately after conservative valve repair (annuloplasty, commissurotomy) or valve replacement. The degree of valvular incompetency can be accurately measured using a combination of two-dimensional and Doppler techniques (**Figs. 5.5** and **5.6**), and the function of the repaired or replaced valve can be quantitatively evaluated.

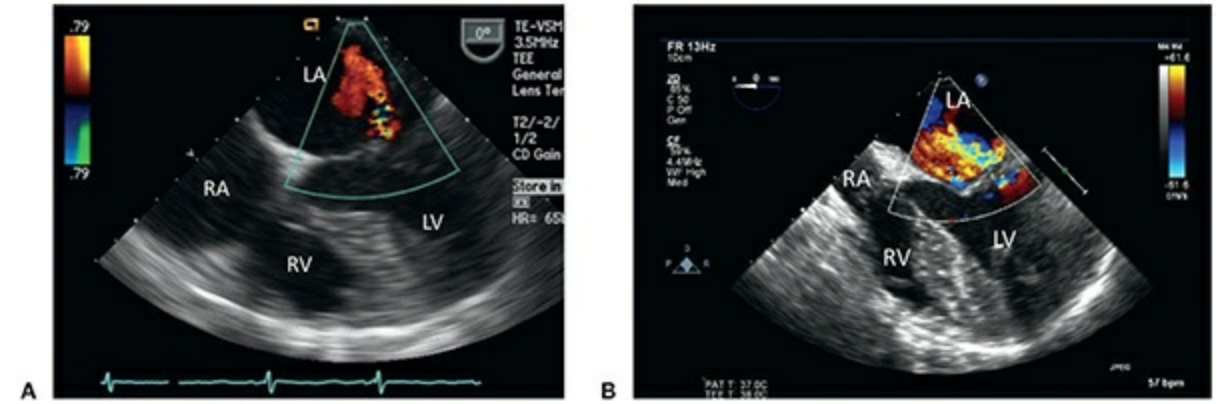

FIGURE 5.5. Color Doppler echocardiography. A. Superimposed on a two-dimensional image (here, the midesophageal view), the relative velocities of the red blood cells from a selected area *(triangle)* are visualized. Timed to the ECG (on the bottom of the sector image), normal or abnormal blood flows can be viewed as they cross orifices. In this case, a small regurgitant jet originating from the mitral valve during systole is seen. The color of the jet displays velocity and direction, according to the scale, on the left side of the figure. The mitral regurgitation jet is moving upward toward the left atrium (LA) and is colored red. **B.** In this midesophageal four-chamber view of the left ventricle (LV), a systolic mitral regurgitant jet is directed inside the LA. RA, right atrium; RV, right ventricle.

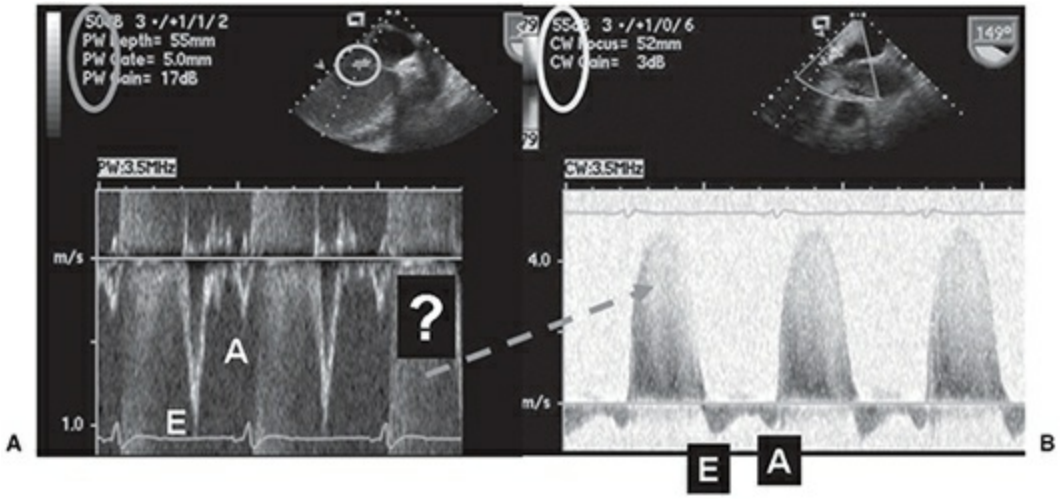

FIGURE 5.6. Doppler mode. A. A typical pulsed-wave (PW) Doppler velocity consists of a spectral recording of varying intensity, depending on the acoustic density of the reflected interface (the mass of blood cells). The most dense (or brightest) portion of the spectral tracing represents the velocity of most blood cells. The velocity is recorded from a specific site *(white circle)*, and the maximum velocity recorded is limited (usually <1.5 m per second). In this PW Doppler spectrum, *E* represents the diastolic early filling, and *A* the diastolic late (due to atrial contraction) velocity. During systole, there is a broad signal *(question mark)* representing systolic flow through the mitral valve (probably mitral regurgitation). However, neither the direction nor the peak velocity can be visualized. **B.** In contrast, continuous-wave (CW) Doppler records the velocities of all the red blood cells moving along the path of the sound beam. A CW Doppler recording always consists of a full spectral envelope with the outer border corresponding to the fastest moving blood cells. The site of origin of a high-velocity jet is inferred from the particular lesion that is being examined. The maximum velocity that can be recorded

can be as high as 8 m per second. Here, the direction (from bottom to top or from the LV toward the left atrium) as well as the maximum systolic velocity (approximately 5 m per second) can be visualized, detailing the mitral regurgitation jet.

- *Valvular stenosis*. Spectral Doppler echocardiography can be used intraoperatively to measure the pressure gradient across a valvular stenosis and calculate the area of the diseased valve.
- *Congenital heart disease*. TEE techniques facilitate complex cardiac reconstructions because the surgeon has the ability to visualize the heart and evaluate adequacy of the surgical repair immediately after the operative procedure.
- *Thoracic aorta*. TEE can accurately diagnose thoracic aortic aneurysm, dissection, disruption, and atheroma. Epiaortic echocardiography is performed to examine the ascending aorta and arch if severe atheroma is found in the descending aorta or arch by TEE. Severe atheroma of the thoracic aorta is an independent predictor of postoperative neurologic outcome. Atheromas are graded as follows: grade I, normal to mild intimal thickening; grade II, severe intimal thickening; grade III, atheroma protruding less than 5 mm into the lumen; grade IV, atheroma protruding greater than 5 mm; and grade V, atheroma with a mobile component (**Fig. 5.7**).

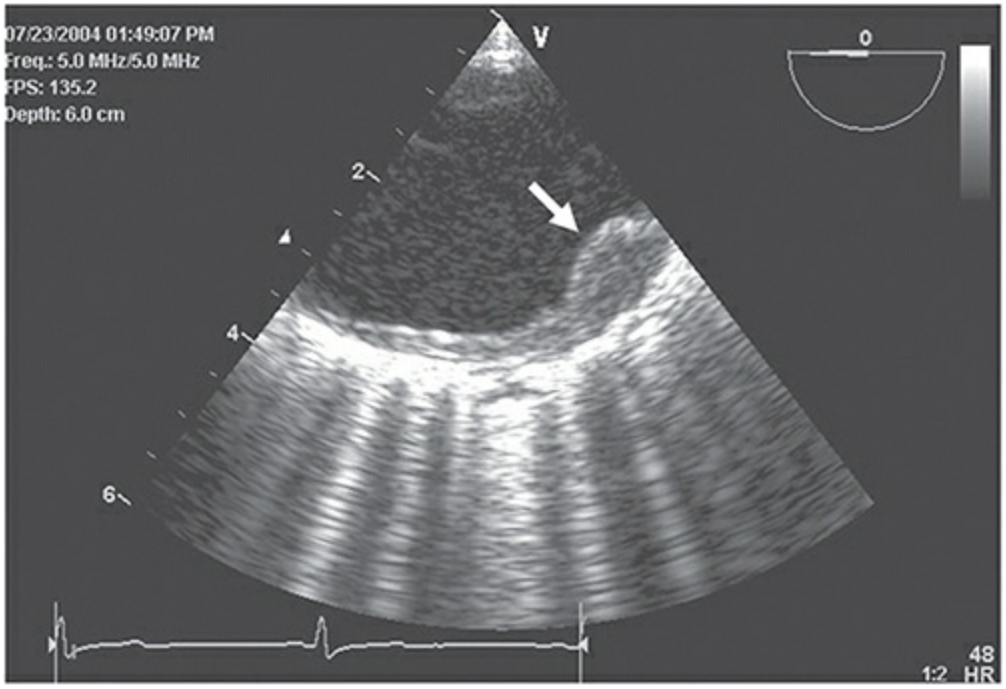

FIGURE 5.7. Atheromatous aortic disease. An echocardiographic picture of the short-axis view of the descending thoracic aorta is shown. The anterior aortic wall is irregularly thickened, and a large atheroma (8 mm) is present at 5 o'clock *(arrow)*. This is a grade IV atheroma.

- *Cardiac tumors*. Atrial myxoma can be easily diagnosed by TEE. Preoperative and postoperative TEE with contrast can assess the presence and severity of mitral regurgitation secondary to valve damage from a ball valve effect of the myxoma.
- *Other cardiac pathology*. Hypertrophic obstructive cardiomyopathy (HOCM) (idiopathic hypertrophic subaortic stenosis) can be identified by the combination of systolic anterior motion of the mitral valve and left ventricular outflow obstruction. Cardiac tamponade caused by a pericardial effusion or hematoma can be detected.
- *Neurosurgery*. TEE was found to be the most sensitive monitor to detect venous air embolism during neurosurgical operations in the sitting position. Patent foramen ovale and paradoxical air embolism can be detected by TEE.

- *Monitoring for noncardiac surgery*. Recent guidelines by Porter et al. suggest the utility of TEE in healthy patients who are acutely hemodynamically unstable during surgery, critically ill patients with significant respiratory and cardiac diseases undergoing noncardiac surgery, and patients undergoing high-risk noncardiac procedures, such as orthopedic surgery and kidney and liver transplants. TEE would be used as a hemodynamic diagnostic and monitoring tool to guide and evaluate effectiveness of therapeutic interventions.

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C.I-10. *How would you induce anesthesia? Is there any advantage/disadvantage to using propofol versus etomidate as the main induction agent? What kind of neuromuscular blocker (NMB) would you use? Why?*

Midazolam 1 to 2 mg is given as soon as the standard

monitors are applied and prior to the arterial line is inserted (under local anesthesia). This is important in alleviating anxiety, which can exacerbate myocardial ischemia. In lieu of the increasing incidence of delirium in the elderly postoperatively, benzodiazepines should be avoided in patients older than 70 years.

A smooth induction is essential to prevent hypotension, hypertension, and tachycardia. Different techniques may be used to achieve a smooth induction. For patients with good left ventricular function, anesthesia is induced with fentanyl, 2 to 5 μg per kg, and propofol, 1 to 2 mg per kg. Propofol may cause a reduction in MAP; however, this is less likely if it is administered at 10 mg per 40 seconds, as recommended in the package insert. Alternatively, etomidate 0.2 mg per kg may be administered for induction. Etomidate causes a transient adrenal insufficiency; however, this does not translate into increased vasopressor requirements or inferior early outcomes. A randomized controlled trial by Hannam et al. comparing the two induction agents in the cardiac surgery population confirmed that propofol has a less favorable hemodynamic profile, although the proportion of patients receiving vasopressors was not significantly different.

After administration of a nondepolarizing muscle relaxant (vecuronium, rocuronium), the trachea is intubated. The choice of nondepolarizing muscle relaxant varies from center to center and among practitioners. Succinylcholine is used less frequently in cardiac surgery.

For patients with poor left ventricular function, all anesthetics, including potent inhalation agents such as isoflurane, sevoflurane, and desflurane, should be used cautiously during induction of anesthesia because of their dose-dependent reduction in myocardial contractility and systemic arterial resistance. There is also the risk of

occupational exposure of inhalational agents due to poor mask design and seal.

See also Chapter 11, section C.6, for other measures to prevent tachycardia and hypertension at the time of intubation.

Basciani RM, Rindlisbacher A, Begert E, et al. Anaesthetic induction with etomidate in cardiac surgery: a randomized controlled trial. *Eur J Anaesthesiol*. 2016;33(6):417–424.

Hannam JA, Mitchell SJ, Cumin D, et al. Haemodynamic profiles of etomidate vs propofol for induction of anaesthesia: a randomised controlled trial in patients undergoing cardiac surgery. *Br J Anaesth*. 2019;122(2):198–205.

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Mangusan RF, Hooper V, Denslow SA, et al. Outcomes associated with postoperative delirium after cardiac surgery. *Am J Crit Care*. 2015;24:156–163.

C.I-11. *How would you maintain anesthesia? Volatile anesthetics or total intravenous anesthesia (TIVA)?*

Hemodynamic stability is essential to achieve a balance between myocardial oxygen demand and supply. Different agents and techniques may be used to accomplish the same goal. A combination of fentanyl (or another synthetic opioid) and isoflurane, sevoflurane, or desflurane (or propofol) is a popular choice (balanced technique). Volatile anesthetics have cardioprotective effects through various mechanisms. A study by Landoni et al. evaluating volatile anesthetics versus TIVA for CABG demonstrated, however, that volatile anesthetics do not improve mortality in this patient population. After the patient is intubated, a mixture of 60% air and 40% oxygen is administered to lessen the possibility of oxygen toxicity. Clearly, this ratio is subject to underlying pulmonary disease and ongoing intraoperative clinical

conditions.

The depth of anesthesia must be titrated to meet the requirements of the varying intensities of surgical stimulation. Skin incision and sternal splitting are very painful. However, the strongest stimulation is usually from sternal retraction with the self-retaining retractor. Fentanyl, around 5 μg (0.1 mL) per kg (or equivalent doses of other opioids), is given right before the skin incision, before sternotomy, and intermittently throughout surgery as needed to maintain adequate analgesia. Very high doses of fentanyl or sufentanil have been successfully used for cardiac anesthesia. There have been significant changes in practice over the past decade, whereby much lower doses of narcotic are administered to facilitate early extubation. Nowadays, maintenance of anesthetic is based on administration of volatile agents and smaller opioid dosages. Longer acting opioids, such as methadone, can be used to reduce the quantity of opioids administered both intraoperatively and postoperatively. A study by Murphy et al. demonstrated that methadone administration during cardiac surgery reduces postoperative opioid requirements and improves pain scores. Vasoactive agents are also used to regulate the hemodynamics (HR, systemic arterial pressure, and filling pressures).

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:731–769.

Landoni G, Lomivorotov VV, Nigro Neto C, et al. Volatile anesthetics versus total intravenous anesthesia for cardiac surgery. *N Engl J Med*. 2019;380:1214–1225.

Murphy GS, Szokol JW, Avram MJ, et al. Intraoperative methadone for the prevention of postoperative pain: a randomized, double-blinded clinical trial in cardiac surgical patients. *Anesthesiology*. 2015;122(5):1112–1122.

Pagel PS. Myocardial protection by volatile anesthetics in patients undergoing cardiac surgery: a critical review of the laboratory and clinical evidence. *J Cardiothorac Vasc Anesth*. 2013;27:972–982.

C.I-12. *What are the cardiovascular effects of volatile anesthetics, morphine, and fentanyl?*

Isoflurane, desflurane, and sevoflurane all produce a dose-related depression in ventricular function and vascular tone due to altered Ca_2+ entry and sarcoplasmic reticulum function in myocytes. Out of all the volatile anesthetics, isoflurane causes the most reduction in vascular tone and coronary vasodilation, suggesting the possibility of steal syndrome in patients with CAD. However, there is not conclusive evidence that isoflurane is more harmful than other anesthetics, assuming that coronary perfusion pressure is maintained. Compared to the other volatile anesthetics, desflurane causes the most increase in HR. Isoflurane and desflurane may cause tachycardia if the inspiratory concentration is increased rapidly. This mechanism is due to increased sympathetic system outflow.

All of the potent drugs decrease arterial pressure in a dose-related manner. The mechanism of BP decrease includes vasodilation, myocardial depression and decreased cardiac output, and decreased sympathetic nervous system tone.

Narcotics such as morphine and fentanyl at their clinical dose have minimal cardiovascular effects. Both may cause bradycardia. Neither sensitizes the heart to catecholamines or depresses myocardial function. The cardiovascular effects of morphine depend on the dose used. Large doses of morphine sulfate have reportedly caused myocardial lactate production and reduction in coronary blood flow in animals. Sethna et al. found that morphine sulfate, 0.25 mg per kg IV, did not produce a global myocardial ischemia in patients with CAD. High doses of morphine, 1 mg per kg, produce a significant

decrease in arterial BP and systemic vascular resistance accompanied by an average 750% increase in plasma histamine. On the other hand, high doses of fentanyl, 50 μg per kg, do not produce any significant changes in BP, vascular resistance, or plasma histamine levels.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:247–291.

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Sethna DH, Moffitt EA, Gray RJ, et al. Cardiovascular effects of morphine in patients with coronary arterial disease. *Anesth Analg*. 1982;61(2):109–114.

C.I-13. *What should you do during sternotomy?*

It is recommended that ventilation be held to protect the lungs from injury by the electric saw for first-time sternotomy.

C.I-14. *Would you use prophylactic nitroglycerin during CABG to prevent intraoperative myocardial ischemia or perioperative MI?*

No. It has been reported that prophylactic administration of nitroglycerin, 0.5 or 1.0 μg/kg/min, during fentanyl anesthesia in patients undergoing CABG did not prevent myocardial ischemia or reduce the incidence of perioperative MI.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:292–356.

C.I-15. *If ST-segment depression is seen during surgery, how would you treat it? What is the relation between perioperative myocardial ischemia and postoperative*

MI?

An ST-segment depression is indicative of ischemia and should be treated by:

- *Increasing coronary oxygen supply*: correct hypotension, hypoxemia, anemia
- *Increasing coronary perfusion pressure*: most often with small boluses of short-acting vasopressor, such as phenylephrine
- *Decreasing coronary oxygen demand*: correct hypertension, tachycardia, and increased PAOP or CVP by deepening anesthesia with a volatile agent or by using vasodilators or β-blockers. All the major determinants of decreased oxygen demand have to be considered and corrected to their normal levels.

If there are no obvious changes in BP, HR, and pulmonary wedge pressure, nitroglycerin is indicated if coronary spasm is suspected. Nitroglycerin may be given by IV drip. IV nicardipine may also be given to relieve coronary spasm.

Slogoff and Keats reported that perioperative myocardial ischemia occurred in 37% of all patients undergoing CABG. They demonstrated that perioperative MI was almost 3 times as frequent in patients with ischemia (6.9%) compared with patients without ischemia (2.5%). Intraoperative tachycardia was associated with a higher incidence of myocardial ischemia and infarction. However, Knight et al. demonstrated that 42% of CABG patients had preoperative episodes of myocardial ischemia, 87% of which were clinically silent. They further found that anesthesia and surgery did not worsen the preoperative ischemic pattern. Furthermore, Slogoff and Keats in another study postulated that approximately 90% of new myocardial ischemia observed during anesthesia was the manifestation of silent ischemia observed in the patient before the operation, and only 10%

was related to anesthetic management. Therefore, the relationship between intraoperative ischemia and postoperative outcome is still unsolved.

It is important to note that ST-segment changes suggestive of myocardial ischemia may be observed with alteration of the patients' position, particularly during retraction of the sternum for internal mammary harvesting. In addition to being attentive to the ECG, addressing presence of ischemia by PA catheter and echocardiography is advised. Segmental wall motion abnormalities may be detected earlier than changes in ECG.

Knight AA, Hollenberg M, London MJ, et al. Perioperative myocardial ischemia: importance of the preoperative ischemia pattern. *Anesthesiology*. 1988;68:681–688.

Mangano DT. Perioperative cardiac morbidity. *Anesthesiology*. 1990;72:153–184.

Slogoff S, Keats AS. Does perioperative myocardial ischemia lead to postoperative myocardial infarction? *Anesthesiology*. 1985;62:107–114.

Slogoff S, Keats AS. Myocardial ischemia revisited. *Anesthesiology*. 2006;105:214–216.

Slogoff S, Keats AS. Randomized trial of primary anesthetic agents on outcome of coronary artery bypass operations. *Anesthesiology*. 1989;70:179–188.

C.I-16. *Discuss autologous transfusion and blood conservation for cardiac surgery.*

Autologous transfusion is the collection and reinfusion of the patient's own blood or blood components. The realization that homologous blood is responsible for transmission of AIDS, hepatitis, transfusion reaction, and autosensitization has led to increased interest in autologous transfusion and blood conservation. Most often, the easiest, safest, and most cost-effective approach for blood conservation is intraoperative normovolemic hemodilution, pharmacologic

treatment, and perioperative blood salvage, whereas options such as preoperative autologous blood donation, preoperative use of erythropoietin, and intraoperative plasmapheresis are rarely used nowadays.

Intraoperative normovolemic hemodilution is the removal of blood through an arterial or venous catheter immediately after induction of anesthesia, before CPB, or the administration of heparin. Depending on the patient's size and hematocrit, 500 to 1,000 mL of blood is collected into blood bags containing citrate phosphate dextrose adenine (CPDA-1) anticoagulant and is kept at room temperature. This blood is spared the rigors of CPB, including hemolysis, platelet destruction, and clotting factor degradation. The autologous blood is transfused after reversal of the heparin with protamine. It has been demonstrated that the effect of 1 unit of fresh whole blood on platelet aggregation after CPB is at least equal, if not superior, to the effect of 8 to 10 stored platelet units. Normovolemic hemodilution is not recommended, however, if the patient's hematocrit is below 33% or the hemoglobin is below 11 g per dL because further decreasing the oxygen-carrying capacity may worsen myocardial ischemia. In addition, hemodilution during CPB will further decrease hematocrit to levels that require homologous blood transfusion. Normovolemic hemodilution should be performed cautiously in patients with critical left main coronary stenosis, aortic stenosis, and HOCM because sudden cardiac arrest has been observed during the procedure.

Perioperative blood salvage is the collection and reinfusion of blood lost during and immediately after surgery. The posttransfusion survival of perioperatively salvaged red blood cells has been shown to be comparable to that of allogeneic red blood cells. At the conclusion of CPB,

all blood remaining in the oxygenator and bypass circuits should be salvaged and, if needed, infused. Blood salvaged intraoperatively may be transfused directly (unwashed) or processed (washed) before infusion. Commercially available equipment exists for each option. Blood collected by intraoperative salvage represents an excellent source of red blood cells. Salvaged blood is, however, deficient in coagulation factors and platelets.

Postoperative blood salvage is another technique of autologous blood transfusion utilizing blood lost following surgery. Blood salvaged following cardiac surgery generally is collected from mediastinal and chest drains and transfused without washing. It does not require anticoagulation before transfusion. Although dilute, the blood is sterile and contains viable red blood cells.

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Lilly KJ, O'Gara PJ, Treanor PR, et al. Cardiopulmonary bypass: it's not the size, it's how you use it! Review of a comprehensive blood-conservation strategy. *J Extra Corpor Technol*. 2006;36(3):263–268.

Shander A, Moskowitz D, Rijhwani TS. The safety and efficacy of "bloodless" cardiac surgery. *Semin Cardiothorac Vasc Anesth*. 2005;9(1):53–63.

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Spahn DR, Casutt M. Eliminating blood transfusions: new aspects and perspectives. *Anesthesiology*. 2000;93:242–255.

Van der Linden P. Perioperative blood conservation strategies: an update for clinicians. *Can J Anaesth*. 2003;50(suppl 6):S1–S2.

C.I-17. *What antifibrinolytic will you use to reduce blood transfusions?*

Antifibrinolytic agents include lysine analogues epsilon

aminocaproic acid (EACA) and tranexamic acid (TXA). Lysine analogues block plasminogen's conversion to plasmin, in turn inhibiting fibrinolysis. These agents reduce bleeding and the amount of blood transfusions. The Society of Thoracic Surgeons/Society of Cardiovascular Anesthesiologists 2011 guidelines on blood conservation strongly recommend antifibrinolytics to be part of a blood conservation strategy.

Extensive dosing variability is reported for TXA. A low-dose strategy consists of a 10-mg per kg loading dose, 1 to 2 mg per kg into the CPB prime, and a 1-mg/kg/hr infusion. On the other hand, a high-dose strategy consists of a 30-mg per kg loading dose, 2 mg per kg into the CPB prime, and a 16-mg/kg/hr infusion. Up to 50% of cardiac surgical patients have renal dysfunction, and TXA is eliminated renally. High doses of TXA may also cause seizures. The mechanism of TXA-associated seizures is not fully understood, although dosage has been demonstrated to be an important variable. A lower dosing strategy should be used in those patients who have renal dysfunction and/or are at risk for seizures. Jerath et al. recommend a dosing strategy of a single 50 mg per kg bolus for patients with chronic renal dysfunction.

Pharmacokinetic data is also sparse for EACA. The loading dose is typically 100 mg per kg with a 5-g or 10-g bolus into the CPB prime and a 1 g per hour or 30-mg/kg/hr infusion. There is risk of renal dysfunction after the administration of EACA.

The 2008 BART trial (Blood conservation using Antifibrinolytics: Randomized trial) compared the 3 available antifibrinolytic agents available at the time: aprotinin, EACA, and TXA. The trial was terminated early due to a higher rate of death in the aprotinin group. Aprotinin was subsequently withdrawn from the market by the

manufacturer.

Fergusson DA, Hébert PC, Mazer CD, et al. A comparison of aprotinin and lysine analogues in high-risk cardiac surgery. *N Engl J Med*. 2008;358:2319–2331.

Gerstein NS, Brierley JK, Windsor J, et al. Antifibrinolytic agents in cardiac and noncardiac surgery: a comprehensive overview and update. *J Cardiothorac Vasc Anesth*. 2017;31:2183–2205.

Jerath A, Yang QJ, Pang KS, et al. Tranexamic acid dosing for cardiac surgical patients with chronic renal dysfunction: a new dosing regimen. *Anesth Analg*. 2018;127(6):1323–1332.

Koster A, Faraoni D, Levy J. Antifibrinolytic therapy for cardiac surgery: an update. *Anesthesiology*. 2015;123(1):214–221.

Lecker I, Wang DS, Whissell, et al. Tranexamic acid-associated seizures: causes and treatment. *Ann Neurol*. 2016;79:18–26.

Society of Thoracic Surgeons Blood Conservation Task Force, Ferraris VA, Brown JR, et al. 2011 update of the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists blood conservation clinical practice guidelines. *Ann Thorac Surg*. 2011;91(3):944–982.

C.I-18. *How do you know that the tip of the PA catheter is in the right ventricle (RV) or the PA?*

There are three main differences in the pressure tracings, as shown in **Figure 5.8**.

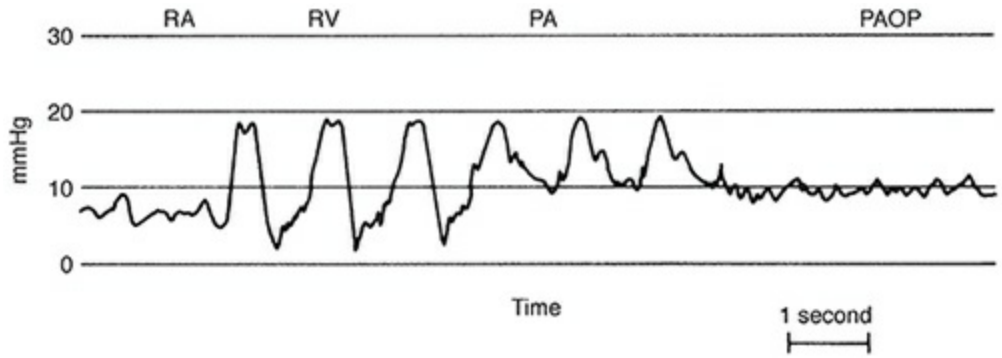

FIGURE 5.8. Pressure tracings of right atrium (RA), right ventricle (RV), pulmonary artery (PA), and pulmonary artery occlusion pressure (PAOP).

Diastolic pressure is higher in PA than in RV because the closed pulmonary valve maintains a diastolic gradient between the PA and the RV.

- PA pressure: 20 to 25/5 to 10 mmHg
- Right ventricular pressure: 20 to 25/0 to 5 mmHg

Pressure Contour

- PA pressure tracing has a dicrotic notch, which is created by the closure of pulmonary valve, and the diastolic part is descending (decreasing).
- Right ventricular pressure tracing has a sharp drop and a plateau in early diastole, and the diastolic part is ascending (increasing).

Ventricular Filling

In the late diastolic phase, PA pressure is decreasing because of diastolic runoff in the pulmonary circulation, whereas the right ventricular pressure is increasing because of ventricular filling.

C.II. During Cardiopulmonary Bypass

C.II-1. *What anticoagulant would you give before cardiopulmonary bypass (CPB)? How much would you give? What is its mechanism?*

Heparin has been used conventionally in doses of 300 (200 to 400) units per kg of body weight, assuming an initial concentration of at least 2 to 4 units per mL of whole blood. Empirically, after 2 hours of the initial dose, subsequent doses of 100 units per kg are given for each additional hour of bypass. Because there is marked individual variation, heparin doses are best monitored by the celite-ACT test.

Heparin acts indirectly by means of a plasma cofactor. The heparin cofactor, or antithrombin III (AT III), is an α_2-globulin and a protease inhibitor that neutralizes several activated clotting factors: XIIa, kallikrein, XIa, IXa, Xa, IIa, and XIIIa. AT III forms irreversible complexes with thrombin (IIa) and, as a result, both proteins are inactivated.

Inhibition of thrombin and factor Xa accounts for most of the anticoagulant effect of heparin. Heparin increases the rates of the thrombin–antithrombin reaction at least 1,000-fold by serving as a catalytic template to which both the inhibitor and the protease bind. Heparin also binds to cofactor II, a glycoprotein that inactivates thrombin independently of AT III. This reaction occurs more slowly and requires higher heparin concentrates than does thrombin inhibition through the heparin–AT III complex.

Spiess BD, Horrow JC, Kaplan JA. Transfusion medicine and coagulation disorders. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:949–991.

C.II-2. *What is the half-life of heparin? How is it eliminated?*

The biologic half-life of heparin varies with dosages and temperature. It has a remarkable individual variation. The average half-life is approximately 100 minutes in a normothermic man for the initial doses of 300 units per kg, increasing with higher doses and decreasing temperature. When 100, 400, or 800 units per kg of heparin are given intravenously, the approximate half-life is 1, 2.5, and 5 hours, respectively. Heparin concentrations decline progressively at all temperatures, but the rate of decline is delayed in proportion to the hypothermia.

The primary mechanism for heparin elimination remains uncertain. Heparin appears to be cleared and degraded primarily by the reticuloendothelial system. A small amount of heparin also appears in the urine.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1248–1290.

C.II-3. *How do you monitor heparin dosage? What is the activated coagulation time (ACT) test?*

Heparin therapy can be assessed by the partial thromboplastin time, heparin assay, heparin–protamine titration, and the ACT test. The most convenient and practical method used to monitor heparin therapy in the operating room is the celite-ACT test. There is a very good correlation among the ACT, plasma heparin units, and thrombin time. After central venous injection of a heparin bolus, the onset of maximal ACT prolongation occurs within 1 minute.

Two milliliters of blood are put into a test tube containing celite to activate coagulation. Then, the tube is kept at 37°C (98.6°F) and clot formation is watched for ACT. The normal control value of ACT is 105 to 167 seconds. A baseline value is determined before the administration of heparin, and the test is repeated 3 to 5 minutes after heparin is given and at intervals of 30 to 60 minutes thereafter. With the dose of heparin in milligrams per kilogram on the vertical axis and ACT in seconds on the horizontal axis, a dose-response curve can be plotted. ACT values are maintained at approximately twice the control value and should never decrease less than 300 seconds during normothermia.

Precise determination of plasma heparin concentration can also be used. The patient's plasma is incubated with factor Xa in the presence of its inhibitor, Xai. Heparin accelerates factor Xa inhibition, and residual factor Xa remaining after 2 minutes is measured and converted to a heparin concentration, expressed in units per milliliter. This method has been shown to decrease the amount of heparin used compared to heparin-ACT dose-response curves. The major disadvantage of this technique is the time delay before results are available.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:452–454.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:698–730.

C.II-4. *What is total CPB? What is partial bypass?*

Total bypass indicates that all the venous return from superior and inferior venae cavae and the coronary sinus is drained to the oxygenator. No blood is pumped by the RV to the lungs. The PA and systemic pressure tracings become nonpulsatile. Partial bypass means that some of the blood return is still pumped by both RV and LV. This venous blood is drained to the oxygenator and pumped back to the arterial side. Femoral–femoral bypass is one example of partial CPB.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:665.

C.II-5. *What kinds of pumps are used in CPB? Are they pulsatile or not?*

There are three types of pumps available for modern CPB machines: the double-headed non-occlusive roller pump, the centrifugal blood pump, and the ventricular-type pneumatic or hydraulic pump. Only the first two types are in common use.

The roller pump is the most commonly used pump. It is driven by an afterload-independent motor. Once the pump speed is set, it will continue the forward displacement of the same blood volume (or air volume) even if the resistance is increased by kinking or clamping the arterial line. This will result in the rupture of connections between sections of tubing. Some centers use pressure gauges on the arterial

inflow line to avoid this type of disaster.

The centrifugal pump is a kinetic pump that operates on the constrained vortex principle. Blood is driven through the pump by centrifugal forces generated by a vortex in the pump. The advantages of centrifugal pumps are as follows:

- Less trauma to blood components than the roller pump
- Less risk of increasing arterial line pressure because blood flow decreases when line resistance is increased
- Inflow responsiveness—if a large quantity of air is introduced into the pump, cohesive forces will no longer exist between layers of blood and pumping will stop
- Less risk of micro-air embolism because small, low-density air bubbles are trapped in the center of the vortex

Ventricular-type pumps, although potentially more powerful, are rather cumbersome and have not been well accepted. This type of pump is mainly used for pulsatile bypass.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:8–10.

Hornick P, Taylor K. Pulsatile and nonpulsatile perfusion: the continuing controversy. *J Cardiothorac Vasc Anesth*. 1997;11:310–315.

Ji B, Undar A. An evaluation of the benefits of pulsatile versus nonpulsatile perfusion during cardiopulmonary bypass procedures in pediatric and adult cardiac patients. *ASAIO J*. 2006;52(4):357–361.

C.II-6. *What is the purpose of venting the LV? How can it be done?*

Although all the venous return is bypassed from the RV, 2% to 5% of cardiac output is draining to the LV. This represents the physiologic shunt from the bronchial, thebesian, and pleural veins. Other sources of blood flow to the left heart during CPB include aortic regurgitation from aortic insufficiency and extracardiac left-to-right shunts such as

patent ductus arteriosus and Blalock-Taussig, Waterston, and Potts shunts. The left ventricular sump drain (left ventricular "vent") prevents overdistention of the LV, which may cause post-ECC heart failure. A suction needle inserted proximal to the aortic cross-clamp may serve the same purpose.

Venting of the LV can be accomplished by inserting a catheter to the following sites:

- Aortic root such as cardioplegia cannula for CABG
- Junction of the right superior pulmonary vein and the left atrium and advancing through the left atrium and mitral valve into the LV
- Apex of the LV
- PA or the left atrium only

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:667–668.

C.II-7. *How many types of oxygenators are there? What are the advantages of each type?*

There are two basic types of oxygenators in terms of their interface with blood.

Direct Gas Interface

- Disk
- Vertical screen
- Bubble

Without Gas Interface

- Membrane—solid or microporous
- Fluid—using fluorocarbon liquid

The disk and screen oxygenators are not disposable and have proven to be somewhat difficult to clean, prepare, and resterilize. The bubble oxygenator has the advantages of simplicity, disposability, and relatively low cost.

The disadvantages of gas interface oxygenators include the following:

- Protein denaturation
- Increased fragility of cells
- Susceptibility to hemolysis
- Denaturation of platelet membrane materials resulting in platelet aggregation, clumping
- Formation of air embolism
- Large priming volume
- Variable reservoir level resulting in potential shifts of blood volume between intracorporeal and extracorporeal circuit

Direct gas interface oxygenators are not used anymore. The membrane oxygenator has become more popular, economical, efficient, and less traumatic to blood. Its advantages include the following:

- Less trauma to blood components
- No defoaming
- Decreased complement activation
- Independent control of oxygen and CO_2 exchange
- Use of air–oxygen mixture without the risk of gaseous microemboli

The advantage of a membrane oxygenator for a short bypass (<2 hours) is unclear, however, although lower plasma hemoglobin levels are present using membrane oxygenators.

The disadvantages of membrane oxygenators include the following:

- Expense
- Potential difficulty in eliminating all bubbles during priming
- Moderately large priming volume

The major differences in changes of clotting factors

between the bubble and membrane oxygenators become apparent after 4 to 6 hours of ECC.

Barry AE, Chaney MA, London MJ. Anesthetic management during cardiopulmonary bypass: a systematic review. *Anesth Analg*. 2015;120:749–769.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:95–106.

C.II-8. *What kind of priming solution would you use? How much priming solution would you use? When would you prime with blood? Why?*

The usual priming solution includes a balanced salt solution, albumin, and mannitol. The priming volumes vary with the size of the oxygenators used and the tubing volume. Most oxygenators for adults have priming volumes of 500 to 1,000 mL. In general, blood is added to the oxygenator if the patient is markedly anemic (prepump hematocrit below 30%) or if the priming volume is large in relation to the patient's blood volume, such as in pediatric patients. In order to maintain oxygen-carrying capacity, the hematocrit is kept at levels above 18% to 20%. Mannitol has long been used as an osmotic diuretic in situations where hemolysis or diminished renal function is expected. Mannitol has been found to decrease the incidence of renal failure during hypotension by promoting osmotic diuresis and increasing renal blood flow by decreasing renal vascular resistance. Heparin, 3,000 to 10,000 units, is added to the prime depending on the size of the prime volume. This allows heparin to be distributed over the thrombogenic surfaces of the CPB circuit.

Del Nido solution is an extracellular cardioplegia based on Plasma-Lyte A. It has a 1:4 blood-to-crystalloid composition. Similar outcomes having been reported in the CABG population when using del Nido compared to traditional

solutions.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:426–430.

Ramanathan R, Parrish DW, Armour TK, et al. Use of del Nido cardioplegia in adult cardiac surgery. *Thorac Cardiovasc Surg*. 2015;63:624–627.

Timek T, Willekes C, Hulme O, et al. Propensity matched analysis of del Nido cardioplegia in adult coronary artery bypass grafting: initial experience with 100 consecutive patients. *Ann Thorac Surg*. 2016;101:2237–2241.

C.II-9. *What are the advantages and disadvantages of hemodilution?*

Advantages of Hemodilution

- An increase in microcirculation due to a reduction of blood viscosity
- Improved oxygen delivery to tissues
- Decreased metabolic acidosis
- Reduced risk of hypertension
- Reduced blood demands
- Reduced incidence of hepatitis, AIDS, or reactions from blood transfusions
- Reduced postoperative blood loss
- Improved blood flow at lower perfusion pressure, especially during hypothermic perfusion

Disadvantages of Hemodilution

- Decreased oxygen-carrying capacity
- Postoperative extracellular fluid overload
- Possible pulmonary edema
- Increased risk of postoperative renal dysfunction
- Hypotension from decreased viscosity and peripheral resistance

- Decreased concentration of calcium, magnesium, phosphate, and zinc

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:427–428.

Habib RH, Zacharias A, Schwann TA, et al. Role of hemodilutional anemia and transfusion during cardiopulmonary bypass in renal injury after coronary revascularization: implications on operative outcomes. *Crit Care Med*. 2005;33:1749–1756.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1111–1161.

Karkouti K, Beattie WS, Wijeysundera DN, et al. Hemodilution during cardiopulmonary bypass is an independent risk factor for acute renal failure in adult cardiac surgery. *J Thorac Cardiovasc Surg*. 2005;129:391–400.

Murphy GS, Hessel EA II, Groom RC. Optimal perfusion during cardiopulmonary bypass: an evidence-based approach. *Anesth Analg*. 2009;108:1394–1417.

Vermeer H, Teerenstra S, de Sévaux RG, et al. The effect of hemodilution during normothermic cardiac surgery on renal physiology and function: a review. *Perfusion*. 2008;23:329–338.

C.II-10. *How do you monitor the patient during CPB?*

Clinical Monitoring

- ECG
- MAP should be kept between 50 and 100 mmHg to maintain tissue perfusion. In hypertensive patients and in older patients, a higher MAP is frequently utilized. There is very little support for this in the literature.
- Bladder and esophageal temperatures are recorded (tympanic also may be used).
- CVP should be low or zero to make sure there is no obstruction to venous return from the head (when monitored from a site proximal to the RA) or there is adequate drainage of blood to the CPB circuit (when

monitored from inside the RA).

- PA pressure should be low or zero to prevent over distention of the LV.
- Urine output should be maintained above 1 mL/kg/hr by adequate perfusion.
- TEE may be used to detect aortic and cerebral embolism.
- Cerebral oximetry can be used to help monitor for adequate brain oxygen saturation (<20% change from baseline).
- Pump-flow rate should be adequate for tissue perfusion and oxygenation.

Laboratory Monitoring at Least Once Every Hour

- Arterial blood gases are kept at normal range.
- Venous P_{O_2} should be 40 to 45 mmHg.
- Hematocrit maintained between 20% and 24%
- Electrolytes Na^+, K^+, ionized Ca^{2+}
- ACT measured each hour and maintained above 400 to 480 seconds
- Glucose should be kept below 250 mg per dL.

Barry AE, Chaney MA, London MJ. Anesthetic management during cardiopulmonary bypass: a systematic review. *Anesth Analg*. 2015;120:749–769.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:315–337.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1111–1161.

Murkin JM, Adams SJ, Novick RJ, et al. Monitoring brain oxygen saturation during coronary bypass surgery: a randomized, prospective study. *Anesth Analg*. 2007;104:51–58.

Yao FS, Tseng CC, Ho CY, et al. Cerebral oxygen desaturation is associated with early postoperative neuropsychological dysfunction in

patients undergoing cardiac surgery. *J Cardiothorac Vasc Anesth*. 2004;18(8):552–558.

C.II-11. *What should your target BP be during CPB?*

Controversy continues over what constitutes adequate pressures while the patient is on bypass. The MAP is usually maintained at approximately 50 to 100 mmHg to ensure adequate tissue perfusion. BP depends on cardiac output (pump flow) and total peripheral resistance (TPR). Adequate cardiac output (pump flow) is more important for tissue perfusion than BP.

During hypothermic cardioplegia, higher systemic pressures (mean BP >70 mmHg) are often avoided because of increased noncoronary collateral blood flow into the heart through the pericardium and pulmonary venous drainage. Such collateral flow of relatively warm blood tends to wash the colder cardioplegic solution out of the heart and decreases the hypothermic protection against myocardial ischemia.

Gold et al. studied 248 patients randomized to either low MAP (50 to 70 mmHg) or high MAP (80 to 100 mmHg) during CPB and found a trend toward improvement in cardiac and neurologic outcome with higher MAP. However, MAP had no significant effect on neurologic outcome in those patients at low risk for cerebral embolization (normal to mild aortic atherosclerosis by TEE). Patients at high risk for adverse neurologic outcome (severe aortic atherosclerosis by TEE) had a significantly lower risk of worse neurologic outcome when randomized to higher MAP.

However, keeping the MAP high during CPB, above the limit of cerebral autoregulation, is associated with a risk of delirium. The range of cerebrovascular autoregulation during hypothermia is controversial. Although pooled data from clinical studies indicate a lower autoregulatory threshold of

20 to 30 mmHg in patients without cerebrovascular disease or preexisting hypertension, other studies suggest a pressure-dependent cerebral circulation when MAP is less than 50 mmHg. Until prospective studies clearly define the autoregulatory threshold under various clinical conditions, a BP of less than 50 mmHg should be regarded as a potential physiologic trespass, which may compromise cerebral circulation. Higher perfusion pressure is recommended in patients with cerebrovascular disease and/or hypertension. Real-time monitoring of autoregulation with transcranial Doppler allows for tailoring of the target MAP for the patient during CPB. This may improve patient outcomes.

With the recent introduction of noninvasive cerebral oximetry, the frontal cortex oxygen saturation can be monitored by near-infrared spectroscopy. The technique measures the oxygen saturation of the mixed arterial and venous blood in the brain cortex. Because the volume of blood is predominantly venous, it reflects the balance between oxygen supply and demand in the brain. Yao et al. showed good correlation between brain oxygen saturations and neurologic and cognitive outcomes. The MAP should be kept at levels enough to maintain adequate cerebral oxygen saturations (at least within 20% change of baseline values). Murkin et al. demonstrated in a randomized controlled trial that profound cerebral desaturation was avoided in patients undergoing CABG in whom cerebral regional oxygen saturation was monitored. This resulted in significantly fewer incidences of major organ dysfunction and death.

Aronson S, Fontes ML. Hypertension: a new look at an old problem. *Curr Opin Anaesthesiol*. 2006;19:59–64.

Berger M, Terrando N, Smith SK, et al. Neurocognitive function after cardiac surgery: from phenotypes to mechanisms. *Anesthesiology*. 2018;129(4):829–851.

Fontes ML. New insights in hypertension. *ASA Refresher Courses Anesthesiol*. 2006;34:43–53.

Gold JP, Charlson ME, Williams-Russo P, et al. Improvement of outcomes after coronary artery bypass. A randomized trial comparing intraoperative high versus low mean arterial pressure. *J Thorac Cardiovasc Surg*. 1995;110:1302–1311.

Hartman GS, Yao FS, Bruefach M, et al. Cardiopulmonary bypass at high pressure reduces stroke incidence in patients with TEE diagnosed severe aortic atheromatous disease. *Anesthesiology*. 1995;83:A141.

Hori D, Brown C, Ono M, et al. Arterial pressure above the upper cerebral autoregulation limit during cardiopulmonary bypass is associated with postoperative delirium. *Br J Anaesth*. 2014;113(6):1009–1117.

Hori D, Nomura Y, Ono M, et al. Optimal blood pressure during cardiopulmonary bypass defined by cerebral autoregulation monitoring. *J Thorac Cardiovasc Surg*. 2017;154(5):1590–1598.

Joshi B, Ono M, Brown C, et al. Predicting the limits of cerebral autoregulation during cardiopulmonary bypass. *Anesth Analg*. 2012;114:503–510.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1111–1161.

Murkin JM, Adams SJ, Novick RJ, et al. Monitoring brain oxygen saturation during coronary bypass surgery: a randomized, prospective study. *Anesth Analg*. 2007;104:51–58.

Murkin JM, Farrar JK, Tweed WA, et al. Cerebral autoregulation and flow/metabolism coupling during cardiopulmonary bypass: the influence of $PaCO_2$. *Anesth Analg*. 1987;66:825–832.

Murphy GS, Hessel EA II, Groom RC. Optimal perfusion during cardiopulmonary bypass: an evidence-based approach. *Anesth Analg*. 2009;108:1394–1417.

Newman MF, Kramer D, Croughwell ND, et al. Differential age effects of mean arterial pressure and rewarming on cognitive dysfunction after cardiac surgery. *Anesth Analg*. 1995;81:236–242.

Yao FS, Tseng CC, Ho CY, et al. Cerebral oxygen desaturation is associated with early postoperative neuropsychological dysfunction in patients undergoing cardiac surgery. *J Cardiothorac Vasc Anesth*. 2004;18(5):552–558.

C.II-12. *How would you treat hypotension during CPB?*

Mean arterial pressure (MAP) = cardiac output (CO) × total peripheral resistance (TPR)

Hypotension may be caused by low cardiac output or low peripheral resistance. Cardiac output should first be corrected by increasing the pump-flow rate. If the cardiac output is adequate, then peripheral resistance can be raised by giving primarily an α-adrenergic vasopressor, typically phenylephrine in increments of 0.1 mg to raise the MAP to 50 mmHg. In cases of more profound vasoplegia, agents such as norepinephrine and vasopressin may be required. According to Poiseuille law, low systemic vascular resistance usually is due to decreased viscosity or increased vascular diameter (vasodilation). Total viscosity is reduced by hemodilution during CPB using blood-free priming solutions, although plasma viscosity is increased by hypothermia. A short period of hypotension with a MAP of approximately 30 to 40 mmHg is usually observed in the first 5 to 10 minutes of bypass. It is due to the following causes:

- Inadequate pump flow at the beginning of bypass
- Hypoxic vasodilation from initial perfusion with blood-free priming
- Vasodilation from vasoactive materials released because of the initial reaction of the serum proteins, blood cells, and platelets with the foreign surfaces of the heart–lung machine
- Decreased plasma levels of catecholamines by hemodilution

Balasaraswathi K, Glisson SN, El-Etr AA, et al. Effect of priming volume on serum catecholamine during cardiopulmonary bypass. *Can Anaesth Soc J*. 1980;27:135–139.

Barry AE, Chaney MA, London MJ. Anesthetic management during cardiopulmonary bypass: a systematic review. *Anesth Analg*.

2015;120:749–769.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1111–1161.

C.II-13. *How would you treat hypertension (a mean arterial pressure [MAP] of over 100 mmHg)?*

Hypertension during bypass is usually the result of inadequate depth of anesthesia, which causes increased catecholamine output and increased vascular resistance. Pump-flow rate should not be reduced to lower the pressure. Low pump flow may cause tissue hypoxia even though BP is high. The most effective treatment involves administering an inhalational agent through the vaporizer in the heart-lung machine. IV agents such as propofol, midazolam, and narcotics may be used, but they are frequently not as effective and have to be supplemented with vasodilator drugs. Previously, nitroprusside and nitroglycerin were commonly used, but more recently, the IV calcium channel blockers (nicardipine and clevidipine) are frequently used.

Aronson S, Dyke CM, Stierer KA, et al. The ECLIPSE trials: comparative studies of clevidipine to nitroglycerin, sodium nitroprusside, and nicardipine for acute hypertension treatment in cardiac surgery patients. *Anesth Analg*. 2008;107:1110–1121.

Singla N, Warltier DC, Gandhi SD, et al. Treatment of acute postoperative hypertension in cardiac surgery patients: an efficacy study of clevidipine assessing its postoperative antihypertensive effect in cardiac surgery-2 (ESCAPE-2), a randomized, double-blind, placebo-controlled trial. *Anesth Analg*. 2008;107(1):59–67.

C.II-14. *How do you prepare an IV infusion of sodium nitroprusside, nicardipine, and nitroglycerin? What are the usual doses? Which do you prefer to use?*

IV solutions may be prepared by adding to 250 mL of 5% dextrose in water 50 mg of nitroglycerin or sodium nitroprusside, or 25 mg of nicardipine, to make a

concentration of 200 μg per mL (nitroglycerin or nitroprusside) or 100 μg per mL nicardipine. The usual doses are nitroglycerin or nitroprusside 0.5 to 10 μg/kg/min, or 0.05 μg/kg/min nicardipine, determined by careful titration (**Table 5.1**).

TABLE 5.1 Cardiac Anesthesia Intravenous Medications[a]

Drug	Amount to Add	Total Volume with D_5W	Concentration	Dosage Range
Amicar (EACA)	15 g	150 mL	1 mL = 100 mg 10 mL = 1 g	Load: 10 g over 1/2 hr Maintenance: 1 g/hr × 5 hr
Amiodarone	450 mg	250 mL	1 mL = 1.8 mg	Initial: 150 mg over 10 min Followed by: 1 mg/min × 6 hr (360 mg) Then: 0.5 mg/min × 18 hr
Dexmedetomidine			1 mL = 4 μg	Load: 1.0 μg/kg over 10 min Maintenance: 0.2–0.7 μg/kg/hr
Diltiazem	25 mg	100 mL	1 mL = 0.25 mg	Load: 0.1−0.15 mg/kg Maintenance: 0.5−0.25 μg/kg/min
Dobutamine	500 mg	250 mL	1 gt = 33.3 μg 1 mL = 2 mg	5–20 μg/kg/min
Dopamine	400 mg	250 mL (premixed)	1 gt = 26.6 μg 1 mL = 1.6 mg	Renal: 1−5 μg/kg/min β: 10 μg/kg/min α: 10−15 μg/kg/min
Epinephrine	2 mg	250 mL	8 gtt = 1 μg	2–8 μg/min
Esmolol	5 g	250 mL	1 gt = 333 μg 1 mL = 20 mg	50−300 μg/kg/min
Levophed	8 mg	250 mL	2 gtt = 1 μg	4–32 μg/min
Lidocaine	2 g	500 mL (premixed)	15 gtt = 1 mg 1 mL = 4 mg	1−4 mg/min
Milrinone	20 mg	100 mL	3 gtt = 1 μg 1 mL = 200 μg	0.375−1 μg/kg/min
Nicardipine	25 mg	250 mL	1 gt = 1.66 μg	Load: 5 mg/hr Maintenance: Increase by 2.5 mg/hr every 15 min Maximum amount: 15 mg/hr
Nitroprusside	50 mg	250 mL (premixed)	1 gt = 3.33 μg	1−10 μg/kg/min

Nitroglycerin	50 mg	250 mL (premixed)	1 gt = 3.33 μg	10−80 μg/min
Phenylephrine	20 mg	250 mL	19 gtt = 25 μg	25−125 μg/min
Procainamide	2 g	500 mL (premixed)	15 gtt = 1 mg 1 mL = 4 mg	Load: 500−1,000 mg (20 mg/min) Dosage: 1−4 mg/min
Sodium bicarbonate	100 mEq	100 mL undiluted	1 mL = 1 mEq	1−3 mEq/kg/hr (titrate to pH)
Tranexamic acid			1 mL = 100 mg	Load: 10 mg/kg Maintenance: 1 mg/kg/hr
Vasopressin	100 units	100 mL	1 mL = 1 unit	Initial dose: 0.04 U/min, 2.4 U/hr Titrate: 0.005–0.01 U/min (0.3−0.6 mL/hr) every 10 min to max of 0.1 U/min or 6 U/hr

[a]There are 60 gtt/mL; therefore, gtt/min = mL/hr.
D_5W, dextrose 5% in water; EACA, ε-aminocaproic acid.

Nitroglycerin or nicardipine infusion is preferred. Sodium nitroprusside dilates both arterial and venous smooth muscle. It is very effective in reducing both preload and afterload. At high doses and prolonged duration, it may cause cyanide and thiocyanate toxicity. Because nitroprusside dilates the intramyocardial arterioles, intracoronary steal may occur. The solution has to be covered with aluminum foil to prevent decomposition from exposure to light. Nitroglycerin primarily causes venodilation, resulting in reduction of preload and myocardial oxygen consumption. At larger doses and by the IV route, it has mild arteriolar dilation and reduces afterload. It has no known toxicity and does not produce intracoronary steal because it dilates epicardial arteries. It may redistribute blood flow to the subendocardium and increase collateral circulation through the myocardium. Nicardipine is a systemic and coronary arterial dilator. The afterload is decreased, whereas the preload is not affected. It may cause a slight increase in HR (reflex tachycardia).

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:247–356.

C.II-15. *How much pump flow would you maintain during CPB? During hemodilution? During hypothermia?*

The pump blood flow is equivalent to cardiac output and to supply tissue oxygenation. The normal average cardiac output for adults is 70 mL/kg/min or 3.1 L/min/m^2. Seventy percent of normal cardiac output is usually enough to maintain tissue oxygenation. When body surface is used, both pediatric and adult patients require about the same pump flow—2.2 to 3.1 L/min/m^2. In summary, at normothermia and normal hemoglobin levels, the pump flow is as follows:

Adults 50 to 70 mL/kg/min	or 2.2 to 3.1 L/min/m^2
Children 100 to 150 mL/kg/min	or 2.2 to 3.1 L/min/m^2

Some perfusion teams, however, use low-flow (40 mL/kg/min), low-pressure (approximately 40 mmHg) bypass quite successfully. This technique has the advantages of less bleeding through intracardiac collaterals, less trauma to blood cells and platelets, and lower fluid requirement. It also, however, may lead to inadequate organ perfusion. Although there have been studies demonstrating good clinical results with low-flow and low-pressure techniques used in conjunction with hypothermia and hemodilution, the minimal safe flow rate during CPB has not been established.

$$\text{Oxygen delivery} = \text{cardiac output} \times \text{arterial oxygen content}$$

$$\text{Arterial oxygen content} = 1.34 \times \text{hemoglobin} \times O_2 \text{ saturation} + (0.003 \times Pa_{O_2})$$

Hemodilution reduces hemoglobin concentration and

hence decreases oxygen content. In order to deliver the same amount of oxygen, the pump flow has to be increased accordingly during hemodilution. For example, if the hematocrit is diluted from 40% to 20% during CPB, the pump flow has to be doubled (increased by a factor of 40 / 20 = 2). Clinically, both hypothermia and hemodilution are applied simultaneously so that the adjustment has to be done at the same time. For example, the pump flow for adults at a temperature of 30°C (86°F) and a hematocrit of 25% will be as follows:

50 to 70 mL/kg/min × 50% × 40/25 = 40 to 56 mL/kg/min

Hypothermia decreases oxygen consumption. Therefore, the pump flow may be decreased proportionally if the blood oxygen content does not change. The oxygen consumption at different body temperatures is listed in the following text:

Temperature (°C)	37	32	30	28	25	20	10
O_2 consumption (%)	100	60	50	40	25–30	20	10

Because the O_2 consumption at 30°C (86°F) is half of that at 37°C (98.6°F), the required pump flow at 30°C (86°F) is 50% of the flow at 37°C (98.6°F) (50 to 70 mL/kg/min). Therefore, a pump flow of 25 to 35 mL/kg/min is adequate for adults at 30°C (86°F) if there is no hemodilution. During profound hypothermia (10°C to 20°C [50°F to 68°F]), patients can usually tolerate total circulatory arrest without pump support for approximately 60 to 90 minutes. The decrease in metabolism during hypothermia is not a linear process. From 37°C to 30°C (98.6°F to 86°F), the metabolism decreases approximately 7% by each degree

centigrade. Below 30°C (86°F), the rate of metabolism decrease slows down. Usually, every 7°C to 8°C (44.4°F to 46.4°F) decrease in temperature reduces oxygen consumption by 50%. Clinically, it has been demonstrated that pump flows as low as 30 mL/kg/min or 1.2 L/min/m^2 will not compromise whole-body oxygen delivery when moderate systemic hypothermia is employed.

Barry AE, Chaney MA, London MJ. Anesthetic management during cardiopulmonary bypass: a systematic review. *Anesth Analg*. 2015;120:749–769.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:665–666.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1111–1161.

Kolkka R, Hilberman M. Neurologic dysfunction following cardiac operation with low-flow, low-pressure cardiopulmonary bypass. *J Thorac Cardiovasc Surg*. 1980;79:432–437.

C.II-16. *How does blood viscosity change during hemodilution and hypothermia?*

Blood viscosity varies inversely with temperature; a 2% increase occurs for every 1°C (1.8°F) decrease in temperature. At a hematocrit of 40%, a decrease in temperature from 37°C to 27°C (98.6°F to 80.6°F) increases viscosity by approximately 25%. Hemodilution with balanced salt solution will decrease blood viscosity. Decreasing the hematocrit from 40% to 20% at 27°C (80.6°F) decreases viscosity by approximately 40%. It has been recommended that the hematocrit be adjusted to the same numerical value as the core body temperature in degree centigrade if blood viscosity is to be kept approximately constant. For example, normal viscosity at 37°C (98.6°F) with hematocrit of 40% approximates that seen at 25°C

(77°F) with hematocrit of 25%.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:395.

C.II-17. *How is anesthesia provided during CPB?*

Anesthesia is maintained with intermittent administration of IV propofol, benzodiazepines, narcotic, and/or inhalation agents through the pump oxygenator to achieve unconsciousness and analgesia, to control BP, and to prevent shivering. IV agents are diluted by the priming solution during CPB. Meanwhile, hypothermia itself produces anesthesia and prolongs the action of duration of IV agents by decreasing hepatic metabolism and urinary excretion.

Cardiac surgery patients are at increased risk for intraoperative awareness. Processed EEG monitors may reduce the incidence of awareness. However, these monitors have important limitations, such as unresponsiveness to certain hypnotic agents, interference artifacts, indices that are relatively unvarying, and cost-effectiveness. A large multicenter randomized trial by Avidan et al. demonstrated that the superiority of a processed EEG monitor such as the bispectral index is not established. Vigilance is required at all stages of anesthesia to prevent intraoperative awareness, especially in CPB during the rewarming phase.

Avidan MS, Jacobsohn E, Glick D, et al. Prevention of intraoperative awareness in a high-risk surgical population. *N Engl J Med*. 2011;365(7):591–600.

Serfontein L. Awareness in cardiac anesthesia. *Curr Opin Anaesthesiol*. 2010;23(1):103–108.

C.II-18. *Would you give muscle relaxants during CPB? How is the action of muscle relaxants affected during CPB?*

Yes. Muscle relaxants are given to prevent diaphragmatic movement that interferes with surgery and to prevent shivering during hypothermia. Shivering may increase oxygen consumption to as high as 486% of normal. The effect of a muscle relaxant is altered by both hypothermia and hemodilution. The plasma concentration of muscle relaxants is diluted by the priming solution. Therefore, more relaxant is required to maintain the same degree of relaxation. Hypothermia does prolong the onset of paralysis. Moreover, hypothermic CPB per se facilitates neuromuscular transmission at the electrochemical level yet compromises mechanical contractility. The duration of action of rocuronium is prolonged by hypothermic CPB. Modifications of partial neuromuscular blockade by hypothermic bypass are the result of muscle relaxation enhancing or interfering with the impact of hypothermia on normal neuromuscular transmission. The best way to monitor muscle relaxation is by using a peripheral nerve stimulator.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:249.

Hemmerling TM, Russo G, Bracco D. Neuromuscular blockade in cardiac surgery: an update for clinicians. *Ann Card Anaesth*. 2008;11(2):80–90.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1111–1161.

C.II-19. *How do you know the patient is well perfused during CPB?*

If the perfusion pressure is maintained between 50 and 100 mmHg, and the pump-flow rate is adequately maintained according to the degree of hypothermia and hemodilution, there should be adequate urine output, greater than 1

mL/kg/hr, no metabolic acidosis, and normal mixed venous oxygen tension of 40 to 45 mmHg. However, cerebral perfusion is not routinely monitored, and the autoregulation range of BP may be higher than the normal range in the elder and high-risk patients. Cerebral oximetry should be used for patients with increased risk for neurologic and cognitive outcomes. It is recommended to keep cerebral oxygen saturation over 40%.

Joshi B, Ono M, Brown C, et al. Predicting the limits of cerebral autoregulation during cardiopulmonary bypass. *Anesth Analg*. 2012;114:503–510.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1111–1161.

Murphy GS, Hessel EA II, Groom RC. Optimal perfusion during cardiopulmonary bypass: an evidence-based approach. *Anesth Analg*. 2009;108:1394–1417.

Yao FS, Tseng CC, Boyd WC, et al. Neurological complications following cardiac surgery is associated with cerebral oxygen desaturation. *Anesth Analg*. 2000;90:76.

Yao FS, Tseng CC, Ho CY, et al. Cerebral oxygen desaturation is associated with early postoperative neuropsychological dysfunction in patients undergoing cardiac surgery. *J Cardiothorac Vasc Anesth*. 2004;18(8):552–558.

C.II-20. *How much gas flow would you use for the oxygenator? What kind of gas would you use? Why?*

Normal alveolar ventilation is 4 L per minute, and pulmonary circulation is 5 L per minute. That ratio is 0.8. The oxygenator is not as efficient as human lungs. Usually, 2 L of gas are used for each liter of pump-flow rate and then the gas flow rate is adjusted according to blood $Paco_2$ and Pao_2. The gas flow may be decreased if the $Paco_2$ is low and the Pao_2 is too high. The ratio may be increased if the $Paco_2$ is over 40 mmHg or the Pao_2 is under 100 mmHg. Meanwhile, air–

oxygen mixtures allow for better control of oxygen tension during CPB. It is not necessary to add CO_2 to the ventilating gas during hypothermia to elevate $PaCO_2$ and decrease the pH because α-stat regulation is used for acid–base management.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:97, 101.

C.II-21. *What are the disadvantages of hypocapnia during CPB?*

- Cerebral blood flow decreases approximately 2% to 4% for each mmHg decrease in $PaCO_2$ when $PaCO_2$ is in the range of 20 to 60 mmHg due to cerebral vasoconstriction. Cerebral O_2 saturation decreases approximately 1% for each mmHg decrease in $PaCO_2$.
- Respiratory alkalosis shifts the oxygen dissociation curve to the left, which increases the O_2 affinity to hemoglobin and decreases the release of O_2 to the tissues.
- Hypokalemia occurs because alkalosis shifts the potassium intracellular.
- Alkalosis decreases ionized calcium.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:394–395.

Smith AL, Wollman H. Cerebral blood flow and metabolism: effects of anesthetic drugs and techniques. *Anesthesiology*. 1972;36:378–400.

Yao FSF, Tseng CC, Yu J, et al. Relationship between $ETCO_2$ and cerebral oxygen saturation. *Anesthesiology*. 2000;93(3A):A320.

C.II-22. *How would you preserve the myocardium during CPB?*

The most popular and effective method of protecting the myocardium is to reduce myocardial oxygen demand by

hypothermia and cardioplegia. Hypothermia is induced by a combination of the following: (1) systemic blood cooling by heat exchangers in the oxygenator; (2) local application of cold saline solution or iced slush to the external surface and chambers of the heart (if the heart is open); (3) infusion of cold cardioplegic solution through the aortic root, venous grafts, retrograde coronary sinus, and/or coronary ostium to the coronary arterial tree. The myocardial temperature may be decreased to 10°C to 15°C (50°F to 59°F).

In addition to inducing hypothermia and cardioplegia, one may take the following measures before aortic cross-clamping:

- Avoid tachycardia or increased contractility by discontinuing pacing at rapid rate and discontinuing inotropes if they were utilized.
- Initiate rapid arrest (asystole).
- Utilize proper venting methods and ensure adequate venous drainage to the pump to avoid ventricular distention, which decreases subendocardial blood supply.
- Prevent and treat ventricular fibrillation, which increases oxygen demand in normothermic myocardium.
- Maintain adequate coronary perfusion pressure of at least 50 mmHg and greater than 70 mmHg in the presence of severe coronary disease or left ventricular hypertrophy.

Barry AE, Chaney MA, London MJ. Anesthetic management during cardiopulmonary bypass: a systematic review. *Anesth Analg*. 2015;120:749–769.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:148–149.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1111–1161.

C.II-23. *What is cardioplegia? How much would you use?*

Cardioplegic solution usually contains high concentrations of potassium (10 to 30 mEq per L) or magnesium (160 mEq per L) to arrest the heart. Cardioplegia reduces myocardial oxygen consumption and provides optimal conditions for surgery. Bicarbonate or tris(hydroxymethyl)-aminomethane (THAM) is usually added to raise the pH to levels between 7.40 and 7.80 to increase the intracellular shift of potassium and to decrease the metabolic acidosis from ischemia. Steroids, calcium, and procaine may be added to stabilize lysosomal and cell membranes. Glucose and insulin are added to provide energy and improve the intracellular shift of potassium. Nitroglycerin is added to dilate coronary vessels, resulting in better perfusion to the myocardium, including ischemic areas.

When blood cardioplegia is used, four parts of bypass blood are mixed with one part of cardioplegic solution. Blood cardioplegia seems to have several advantages over crystalloid cardioplegia. The heart is arrested while being oxygenated, so that adenosine triphosphate (ATP) is not depleted before asystole. Repeated infusions provide a source of oxygen and glucose for continued metabolism and ATP repletion. Although little oxygen is released from hemoglobin during hypothermia, enough is probably dissolved in the plasma to sustain metabolism when reinfusion is performed every 30 minutes. Buffering capacity is improved because of the presence of the histidine buffering system present in red blood cells. Myocardial edema is reduced because of the osmolarity of blood. The risk of calcium paradox following ischemia is reduced and functional recovery is improved because of the physiologic calcium concentration provided by blood. The presence of red blood cell enzyme catalase may scavenge free radicals

produced by ischemia. Capillary perfusion is improved and more homogeneous because of the presence of red blood cells. However, results of clinical studies in which blood cardioplegia was compared with crystalloid cardioplegia either detected no significant difference or showed that blood cardioplegia improved contractility late in the postoperative course. Multiple-dose cardioplegia is required for satisfactory results, whereas single-dose blood cardioplegia results in poor ventricular function.

Intermittent, continuous, or single infusions of cardioplegic solution have been used. Usually 300 to 600 mL of cold cardioplegic solution is needed to paralyze the myocardium and cool the myocardium to 10°C to 20°C (50°F to 68°F).

In the case of severe obstructive coronary lesions, antegrade infusion into the aortic root may cause poor distribution of the cardioplegia. Therefore, retrograde infusion through the coronary sinus into the coronary veins may be additionally employed to ensure homogeneous distribution of cardioplegia.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:688–690.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1111–1161.

C.II-24. *The arterial blood gases and electrolytes during CPB are as follows: pH, 7.36; $PaCO_2$, 42 mmHg; PaO_2, 449 mmHg; CO_2 content, 24 mEq per L; sodium (Na), 128 mEq per L; potassium (K), 5.8 mEq per L; glucose, 180 mg/dL; and hematocrit, 20%. The patient's temperature is 27°C (80.6°F). At*

what temperature are blood gases measured? How would you correct the blood gases according to patient's body temperature? Would you treat the arterial blood gases at 37°C (98.6°F) or at patient's body temperature?

Blood gases are measured at a constant temperature of 37°C (98.6°F). They may be corrected according to body temperature. Each degree centigrade below 37°C (98.6°F) increases blood pH by 0.015. If pH is 7.40 at 37°C (98.6°F) in vitro, in vivo pH will be 7.55 at 27°C (80.6°F) body temperature ($7.40 + 0.015 \times [37 - 27] = 7.55$). The pH increases at lower temperatures because of increased pKa and decreased CO_2 tension from increased CO_2 blood solubility during hypothermia. In vivo Pa_{O_2} is decreased because of increased oxygen solubility during hypothermia. Nowadays, blood gases are measured at 37°C (98.6°F) and interpreted at 37°C (98.6°F) without correcting them to body temperature. The normal values of blood gases at 37°C (98.6°F) are as follows: pH, 7.40 ± 0.05; Pa_{CO_2}, 40 ± 5; and Pa_{O_2}, 95 ± 5. During hypothermia, the normal values of blood gases are not the same as those at 37°C (98.6°F). The same blood specimen has different P_{O_2} values when measured at different temperatures. Yet, the oxygen content remains unchanged. It is easier to calculate the oxygen content at 37°C (98.6°F) than at other temperatures where oxygen dissociation curves are shifted.

Optimal management of pH and Pa_{CO_2} for patients undergoing hypothermic CPB remains controversial. The two strategies for interpreting blood gases are the pH-stat (temperature-corrected) method and the α-stat (temperature-uncorrected) method. The pH-stat strategy aims at keeping

constant arterial pH at 7.40 and $PaCO_2$ at 40 mmHg at any given temperature. A $PaCO_2$ of 60 mmHg analyzed at 37°C (98.6°F) would be equivalent to a $PaCO_2$ of 40 mmHg if "corrected" for a body temperature of 27°C (80.6°F). The *α*-stat strategy aims at keeping a constant ratio of $[OH^-]:[H^+]$ at approximately 16:1. This is based on the premise that the pH of blood is regulated to keep the state of dissociation of the imidazole moiety (i.e., the alpha of imidazole) constant. Histidine, which contains the imidazole moiety, is an integral part of the active site of many enzyme systems. The function of enzyme systems has been shown to be optimal when the ratio of $[OH^-]:[H^+]$ is approximately 16:1. This ratio represents different pH values at different temperatures.

The differences between pH-stat and *α*-stat strategies are listed in **Table 5.2**. With the pH-stat strategy, the blood gas values are corrected to the patient's temperature; the patient is treated as a hibernating animal. With the *α*-stat strategy, the blood gas values are not corrected regardless of the patient's actual temperature; the patient is treated as a poikilotherm. Studies indicate that myocardial function is better preserved when the *α*-stat strategy is employed. Moreover, maintenance of cerebral blood flow autoregulation appears to remain intact with *α*-stat management, whereas flow becomes pressure dependent with pH-stat management. *α*-Stat blood gas management preserves cerebral blood flow-metabolism coupling such that hypothermic-induced decreases in metabolic rate are accompanied by proportionate decreases in cerebral blood flow. As a result, most medical centers use *α*-stat management of blood gases during hypothermic CPB. However, Bashein et al. found no difference in neuropsychological outcome between patients randomized to

α-stat versus pH-stat management.

TABLE 5.2 Different Hypothermic Acid–Base Regulatory Strategies

Strategy	Aim	Total CO_2 Content	pH and $PaCO_2$ Maintenance	Intracellular State	α-Imidazole and Buffering	Enzyme Structure and Function	C F C
pH-stat	Constant pH	Increases	Normal corrected values	Acidotic (excess H^+)	Excess (+) charge Buffering decreased	Altered and activity decreased	F n ? m u
α-Stat	Constant OH^-/H^+	Constant	Normal uncorrected values	Neutral (H^- = OH^-)	Constant net charge Buffering constant	Normal and activity maximal	F d (? m c

?, questionable.
From Tinker JH, ed. *Cardiopulmonary Bypass: Current Concepts and Controversies*. Philadelphia, PA: JB Lippincott; 1989:16, with permission.

Other studies have shown less decline in cognitive performance when α-stat management is used, especially in cases with prolonged CPB times. These data may support an embolic threshold above which recognizable neurologic injury occurs.

During deep hypothermic circulatory arrest, both animal and clinical studies have shown that pH-stat is associated with better neurologic outcome likely because of increased cerebral blood flow, leading to better brain cooling and greater cellular oxygen availability. In summary, most recent outcome studies support the utilization of α-stat for adult CPB and pH-stat for children under deep hypothermic circulatory arrest.

Bashein G, Townes BD, Nessly ML, et al. A randomized study of carbon dioxide management during hypothermic cardiopulmonary bypass. *Anesthesiology*. 1990;72:7–15.

Dahlbacka S, Heikkinen J, Kaakinen T, et al. pH-stat versus alpha-stat acid-base management strategy during hypothermic circulatory arrest combined with embolic brain injury. *Ann Thorac Surg*. 2005;79(4):1316–1325.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:665–667.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1111–1161.

Murkin JM. Central nervous system dysfunction after cardiopulmonary bypass. In: Kaplan JA, Reich DL, Savino JS, eds. *Kaplan's Cardiac Anesthesia: The Echo Era*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2011:1061–1085.

Newman MF, Kirschner JL, Phillips-Bute B, et al. Longitudinal assessment of neurocognitive function after coronary-artery bypass surgery. *N Engl J Med*. 2001;344:395–402.

C.II-25. *How does the blood sugar level change during CPB? Why? What is optimal glucose control intraoperatively? Does hyperglycemia increase neurologic complications during CPB?*

Blood sugar levels are elevated during the perioperative period in patients undergoing cardiac surgery with the use of CPB. Hyperglycemia is most profound during hypothermic CPB, with approximately 100% of patients (diabetic and nondiabetic) achieving plasma glucose levels greater than 200 mg per dL. There are several reasons for this: First, the practice of making patients nothing by mouth (NPO) overnight induces a state of starvation, marked by peripheral resistance to insulin at the level of muscle and fatty tissues, therefore allowing glucose uptake by the brain. Second, sympathoadrenal activation, in response to surgical stress, also tends to induce a diabetogenic state. Third, active

cooling the body during bypass causes a profound reduction in insulin production, induces peripheral insulin resistance, and is associated with renal tubular impairment in glucose regulation. And lastly, use of dextrose-containing cardioplegia is a major contributor to intraoperative hyperglycemia. Of interest, postoperative hyperglycemia continues despite insulin administration and has been shown to remain above normal up to several weeks postoperatively. At the cellular level, the alterations in insulin receptor/resistance are very similar to that of type 2 diabetes. It is controversial whether hyperglycemia increases neurologic complications during CPB. Under conditions of limited cerebral oxygen delivery, anaerobic glucose oxidation becomes the primary method of ATP production, resulting in intracellular lactic acidosis. Hyperglycemia, by providing more glucose for anaerobic oxidation, increases the degree of intracellular acidosis, which, in numerous animal studies, correlates with the severity of subsequent injury.

Given the tendency of hyperglycemia during cardiac surgery, there have been several large-scale studies evaluating the question of how much of glycemic control is optimal during CPB. The first by Ouattara et al., an observational study of 200 consecutive diabetic patients undergoing cardiac surgery, demonstrated that poor intraoperative control of blood glucose concentrations was associated with an increased incidence of in-hospital morbidity, including neurologic, cardiovascular, infectious, respiratory, and/or renal complications. Based on these findings, “tight” glucose control had been recommended for all patients undergoing CPB. More recently, tight intraoperative glycemic control for all patients has come under scrutiny due to equivocal results in nondiabetic

patients, finding that tight glucose control intraoperatively either did not make a difference or was related to increased morbidity and mortality.

Butterworth et al. studied the effects of tight glucose control in 381 patients without diabetes undergoing isolated CABG surgery with one group receiving an insulin infusion for glucose levels above 100 mg per dL and the other group receiving no insulin. Although glucose levels were lower in the patients who received insulin infusions, there was no difference between the incidences of neurologic complications, mortality, need for inotropic support, or length of hospital stay between the groups.

Gandhi et al. studied the effects of strict glucose control in 400 CABG patients (20% diabetic) randomized to a continuous insulin group (glucose levels maintained between 80 and 100 mg per dL) and a conventional group (glucose <200 mg per dL) using boluses of insulin. They found no difference in number of deaths, hospital length of stay, sternal wound infections, prolonged ventilation, cardiac arrhythmias, strokes, or renal failure within 30 days of surgery. There was a tendency for more deaths and strokes in the intensive insulin group.

As a result of these studies, the STS revised guidelines in 2009 state that glycemic control is best achieved with the use of an insulin drip (Level A) and diabetic patients should receive insulin infusions intraoperatively (Level B). However, insulin infusions are not necessary intraoperatively for patients without diabetes for glucose levels <180. These patients can be treated initially with an IV insulin bolus. However, an insulin infusion should be instituted (Level B) in those patients with persistently elevated serum glucose levels (>180 mg per dL) after CPB.

Most recently, the focus has shifted to evaluating glucose

variability, with increased variability being linked to conditions such as postoperative atrial fibrillation, acute kidney injury, and intensive care unit (ICU) length of stay.

Butterworth J, Wagenknecht LE, Legault C, et al. Attempted control of hyperglycemia during cardiopulmonary bypass fails to improve neurologic or neurobehavioral outcomes in patients without diabetes mellitus undergoing coronary artery bypass grafting. *J Thorac Cardiovasc Surg*. 2005;130:1319.

Carvalho G, Moore A, Qizilbash B, et al. Maintenance of normoglycemia during cardiac surgery. *Anesth Analg*. 2004;99:319–324.

Clement KC, Alejo D, DiNatale J, et al. Increased glucose variability is associated with atrial fibrillation after coronary artery bypass. *J Card Surg*. 2019;34(7):549–554.

Fontes ML, Koval KJ, Desvarieux T, et al. Epidemiology of hyperglycemia in non-diabetic patients undergoing hypothermic cardiopulmonary bypass. *Anesthesiology*. 2006;105:A749.

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Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:322–323.

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Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1111–1161.

Lanier WL. Glucose management during cardiopulmonary bypass: cardiovascular and neurologic implications. *Anesth Analg*. 1991;72:423–427.

Lazar HL, Chipkin SR, Fitzgerald CA, et al. Tight glycemic control in diabetic coronary artery bypass graft patients improves perioperative outcomes and decreases recurrent ischemic events. *Circulation*.

2004;109:1497–1502.

Lazar HL, McDonnell M, Chipkin SR, et al. The Society of Thoracic Surgeons practice guideline series: blood glucose management during adult cardiac surgery. *Ann Thorac Surg*. 2009;87:663–669.

Murkin JM. Pro: tight intraoperative glucose control improves outcome in cardiovascular surgery. *J Cardiothorac Vasc Anesth*. 2000;14:475–478.

Nam K, Jeon Y, Kim WH, et al. Intraoperative glucose variability, but not average glucose concentration, may be a risk factor for acute kidney injury after cardiac surgery: a retrospective study. *Can J Anaesth*. 2019;66(8):921–933.

Ouattara A, Lecomte P, Le Manach Y, et al. Poor intraoperative blood glucose control is associated with a worsened hospital outcome after cardiac surgery in diabetic patients. *Anesthesiology*. 2005;103:687–694.

Shann KG, Likosky DS, Murkin JM, et al. An evidence-based review of the practice of cardiopulmonary bypass in adults: a focus on neurologic injury, glycemic control, hemodilution, and the inflammatory response. *J Thorac Cardiovasc Surg*. 2006;132:283–290.

Sim MA, Liu W, Chew STH, et al. Wider perioperative glycemic fluctuations increase risk of posteoperative atrial fibrillation and ICU length of stay. *PloS One*. 2018;13(6):e0198533.

van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in critically ill patients. *N Engl J Med*. 2001;345:1359–1367.

C.II-26. *What are the effects of CPB on platelet and coagulation factors?*

Platelet dysfunction and thrombocytopenia occur during and after CPB. The level of coagulation factors decreases at the beginning of bypass due to hemodilution; surface absorption by the plastic, glass, and metal; and protein denaturation induced by the blood–gas interface. Transient defects in platelet plug formation and aggregation are seen in all patients placed on CPB. It is important to rule out bleeding due to insufficient heparin reversal and/or surgical bleeding; however, after those causes have been excluded, platelet dysfunction is the most common cause of bleeding issues after CPB. Platelet function generally returns to near-normal

status 2 to 4 hours following CPB. The dysfunction is exacerbated and prolonged by medications such as aspirin and platelet glycoprotein GPIIb/IIIa inhibitors (clopidogrel, tirofiban).

Platelet counts fall more with the bubble-type oxygenator than with the membrane-type oxygenator but rarely below the levels clinically required for hemostasis. Thrombocytopenia is mainly caused by hemodilution, aggregation, adhesion, and the adenosine diphosphate–release reaction induced by the foreign surfaces and the blood–gas interface. Membrane oxygenators cause few changes in clotting factors.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:433–445.

C.II-27. *If the blood level of the venous reservoir is low, what would you replace it with? Blood or balanced salt solution?*

The hematocrit should be maintained around 18% to 20% during hemodilution. If the hematocrit decreases below 18%, blood is added to the CPB circuit. If the hematocrit is above 20%, a balanced salt solution is added to the oxygenator. Hematocrit values in the range of 15% to 18% appear to be well tolerated clinically. When cerebral oxygen saturation (rSO_2) decreases to more than 20% baseline, packed red blood cells are used to improve oxygen-carrying capacity. When rSO_2 is within 20%, the patient has acceptable cerebral oxygenation, even if the hematocrit is below 18%.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:421–431.

Likosky DS, FitzGerald DC, Groom RC, et al. Effect of the

perioperative blood transfusion and blood conservation in cardiac surgery clinical practice guidelines of the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists upon clinical practices. *Anesth Analg*. 2010;111:316–323.

Murphy GS, Hessel EA II, Groom RC. Optimal perfusion during cardiopulmonary bypass: an evidence-based approach. *Anesth Analg*. 2009;108:1394–1417.

Yao FSF, Tseng CC, Woo D, et al. Maintaining cerebral oxygen saturation during cardiac surgery decreased neurological complications. *Anesthesiology*. 2001;95:A152.

C.II-28. *How do you estimate the fluid balance during CPB?*

All IV lines are turned off during CPB. The input consists of the decreased blood level in the oxygenator and the cardioplegic solution, fluid or blood added to the oxygenator during CPB. The output consists of the increased blood level in the oxygenator and urine.

C.II-29. *For how long a period can the aorta be cross-clamped?*

The limits of "safe" ischemic time during aortic cross-clamping are between 15 and 45 minutes. This can be increased to as much as 240 minutes in animal models with normal ventricular function when cardioprotective strategies are employed, such as intermittent hypothermic blood cardioplegia, initiation of rapid arrest, and left ventricular venting. However, many patients have preoperative ventricular dysfunction and the protection from hypothermic cardioplegia may not be optimal due to coronary artery obstruction. Clinically, the aorta may be safely cross-clamped for 60 to 120 minutes without perfusion. The myocardial function will be better the shorter the cross-clamping time.

Nissinen et al. evaluated the impact of prolonged CBP and aortic cross-clamp times (XCT) in 3,280 patients undergoing adult cardiac surgery, with myocardial protection provided

by continuous anterograde and retrograde cardioplegia. They found that XCT greater than 150 minutes and bypass times greater than 240 minutes were both associated with higher 30-day mortality (1.8% vs. 12.2% for increased XCT and 1.9% vs. 31.5% for CPB). Both increased XCT and CBP times also correlated significantly to increased transfusion of blood products, hospital length of stay, time to extubation, and postoperative morbidity such as stroke.

Nissinen J, Biancari F, Wistbacka JO, et al. Safe time limits of aortic cross-clamping and cardiopulmonary bypass in adult cardiac surgery. *Perfusion*. 2009;24(5):297–305.

Salis S, Mazzanti VV, Merli G, et al. Cardiopulmonary bypass duration is an independent predictor of morbidity and mortality after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2008;22(6):814–822.

C.II-30. *Why does the urine turn pink in some cases of CPB? What is the renal threshold for plasma hemoglobin?*

Pink urine is a sign of massive hemolysis. Hemolysis is mainly associated with the negative pressures generated by the suction apparatus and is associated to a lesser degree with the action of the pumps and/or with the gas–blood interface effects in the oxygenator. The renal threshold for hemoglobin is 100 to 150 mg per 100 mL. It is advisable to maintain a high output of alkaline urine to prevent possible tubular damage from acid hematin crystals, which are converted from hemoglobin.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:104, 548.

C.II-31. *Why does it take longer to rewarm than to cool the patient via the pump oxygenator?*

It usually takes 5 to 10 minutes to cool the patient from 37°C to 25°C (98.6°F to 77°F) of average body temperature,

whereas it takes 20 to 40 minutes to rewarm the patient from 28°C to 35°C (82.4°F to 95°F). The speed of heat exchange by the bloodstream depends on the temperature gradient between venous blood and water in the heat exchanger, the pump blood-flow rate, and the water-flow rate of the heat exchanger. The initial venous blood temperature is 37°C (98.6°F), and the water temperature of the heat exchanger is 0°C to 4°C (32°F to 39.2°F) during cooling, creating a temperature gradient of 34°C to 37°C (93.2°F to 98.6°F). During rewarming, the water temperature is limited to 42°C (107.6°F) or less to prevent denaturation and destruction of blood proteins. The temperature gradient is limited to 10°C (18°F) or less to prevent gas embolism from a decrease of gas solubility in the blood associated with a sharp increase in temperature. The heat exchanger water flow does not differ much during cooling and rewarming. However, the pump blood flow is usually maintained to a very high level during the initial cooling because of low BP in the beginning of cooling. During rewarming, the pump blood flow is frequently maintained at a low level because the BP is usually high and the body temperature is still low. Rewarming may be accelerated by administering inhalation anesthetics, or employing vasodilators, to decrease vascular resistance and thereby increase pump flow to maintain the same BP. Because the increased vascular resistance is usually due to inadequate anesthesia during rewarming, inhalation anesthetics are preferred over vasodilators in patients with good ventricular function. In cases of poor ventricular function, inhalation agents are avoided because of the potential cardiac depression after CPB.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:547–548.

C.II-32. *At what temperature can the patient be weaned from CPB?*

An esophageal or nasopharyngeal temperature of 37°C (98.6°F) and a rectal or bladder temperature at least 35°C (95°F) must be reached before the patient can come off the pump. After discontinuation of the pump, surface warming should be continued in pediatric patients to prevent hypothermia owing to redistribution of heat in the body. However, in adults, the use of warming blankets and warmed humidified airway gases has not been found beneficial in preventing the expected temperature "after drop." Esophageal or nasopharyngeal temperature usually will decrease and rectal or bladder temperature will increase during heat redistribution.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:603.

C.II-33. *How would you defibrillate the heart internally during CPB?*

The heart is defibrillated internally by a direct current (DC) defibrillator, with 5 to 10 watt-seconds (joules). If the heart remains in ventricular fibrillation, blood gases, electrolytes, and temperature are rechecked and lidocaine, 1 to 2 mg per kg, is administered before repeated DC defibrillation attempts. MAP is usually increased to 80 mmHg. Amiodarone is occasionally added to treat intractable ventricular fibrillation.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1291–1312.

C.II-34. *If the HR is 40 beats per minute, what should you*

do?

A temporary AV block is often found at the end of bypass because of potassium cardioplegia and the ischemic insult that occurs during aortic cross-clamping. Although atropine may be theoretically administered to treat sinus or nodal bradycardia, a temporary epicardial pacemaker is usually employed. Atrial pacing is preferred because of improved cardiac output when the atrial kick is preserved. Ventricular pacing is necessary if there is complete AV block. AV sequential pacing is indicated when ventricular pacing does not provide adequate cardiac output.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1291–1312.

C.II-35. *How would you prepare for termination of CPB?*

Before termination of CPB, cardiac and pulmonary function must be optimized. To ensure that all important steps are not inadvertently omitted, the patient and all monitors should be carefully checked. The mnemonic LAMPS for Laboratory data, Anesthesia machine, Monitors, Patient (Pump), and Support is one useful approach.

Laboratory Data

- Arterial pH, P_{CO_2}, P_{O_2} within normal limits
- Hematocrit—20% to 25%
- K^+—4.0 to 5.5 mEq per L
- Ionized calcium 1.1 to 1.2 mmol per L
- Pump mixed venous O_2 saturation greater than 70%

Anesthesia Machine

- Anesthesia machine functional
- Adequate depth of anesthesia

Monitors

- ECG—stable rate and rhythm (use pacing if necessary)
- Systemic BP restored to normothermic levels
- PA catheter functional
- Transducers zeroed and calibrated
- TEE out of freeze mode
- Nasopharyngeal/PA catheter temperature 36°C to 37°C (96.8°F to 98.6°F)
- Bladder/rectal temperature greater than 35°C (95°F)

Patient/Pump

- The heart—contractility, size, rhythm, and air removed
- The lungs—atelectasis minimized, fluid in thoracic cavities drained, ventilation reinstituted

Support

- Inotropes/vasopressors/vasodilators
- IABP if needed

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:603–620.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1291–1312.

C.II-36. *How would you decide the need for inotropic support?*

The need for inotropic support after CPB is usually assessed by the following (**Fig. 5.9**):

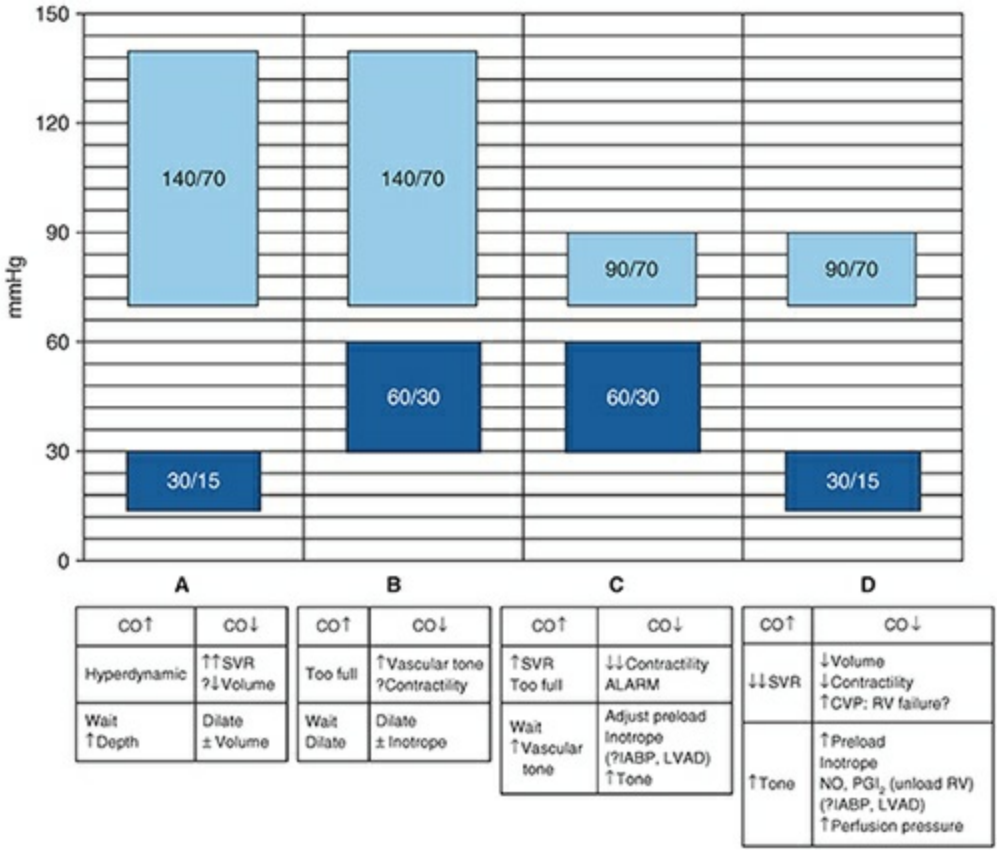


FIGURE 5.9. Hemodynamic management during weaning from CPB. The hemodynamic evaluation is performed by combining information from the systemic *(light shade boxes)* and pulmonary *(dark shade boxes)* arterial pressures. **A.** A combination of elevated systemic arterial and low pulmonary arterial pressure suggests either a hyperdynamic cardiac function (if cardiac output is high) or a vasoconstrictive state (if the peripheral vascular resistance is high). **B.** If systemic hypertension is accompanied by pulmonary hypertension, then either the volume status is elevated (if cardiac output is high) or there is generalized vasoconstriction (if cardiac output is decreased). **C.** In case of systemic hypotension and pulmonary hypertension, the cardiac output may be high (systemic vasodilation) or low (depressed contractility, requiring immediate intervention). **D.** When both systemic and pulmonary pressures are decreased, there is either vasodilation (if the cardiac output is high) or hypovolemia or depressed contractility or right-sided failure is suspected (if cardiac output is decreased). The relative treatment for each hemodynamic derangement is shown in the table. CO, cardiac output; CVP, central venous pressure; IABP, intra-aortic balloon pump; LVAD, left ventricular assist device; NO, nitric oxide; PGI_2, prostacyclin; RV, right ventricle; SVR, systemic vascular resistance; ↑, increase; ↑↑, marked increase; ?, questionable.

- Preoperative ventricular function (ejection fraction)
- Effectiveness of intraoperative myocardial protection
- Adequacy of surgical repair
- Duration of aortic cross-clamping and CPB
- Patient's age

If left ventricular ejection fraction is predicted to be 25% to 35%, milrinone infusion may be added. Norepinephrine infusion is usually needed during milrinone therapy. Generally, IABP is also employed when left ventricular ejection fraction is predicted to be below 25%. The choice of vasoactive and cardioactive agents used is frequently center- and/or physician-specific and is initiated either pre-bypass or while coming off bypass.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:607–608.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1291–1312.

C.III. After Cardiopulmonary Bypass

C.III-1. *How would you reverse heparin? How much protamine would you use? What are the other drugs used to neutralize heparin?*

It has been recommended that 1 mg of protamine sulfate is needed to reverse each 100 units of remaining heparin calculated by ACT dose-response curve or protamine titration test. Protamine, 1 mg, is given to reverse each 100 units or 1 mg of heparin initially administered. Only the initial dose of heparin is counted. Subsequently added doses of heparin, to keep the ACT level above 480 seconds, are not considered due to heparin's metabolism and elimination. The ACT test is repeated 10 minutes after the administration of protamine. ACT usually returns to its control level. If the ACT is still prolonged, additional protamine is given according to the ACT dose-response curve. The ACT is affected, however, by dilution and by hypothermia. Dose-response curves utilizing data obtained during hypothermia may be misleading. In addition, severe thrombocytopenia

also prolongs the ACT because clot formation using the ACT depends on platelet phospholipid surface. Of note, Bolliger and colleagues suggest that an increase in bleeding may occur paradoxically from "extra" protamine administration.

Other drugs that have been used to neutralize heparin include platelet factor 4 (PF4), heparinase, protamine variants, hexadimethrine bromide (Polybrene), and toluidine blue. Human or recombinant PF4 has been used in animals and humans to reverse heparin and does not cause systemic arterial hypotension, or pulmonary hypertension, or changes in white blood cell count, platelet count, or complement levels. Heparinase neutralizes heparin by enzymatic cleavage of α-glycoside linkages at AT III binding site. Heparinase is an effective antagonist of heparin and has minimal effects on platelets, whereas protamine markedly inhibits platelet responsiveness. It appears to be a potential alternative to protamine.

Lastly, reversal for low molecular weight heparin compounds does not exist, but a recombinant antithrombin variant was shown to be a potent antidote to fondaparinux and other heparin derivatives.

Bolliger D, Szlam F, Azran M, et al. The anticoagulant effect of protamine sulfate is attenuated in the presence of platelets or elevated factor VIII concentrations. *Anesth Analg*. 2010;111(3):601–608.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:498–500.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1248–1290.

Nielsen VG, Malayaman SN. Protamine sulfate: crouching clot or hidden hemorrhage? *Anesth Analg*. 2010;111(3):593–594.

C.III-2. *What is the action mechanism of protamine?*

Heparin is a strong organic acid (polyanion). Protamine is a

strong organic base (polycation). They combine ionically to form a stable salt and lose their own anticoagulant activity. Protamine contains two active sites: one that neutralizes heparin and another that exerts a mild anticoagulant effect independent of heparin.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:497–498.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1248–1290.

C.III-3. *What are the complications of too much protamine?*

Protamine itself is an anticoagulant. Protamine administered intravenously in the absence of heparin interacts with platelets and with clotting proteins. It induces transient thrombocytopenia in humans. Platelet aggregation is impaired by the protamine–heparin complex, although protamine alone has no deleterious effects on platelet aggregation. Protamine may bind to thrombin and inhibit thrombin's ability to convert fibrinogen to fibrin.

Bolliger D, Szlam F, Azran M, et al. The anticoagulant effect of protamine sulfate is attenuated in the presence of platelets or elevated factor VIII concentrations. *Anesth Analg*. 2010;111(3):601–608.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:497–498.

Nielsen VG, Malayaman SN. Protamine sulfate: crouching clot or hidden hemorrhage? *Anesth Analg*. 2010;111(3):593–594.

C.III-4. *What is a protamine reaction? How can you prevent this condition? How do you treat it?*

Three different types of circulatory reactions to protamine reversal of heparin have been proposed by Horrow:
Type I: Systemic Hypotension from Rapid Injection: A

Predictable Pharmacologic Reaction

Type II: Anaphylactic or Anaphylactoid Reaction

- Antibody-mediated
- Immediate anaphylactoid response without antibody involvement
- Delayed anaphylactoid response (noncardiac pulmonary edema)

Type III: Catastrophic Pulmonary Vasoconstriction with Systemic Hypotension

Etiologically, however, there are only two types of reaction: (1) pharmacologic side-effect reactions and (2) idiosyncratic reactions. Therefore, an alternative classification was proposed by Lowenstein as follows:

- Pharmacologic histamine release
- True anaphylaxis (immunoglobulin E–mediated)
- Anaphylactoid reactions
  - Pulmonary vasoconstriction
  - Noncardiogenic pulmonary edema

Mild-to-moderate systemic hypotension from pharmacologic side effects is almost always the reaction seen when protamine is given rapidly or is given to patients who are relatively hypovolemic and vasoconstricted. Because it can be elicited in most patients, it is classified as a pharmacologic side effect, not an idiosyncratic reaction. This side effect is possibly mediated by histamine and is characterized by venodilation, reduced cardiac filling pressures, and decreased vascular resistance. Mild cardiac depression by protamine is suggested but probably does not occur. This type of hypotension can be corrected by rapid volume administration from the CPB pump while the arterial cannula is in place and by administration of phenylephrine in 0.1-mg increments. There have been many attempts to modify the hypotensive response (e.g., intra-aortic or left

atrial administration, protamine pretreatment), with little evidence of predictable success. Only slower rates of IV infusion over 5 to 10 minutes and simultaneous maintenance of an adequate blood volume have been shown to decrease the incidence of hypotension.

Anaphylactic or anaphylactoid reaction is uncommon and rarely seen in infants and children. The reaction varies from mild skin flushing and urticaria to severe vascular collapse. Systemic hypotension is usually accompanied by low pulmonary arterial pressure and low right-sided and left-sided filling pressures. This type of hypotension may be treated and prevented with rapid volume infusion and administration of vasoconstrictors. The use of antihistamines and steroids is commonly employed by many cardiovascular anesthesiologists with few, if any, existing data supporting this practice. There are several unanswered questions such as: When should these agents be given? What dose to give? Which agent?

Diabetic patients taking neutral protamine Hagedorn (NPH) insulin may develop antibodies to protamine and would appear to be at increased risk. However, clinical reactions do not predictably occur in these patients. Suspected cross-sensitivity in cases of fish allergy or autosensitization in men after vasectomies does not seem to put most patients at increased risk.

Catastrophic pulmonary hypertension occurs in approximately 0.2% to 4.0% of patients. Several-fold increases in PA pressure leads to right ventricular failure, elevated CVP, low flow across the pulmonary circuit, and low left atrial pressure. Elevated plasma levels of C5a anaphylatoxins and thromboxane are responsible for pulmonary vasoconstriction and accompanied bronchoconstriction. Epinephrine in 0.1-mg increments has

been successfully used. If severe hypotension persists, the patient should be heparinized again and return to bypass to maintain circulation. Slowing the rate of protamine infusion results in a proportional attenuation of the response (**Figs. 5.10** and **5.11**).

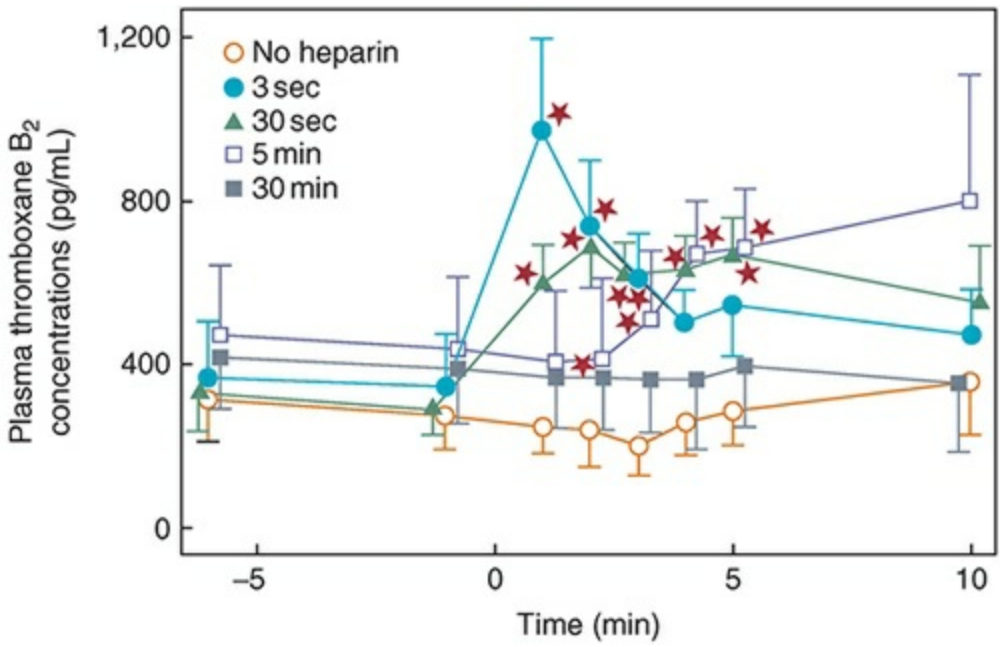


FIGURE 5.10. Plasma thromboxane B_2 concentrations before and after administration of protamine infused over 3 seconds, 30 seconds, 300 seconds, and 30 minutes. Heparin is injected at 5 minutes; protamine infusion is started at 0 minute. Data points represent mean ± *SE* values; n = 6 in each group ($P < .05$ from unheparinized group). (*Reprinted with permission from Morel DR, Costabella PM, Pittet JF. Adverse cardiopulmonary effects and increased plasma thromboxane concentrations following the neutralization of heparin with protamine in awake sheep are infusion rate-dependent.* Anesthesiology. *1990;73:415–424.*)

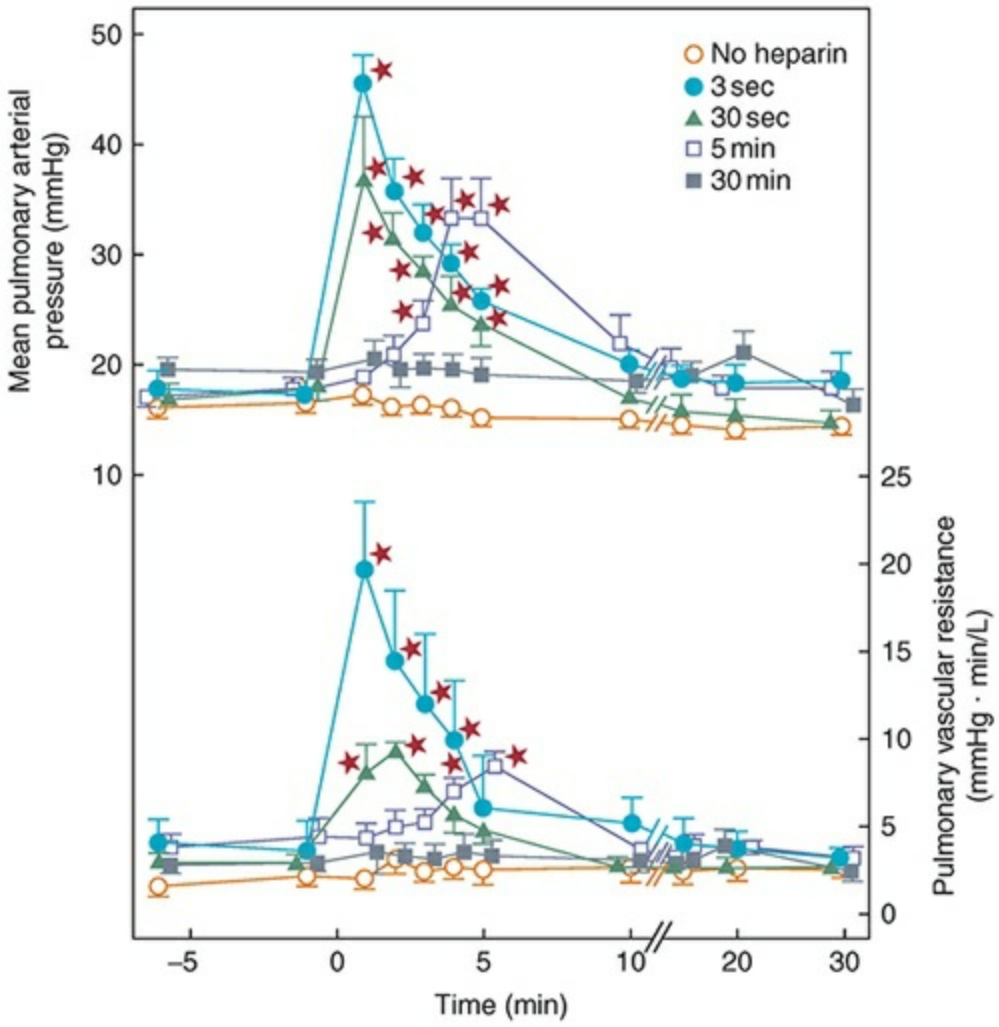


FIGURE 5.11. Pulmonary hemodynamics before and after administration of protamine infused over 3 seconds, 30 seconds, 300 seconds, and 30 minutes. Heparin is injected at 5 minutes; protamine infusion is started at 0 minute. Data points represent mean ± *SE* values; n = 6 in each group (*red star*, $P < .05$ from unheparinized group). (*Reprinted with permission from Morel DR, Costabella PM, Pittet JF. Adverse cardiopulmonary effects and increased plasma thromboxane concentrations following the neutralization of heparin with protamine in awake sheep are infusion rate-dependent.* Anesthesiology. *1990;73:415–424.*)

In conclusion, the treatment of hypotension after protamine administration depends on pulmonary arterial pressure. Hypotension with low pulmonary arterial pressure may be corrected with rapid volume infusion and vasoconstrictors, whereas hypotension with high pulmonary arterial pressure should be treated with inotropes that have a vasodilatory effect. The only effective prevention is a slow

infusion of diluted protamine solution.

Gravlee GP, Davis RF, Hammon J, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2016:504–512.

Horrow JC. Protamine allergy. *J Cardiothorac Anesth*. 1988;2:225–242.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1248–1290.

Lowenstein E. Lessons from studying an infrequent event: adverse hemodynamic response associated with protamine reversal of heparin anticoagulation. *J Cardiothorac Anesth*. 1989;3(1):99–1071.

C.III-5. *What are the indications for intra-aortic balloon pump (IABP)?*

IABP is primarily used for pump failure and myocardial ischemia not responsive to maximal pharmacologic support. The indications include the following:

Ischemic Heart Disease

- Cardiogenic shock
- Acute MI
- Mechanical defects: ventricular or septal rupture, acute mitral insufficiency, or ventricular aneurysm
- Continued ischemic pain and extension of infarction
- Refractory ventricular arrhythmias
- During cardiac catheterization
- Failed PCI and awaiting CABG
- Acute mitral insufficiency with CHF

Cardiac Surgery

- Before CPB and postoperatively
- After CPB: low output syndrome

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed.

Philadelphia, PA: Elsevier; 2017:1042–1063, 1291–1312.

C.III-6. *What are the principles of IABP?*

IABP counterpulsation is designed to increase the myocardial oxygen supply during diastole and to decrease myocardial oxygen demand during systole (Fig. 5.12). The balloon is inflated during diastole to increase the DAP, resulting in increased coronary blood flow. The balloon should be inflated immediately following the closure of the aortic valve at the dicrotic notch of arterial tracing. The balloon is deflated just before the next systole to decrease the intra-aortic pressure and afterload, resulting in decreased myocardial oxygen consumption. The cardiac output is increased because of increased coronary perfusion (diastolic augmentation) and decreased resistance (systolic unloading).

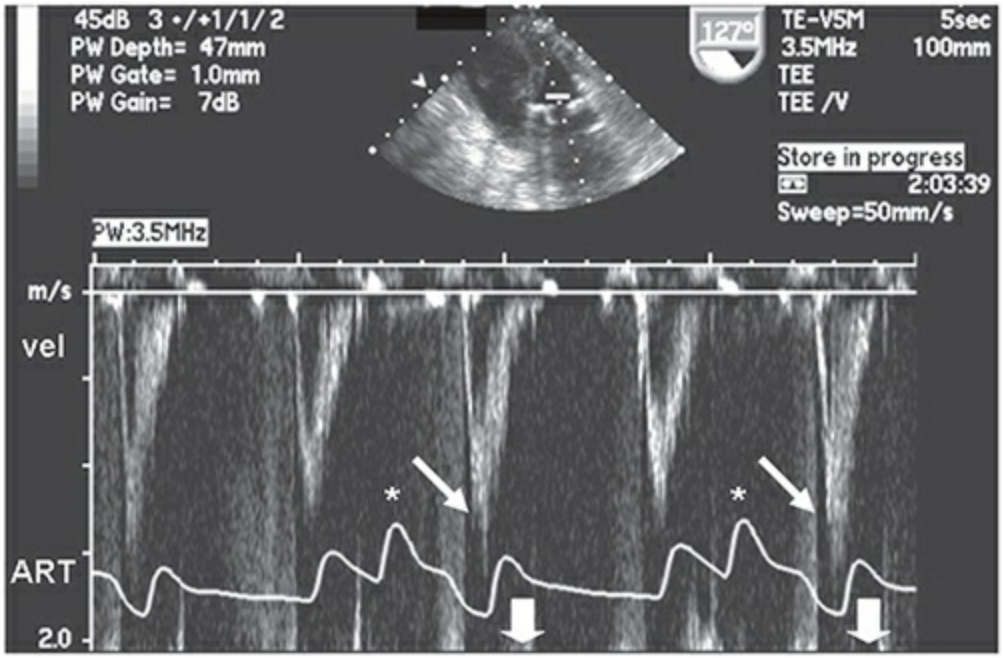


FIGURE 5.12. The function of the intra-aortic balloon pump (IABP). In this patient with an IABP in place, the velocity (vel) of the blood flow, as it exits the left ventricle (LV), is recorded. The arterial waveform is shown in the following text. The IABP is set on a 1:2 ratio; that is, it inflates every other beat, in diastole *(asterisks)*. The velocity (and the amount) of blood exiting the LV is increased *(diagonal arrows)* after the diastolic inflation of the IABP because the LV is ejecting against lower systemic resistance. This is the reason that the systolic arterial pressure following IABP inflation is lower *(down arrows)*.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1042–1063, 1291–1312.

C.III-7. *What are the complications of IABP?*

- Lower extremity ischemia
- Aortic dissection
- Thrombus formation and embolization
- Renal artery occlusion
- Splenic, mesenteric, and spinal cord infarction
- Internal mammary occlusion
- Thrombocytopenia
- Infection
- Gas embolization
- Retroperitoneal bleeding
- Arterial–venous fistula

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1042–1063, 1291–1312.

D. Postoperative Management

D.1. Would you reverse the muscle relaxants? Why?

It depends. If fast-track extubation is planned, reversal agent can be given to ensure that the patient does not experience paralysis while awake. It may be advisable to continue a short-acting sedative/hypnotic agent such as propofol or dexmedetomidine during transport to the ICU and for the immediate period required to establish criteria for extubation. Muscle relaxants should remain in patients who are hemodynamically unstable, with profound hypoxemia (acute respiratory distress syndrome) and/or "open" chest until the clinical state has improved. However, it is important to recognize that prolonged paralysis can lead to marked skeletal myopathy.

Djaiani G, Silverton N, Fedorko L, et al. Dexmedetomidine versus propofol sedation reduces delirium after cardiac surgery: a randomized controlled trial. *Anesthesiology*. 2016;124(2):362–368.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1313–1326.

D.2. When will you wean the patient from the ventilator?

Ventilator management, weaning strategy, and extubation time vary significantly among centers practicing cardiac surgery. Historically, patients were weaned from the respirator the following morning after surgery. More recently, if the operative course is smooth and if the patient is hemodynamically stable, weaning and extubation can be performed early (usually 2 to 6 hours after surgery).

Early tracheal extubation (fast-track) after CABG surgery may have cost benefits and improvement in resource utilization when compared with delayed tracheal extubation. In one report by Cheng et al., early tracheal extubation 1 to 6 hours after surgery reduced total cost per CABG surgery by 25% without increasing the rate or costs of complications in patients younger than 75 years.

Cheng DC, Karski J, Peniston C, et al. Early tracheal extubation after coronary artery bypass graft surgery reduces costs and improves resource use. A prospective, randomized, controlled trial. *Anesthesiology*. 1996;85:1300–1310.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1358–1373.

D.3. What criteria would you use in deciding when to wean the patient from the ventilator?

- Consciousness—awake and alert
- Stable vital signs
- Acceptable arterial blood gases—pH, 7.35 to 7.45; Pa_{O_2}, over 80 mmHg with F_{IO_2}, 0.4; Pa_{CO_2}, 35 to 45 mmHg

- Acceptable respiratory mechanics
- Vital capacity greater than 10 to 15 mL per kg
- Maximal inspiratory force—greater than 20 to 25 cm H_2O
- Hemostasis—less than 100 mL per hour of chest tube drainage
- Stable metabolic state—normal temperature and electrolytes

The patient should tolerate being on continuous positive airway pressure of 5 cm H_2O and pressure support of 5 cm H_2O with 40% oxygen. If the patient tolerates the continuous positive airway pressure well for 30 minutes and arterial blood gases are acceptable, the patient may be extubated.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1358–1373.

D.4. What are potential postoperative complications?

Cardiovascular

CHF, arrhythmias, low output syndrome, myocardial ischemia or infarction due to surgical manipulation, prolonged CPB and aortic cross-clamp (coronary ischemia), use of cardioplegic solution, and occlusion or kinking of grafts.

Pulmonary

Acute lung injury or adult respiratory distress syndrome due to the following:

- Decreased blood flow to the lung during total CPB
- Collapsed alveoli during CPB, resulting in decreased surfactant and decreased distensibility
- Fluid overload
- Hyperoxia during CPB
- Left ventricular failure
- Microemboli
- Reperfusion injury

- Inflammatory response
- Infections
- Transfusion-related lung dysfunction

Renal

- Polyuria from hemodilution and diuretics
- Oliguria from hypoperfusion
- Acute kidney injury
  - Hypoperfusion
  - Ischemia
  - Inflammatory response
  - Nephrotoxins (preoperative contrast dyes, antibiotics)
- Acute tubular necrosis
- Acute or chronic renal insufficiency

Hemorrhage

- Too much or too little protamine to reverse heparin
- Thrombocytopenia and decreased coagulation factors
- Qualitative and quantitative platelet defect
- Disseminated intravascular coagulopathy
- Fibrinolysis with low levels of fibrinogen
- Poor surgical hemostasis

Embolism: due to air, destroyed or aggregated formed blood elements, fat, endogenous and exogenous debris

Neurologic: stroke and neurocognitive dysfunction marked by functional changes in behavior, personality, or other brain functions; cerebral embolism; and seizures

Hyperglycemia: hypothermia, dextrose-containing cardioplegia, increased catecholamine levels, and diabetogenic state associated with surgery and CPB

Hypokalemia: due to hemodilution, alkalosis, and diuretics

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:1327–1357.

6 Mechanical Circulatory Support

Lisa Q. Rong, Mudit Kaushal, and Adam D. Lichtman

A 58-year-old man is scheduled to undergo an upper gastrointestinal (GI) endoscopy under monitored anesthesia care (MAC). The patient underwent aortic and mitral valve replacement for aortic stenosis and mitral regurgitation 4 weeks earlier, and the procedure was complicated by postcardiotomy cardiogenic shock. He was unable to separate from cardiopulmonary bypass (CPB) after maximum vasopressor support and emergent placement of an intra-aortic balloon pump (IABP). He was finally able to separate from bypass after initiation of extracorporeal membrane oxygenation (ECMO) support. Over the next several days, the patient's cardiac function did not recover, and he was brought back to the operating room for placement of a left ventricular assist device (LVAD).

A. Medical Disease and Differential Diagnosis

1. What is an IABP?
2. How is an IABP placed and positioned?
3. Describe an IABP inflation and deflation timing.
4. How does the IABP help improve hemodynamics?
5. What are the indications for IABP placement?

6. What are the contraindications and potential complications of IABP placement?
7. What are the pitfalls of IABP timing?
8. What are the main advantages and disadvantages of IABP support?
9. What is mechanical circulatory support?
10. What is a ventricular assist device (VAD)?
11. What are the types of percutaneous/temporary VADs?
12. What are the types of permanent VADs?
13. How does VAD work?
14. When is circulatory support needed?
15. What are the physiologic considerations in patients requiring a VAD?
16. What are the reasons for suboptimal VAD support?
17. What are common complications from VAD?
18. How long can VADs remain in the patient?

B. Preoperative Evaluation and Preparation

1. What is the focus of the preoperative assessment of an LVAD patient?

C. Intraoperative Management

1. Detail the anesthetic management for a patient undergoing LVAD placement.
2. How is a VAD patient monitored during a general anesthetic?
3. Prescribe an anesthetic for a VAD patient.
4. What is ECMO? What are the indications for ECMO? What are the different types of ECMO?
5. What are the contraindications of ECMO?
6. What are the main complications of ECMO?
7. What are the necessary equipment and teams required to place ECMO? What are the pros and cons of different venoatrial ECMO (VA-ECMO) cannula placement?
8. How are patients monitored and managed while on ECMO?

9. What are the complications of ECMO?
10. How frequently is VA-ECMO being used and how effective is it in cardiogenic shock?

D. Postoperative Management

1. When and how is a patient weaned off IABP support?
2. How is weaning from ECMO accomplished?

A. Medical Disease and Differential Diagnosis

A.1. What is an IABP?

An IABP is a device used to improve the function of a failing heart. It is an 8.5 to 9.5 French dual-lumen catheter with a 40- to 60-mL helium-filled balloon attached at its tip. The IABP provides counterpulsation, whereby the systolic afterload to cardiac ejection is reduced and the perfusion of the coronaries and proximal aortic arteries is augmented.

Kapur NK, Esposito M. Hemodynamic support with percutaneous devices in patients with heart failure. *Heart Fail Clin*. 2015;11:215–230.

White JM, Ruygrok PN. Intra-aortic balloon counterpulsation in contemporary practice—where are we? *Heart Lung Circ*. 2015;24:335–341.

A.2. How is an IABP placed and positioned?

The IABP is placed either percutaneously or under surgical exposure into a large peripheral artery (most commonly femoral) and directed retrograde into the thoracic aorta over a wire. The volume of the balloon used is dictated by the height of the patient (50-mL balloons being most common). The optimal position is with the tip of the balloon positioned just distal to the origin of left subclavian artery and the proximal end of the balloon before the orifice of the renal arteries. IABP positioning is performed either blindly, with subsequent verification of its location with fluoroscopy/x-ray or under the guidance of transesophageal echocardiography (TEE). Incorrect placement

may cause obstruction of the cerebral or visceral vessels, which may result in possible cerebral or visceral organ ischemia and an ineffective counterpulsation. During IABP support, the patient is usually anticoagulated.

Klopman MA, Chen EP, Sniecinski RM. Positioning an intraaortic balloon pump using intraoperative transesophageal echocardiogram guidance. *Anesth Analg*. 2011;113:40–43.

A.3. Describe an IABP inflation and deflation timing.

The balloon is connected to a control console that regulates the inflation and deflation of the balloon at the tip of the IABP. The IABP balloon is inflated in diastole and deflated in systole. The triggers for balloon inflation are (1) the electrocardiogram (ECG) T wave; (2) the dicrotic notch on the arterial waveform, which is recorded from the tip of the IABP; and (3) an internal, predetermined ratio. The balloon deflation is timed to occur prior to the ECG Q wave or the upstroke of the arterial line waveform (**Fig. 6.1**). Improper IABP timing reduces its effectiveness and will increase myocardial oxygen consumption. Examples of this include the following:

- Early inflation: inflation of the IABP before aortic valve closure (**Fig. 6.2A**)
- Late inflation: inflation of the IABP after the closure of the aortic valve (**Fig. 6.2B**)
- Early deflation: premature deflation of the IABP during the diastolic phase (**Fig. 6.2C**)
- Late deflation: deflation of the IABP after the onset of systole (**Fig. 6.2D**)

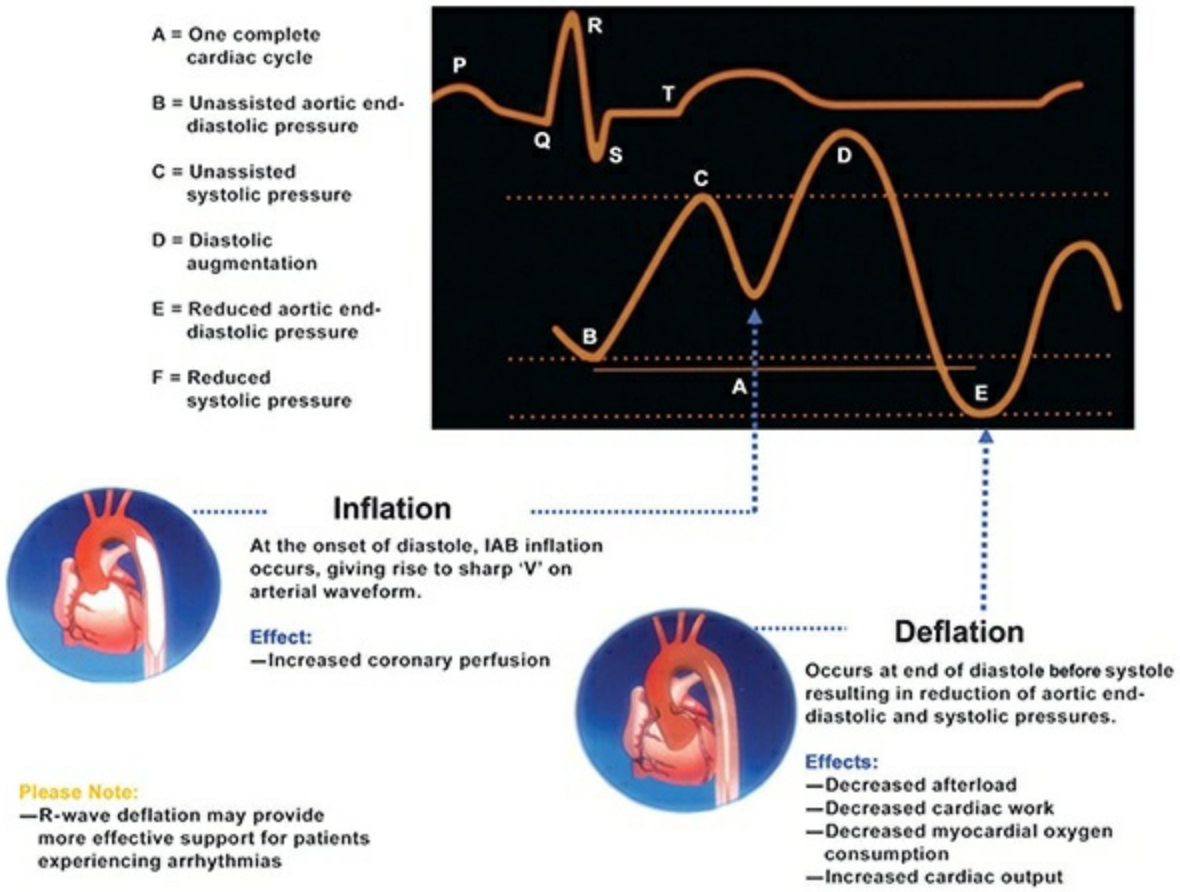


FIGURE 6.1. One complete cardiac cycle and the corresponding waveform of the IABP during the inflation and deflation. *(Reproduced with permission from Datascope®.)*

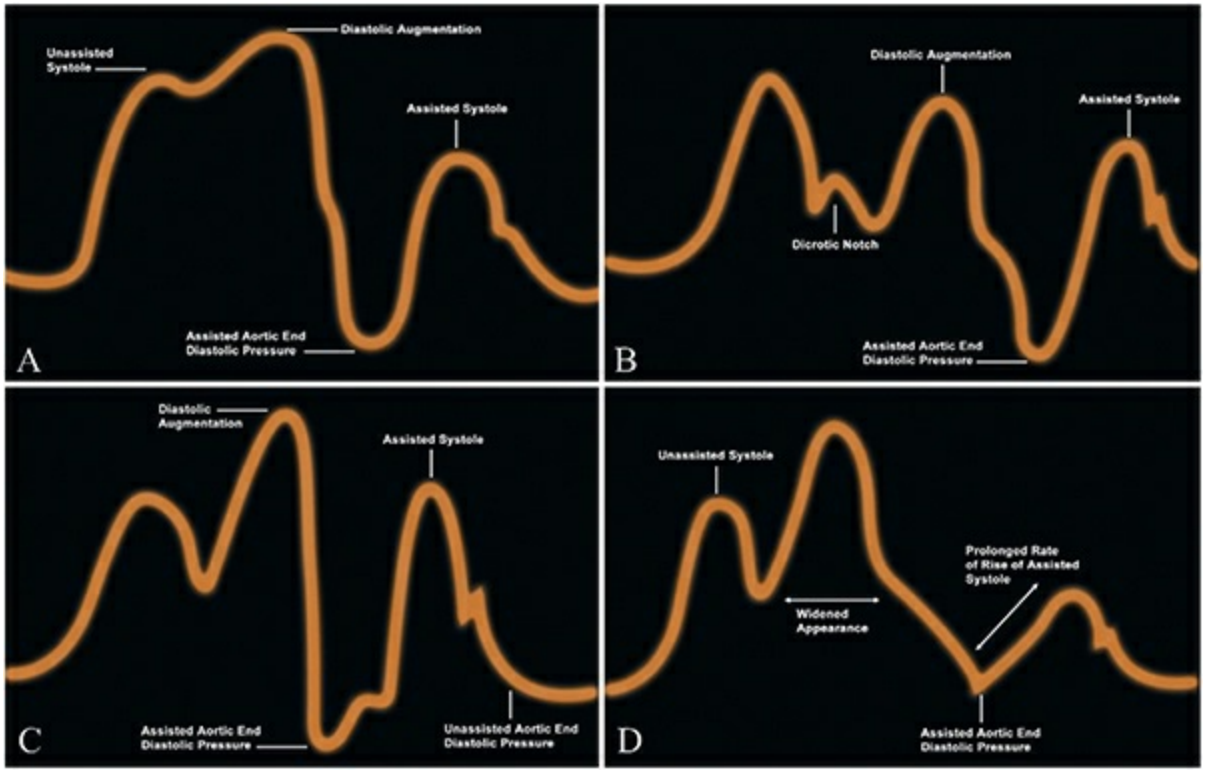


FIGURE 6.2. **A.** *Waveform characteristics:* inflation of IABP before dicrotic notch; diastolic augmentation encroaches onto systole, may be unable to distinguish. *Physiological effects:* potential premature closure of the aortic valve; potential increase in left ventricular end diastolic volume (LVEDV) and left ventricular end diastolic pressure (LVEDP) or pulmonary catheter wedge pressure (PCWP); increased LV wall stress or afterload; aortic regurgitation; increased myocardial oxygen (MVO_2) demand. **B.** *Waveform characteristics:* inflation of IABP after the dicrotic notch; absence of sharp 'V'. *Physiological effects:* suboptimal coronary artery perfusion. **C.** *Waveform characteristics:* deflation of IABP is seen as a sharp decrease after diastolic augmentation; suboptimal diastolic augmentation; assisted aortic end-diastolic pressure may be equal to or less than the unassisted aortic end-diastolic pressure; assisted systolic pressure may increase. *Physiological effects:* suboptimal coronary perfusion; potential for retrograde coronary and carotid blood flow; suboptimal afterload reduction; increased MVO_2 demand. **D.** *Waveform characteristics:* assisted aortic end-diastolic pressure may be equal to the unassisted aortic end-diastolic pressure; rate of increase of assisted systole is prolonged; diastolic augmentation may appear widened. *Physiological effects:* afterload reduction is essentially absent; increased MVO_2 consumption because of the left ventricle ejecting against a greater resistance and a prolonged isovolumetric contraction phase; IABP may impede LV ejection and increase the afterload. (*Reproduced with permission from Datascope®.*)

Krishna M, Zacharowski K. Principles of intra-aortic balloon pump counterpulsation. *Contin Educ Anesth Crit Care Pain*. 2009;9(1):24–28.

White JM, Ruygrok PN. Intra-aortic balloon counterpulsation in contemporary practice—where are we? *Heart Lung Circ*. 2015;24:335–341.

A.4. How does the IABP help improve hemodynamics?

The balloon is timed to inflate in diastole causing an augmented diastolic pressure with resultant increase in blood flow to the coronary arteries, great vessels, and visceral organs. The balloon deflates in systole (just prior to the opening of the aortic valve) causing a "void" or "potential" space in the aorta that reduces left ventricular (LV) afterload, which in turn facilitates ventricular systolic ejection and an increase in stroke volume. The decreased systolic afterload reduces the LV wall tension, decreases the myocardial oxygen demand, and ameliorates the effects of coronary ischemia. IABP counterpulsation intervals can be regulated by the operator, from a 1:1 ratio to a 1:3 ratio (each beat, to every third beat, respectively). In a properly functioning IABP, the operator looks for (1) the counterpulsation to create a diastolic pressure wave, which is usually higher than the preceding systolic wave, that is, the "assisted" diastolic aortic pressure, with a diastolic pressure value lower than the unassisted diastolic pressure; and (2) for the following systolic pressure wave that is lower than the unassisted systolic pressure.

The degree to which the diastolic pressure is augmented depends on a number of variables: (1) balloon position—IABPs placed closer to the aortic valve will produce a greater augmentation of diastolic pressures than those placed further away; (2) balloon volume—maximal augmentation is seen when the balloon volume is equal to the stroke volume; (3) balloon diameter and aortic occlusivity—greatest augmentation is seen with complete aortic occlusion; (4) effective balloon configuration, driving gas, and timing; (5) stroke volume—if the SV is less than 25 mL, minimal augmentation of diastolic pressures is seen. Therefore, the IABP may be less effective in patients in severe cardiogenic shock.

counterpulsation (IABP) for myocardial infarction complicated by cardiogenic shock. *Cochrane Database Syst Rev*. 2011;(7):CD007398.

Weber KT, Janicki JS. Intraaortic balloon counterpulsation: a review of physiological principles, clinical results, and device safety. *Ann Thorac Surg*. 1974;17(6):602–636.

White JM, Ruygrok PN. Intra-aortic balloon counterpulsation in contemporary practice—where are we? *Heart Lung Circ*. 2015;24:335–341.

A.5. What are the indications for IABP placement?

- Cardiogenic shock secondary to acute coronary syndromes (ACS): The most common indication for IABP placement is often after ACS, such as unstable angina refractory to medical therapies and ST-elevation myocardial infarction (MI) with or without acute mitral regurgitation, and ventricular septal defect.
- Postcardiotomy cardiogenic shock: postcardiac surgery where a patient is unable to separate from CPB
- Elective high-risk percutaneous coronary interventions (PCIs) in patients with LV dysfunction and extensive coronary artery disease (CAD) to maintain coronary perfusion and cardiac output during intervention
- Symptomatic severe CAD (i.e., high-grade left main CAD) to increase coronary perfusion before intervention
- Less common indications include bridge to cardiac transplantation and patients with “high-risk” cardiac disease presenting for urgent noncardiac surgical procedures.

In many cases, a patient is on maximal vasoactive support without significant improvement in hemodynamics, peripheral tissue, or organ perfusion measured by cardiac out/mixed venous oxygen saturation, or has a rising lactate and/or decreasing urine output.

Parissis H, Graham V, Lampridis S, et al. IABP: history-evolution-pathophysiology-indications: what we need to know. *J Cardiothorac Surg*. 2016;11(1):122.

Thiele H, Zeymer U, Neumann FJ, et al; for IABP-SHOCK II Trial Investigators. Intraaortic balloon support for myocardial infarction with cardiogenic shock. *N Engl J Med*. 2012;367:1287–1296.

White JM, Ruygrok PN. Intra-aortic balloon counterpulsation in contemporary practice—where are we? *Heart Lung Circ*. 2015;24:335–341.

A.6. What are the contraindications and potential complications of IABP placement?

The contraindications to IABP placement include the following:

- Significant aortic insufficiency (the IABP-induced increased diastolic pressure will worsen the severity of the aortic valvular incompetence and increase the LV diastolic pressure)
- Major aortic pathology (aneurysm, dissection, severe atherosclerotic plaque), which may cause complications during the retrograde advancement of the IABP device retrograde inside the aortic lumen
- Sepsis, with the risk of colonization of the IABP catheter
- Uncontrolled coagulopathy
- Cancer with metastasis

The potential complications include the following:

- Vascular injury at the placement site is the most common complication of IABP placement. This is especially true in patients with severe peripheral vascular disease (reported as 8% to 18% with major limb ischemia reported at 1%). Bleeding at the insertion site is another major complication.
- Thrombocytopenia has been reported in 57.9% of patients receiving IABP but has not been associated with major bleeding events or mortality.
- A rare complication is rupture of IABP causing gas embolism.

Parissis H, Graham V, Lampridis S, et al. IABP: history-evolution-pathophysiology-indications: what we need to know. *J Cardiothorac Surg*. 2016;11(1):122.

White JM, Ruygrok PN. Intra-aortic balloon counterpulsation in contemporary practice—where are we? *Heart Lung Circ*. 2015;24:335–341.

A.7. What are the pitfalls of IABP timing?

Correct diastolic inflation and systolic deflation are critical to optimizing the benefits of IABP counterpulsation. Early diastolic inflation of the IABP balloon (inflation is initiated during late systole) will result in increased LV afterload and increased myocardial oxygen consumption. Late diastolic inflation will result in suboptimal coronary perfusion and diastolic augmentation. Early deflation of the IABP will cause suboptimal diastolic augmentation. In late deflation, there may be a prolonged isovolumetric contraction phase with increased LV afterload and increased myocardial oxygen consumption.

White JM, Ruygrok PN. Intra-aortic balloon counterpulsation in contemporary practice—where are we? *Heart Lung Circ*. 2015;24:335–341.

A.8. What are the main advantages and disadvantages of IABP support?

The main advantages of IABP are its multiple indications and relative ease of use. IABPs are widely used for cardiogenic shock and are easier and quicker to insert (smaller cannula and less complicated procedure) compared to other VADs. An IABP also has relatively low incidence of complications and is easy to manage postoperatively. However, the main disadvantage is it provides limited hemodynamic support at 0.5 to 1.0 L per minute. Despite the fact that there are several indications for the use of IABP in cardiogenic shock including cardiac surgery, there is little evidence of proven benefit. Recently, a large randomized controlled trial, the IABP-SHOCK II trial, did not show improvement in 30-day survival after implantation of IABP after acute MI-related cardiogenic shock.

Werdan K, Gielen S, Ebelt H, et al. Mechanical circulatory support in cardiogenic shock. *Eur Heart J*. 2014;35:156–167.

A.9. What is mechanical circulatory support?

Mechanical circulatory support is a broad term that encompasses the use of devices that provide support ("assist") or replace the function of the failing heart, lungs, or both. The failure of pharmacologic therapy or ventilation techniques to maintain adequate perfusion, oxygenation, and ventilation in order to prevent irreversible end-organ failure has led to the use of mechanical circulatory devices.

The cardiac support systems ("ventricular assist devices" or VAD) can be used as a short-term "bridge" until recovery occurs or as permanent cardiac replacement ("destination" therapy) in the case of end-stage heart failure. The mechanical circulatory support devices include IABPs, VAD (for a single or both ventricles, "biventricular"), extracorporeal membrane oxygenators, and total artificial hearts.

Ferrari M, Kruzliak P, Spiliopoulos K. An insight into short- and long-term mechanical circulatory support systems. *Clin Res Cardiol*. 2015;104:95–111.

A.10. What is a ventricular assist device (VAD)?

A VAD is a device inserted to support one or both ventricles of a failing heart. The cardiac chamber that is supported is used to classify them: An LVAD provides support for a failing left ventricle, a right VAD (RVAD) supports a failing right ventricle, and a biventricular VAD (BiVAD) provides support of both ventricles.

VADs may be fully implantable, with only the electrical or venting components exiting the skin, or may be paracorporeal, with cannulas that direct blood from the patient to an external device. Externally driven VADs are most likely seen following cardiac surgery and as a temporary bridge to recovery or definitive therapy.

Ferrari M, Kruzliak P, Spiliopoulos K. An insight into short- and long-term mechanical circulatory support systems. *Clin Res Cardiol*. 2015;104:95–111.

Slininger KA, Haddadin AS, Mangi AA. Perioperative management of patients with left ventricular assist devices undergoing noncardiac surgery. *J Cardiothorac Vasc Anesth*. 2013;27(4):752–759.

A.11. What are the types of percutaneous/temporary VADs?

The Impella® system (Abiomed, Danvers, MA) is an axial flow pump which provides support by propelling blood from the left ventricle into the ascending aorta. It is positioned retrograde across the aortic valve. There are two versions: the Impella® 2.5 can provide up to 2.5 L per minute of flow and can be inserted percutaneously in the catheterization laboratory, whereas the Impella® 5.0 can deliver up to 5.0 L per minute of flow but requires surgical cutdown of the femoral or axillary artery. When the Impella® 2.5 was compared to the IABP in the ISAR-SHOCK randomized trial on cardiogenic shock patients, the cardiac index and blood pressure were significantly improved in the Impella® group compared to the control group while having no difference in complications. Similarly, the Impella® 5.0 device has been found superior to the IABP in postcardiotomy low-output syndrome patients (cardiac output of 1 L per minute).

The TandemHeart® (CardiacAssist, Pittsburgh, PA) is percutaneously inserted through a transseptal puncture and transfers oxygenated blood from the left atrium and pumps up to 4 L per minute of blood through a continuous-flow centrifugal pump into the lower abdominal aorta or iliac arteries through a femoral cannula. Hemodynamically, the TandemHeart® provides a greater increase in cardiac output and blood pressure compared to IABP and decreases right and LV filling pressures and work. However, both the complexity of the placement of the device and high complication rate (vascular injury, bleeding leading to transfusion, sepsis/systemic inflammatory response syndrome [SIRS], stroke, GI bleeding) have limited its use and

popularity.

Percutaneous biventricular support is possible by using a combination of the TandemHeart® with modified position of the inflow cannula placed in the right atrium and an outflow cannula in the pulmonary artery to support the right ventricle combined with placement of an IABP or Impella® to support the left ventricle.

Lampert BC. Perioperative management of the right and left ventricles. *Cardiol Clin*. 2018;36(4):495–506.

Werdan K, Gielen S, Ebelt H, et al. Mechanical circulatory support in cardiogenic shock. *Eur Heart J*. 2014;35:156–167.

A.12. What are the types of permanent VADs?

Permanent VADs provide pulsatile or continuous flow. Early permanent VADs used pulsatile flow primarily in an effort to mimic the native circulatory pattern but were prone to mechanical failure and infection. The newer VADs rely on the principle of continuous, nonpulsatile flow. Continuous-flow devices can be classified further as either axial (HeartMate® 2 or 3 Left Ventricular Assist System; Thoratec Corp, Pleasanton, CA) or centrifugal flow devices (Heartware Ventricular Assist Device®; Heartware International, Framingham, MA). Both pumps are powered by electric currents that impart motion to a central rotor which displaces blood. In the more common centrifugal pumps, the rotor is levitated by permanent magnets, controlled by the electric currents that cause blood acceleration circumferentially. Blood is removed from the left ventricle through the inflow cannula into the device, propelled around an impeller, and returned into the outflow cannula in the aorta. The pulsatility of the systemic blood pressure is proportional to the amount of intrinsic LV function of the patient. Continuous-flow devices are now the mainstay of VADs because they have been found to have a higher incidence of survival and quality of life

and decreased number of adverse events when compared to first generation pulsatile devices.

Of the implantable continuous-flow LVAD options, the HeartMate® 3 LVAD (St. Jude Medical Inc., St. Paul, MN) has recently emerged as a popular option due to decreased hemolysis, platelet activation, and cleaving of von Willebrand factor as well as a decreased incidence of pump thrombosis.

The Total Artificial Heart (TAH, SynCardia Systems, Tucson, AZ) is a biventricular pulsatile flow pump with all chambers of the native heart mimicked in a single device implanted into the pericardial sac. Anastomoses are made from the caval circulation, pulmonary arterial and venous circulation, and the ascending aorta. Large series studies have shown that when used as a bridge to transplantation, posttransplantation survival is 60% at 5 years after transplantation. Complications include strokes in 8% of the patients and clinically significant hemorrhage in over half of the patients.

Carpentier A, Latrémouille C, Cholley B, et al. First clinical use of a bioprosthetic total artificial heart: report of two cases. *Lancet*. 2015;386(10003):1556–1563.

Ferrari M, Kruzliak P, Spiliopoulos K. An insight into short- and long-term mechanical circulatory support systems. *Clin Res Cardiol*. 2015;104:95–111.

Krabatsch T, Netuka I, Schmitto JD, et al. Heartmate 3 fully magnetically levitated left ventricular assist device for the treatment of advanced heart failure—1 year results from the Ce mark trial. *J Cardiothorac Surg*. 2017;12(1):23.

Lampert BC. Perioperative management of the right and left ventricles. *Cardiol Clin*. 2018;36(4):495–506.

Werdan K, Gielen S, Ebelt H, et al. Mechanical circulatory support in cardiogenic shock. *Eur Heart J*. 2014;35:156–167.

A.13. How does VAD work?

In the case of LV support, blood is drained from either the left atrium or LV apex and routed to the VAD and returned to the systemic circulation via a cannula in the ascending aorta. In the

case of right ventricular (RV) support, blood is drained from the right atrium or right ventricle and is directed to the VAD, from which it is returned to the pulmonary circulation via a cannula in the main pulmonary artery.

Ferrari M, Kruzliak P, Spiliopoulos K. An insight into short- and long-term mechanical circulatory support systems. *Clin Res Cardiol*. 2015;104:95–111.

A.14. When is circulatory support needed?

Circulatory support is indicated for temporary, long-term, and destination therapy. Temporary support is indicated in patients undergoing high-risk interventions, such as PCIs; in patients with severely impaired LV function; or in other complicated percutaneous or surgical interventions. Additional indications for circulatory support include the prevention of the sequelae of cardiogenic shock (i.e., multisystem organ failure) following MI, cardiac surgery, or decompensated heart failure. Due to the severe shortage of donor hearts, long-term circulatory support (usually LVAD or RVAD) is used as a bridge to cardiac transplantation, bridge to candidacy for transplant, or destination therapy in patients not eligible for cardiac transplantation. The goal when using long- or short-term circulatory support in patients who require hemodynamic support is to avoid the "bridge to nowhere" scenario, when circulatory support is initiated with no clear therapeutic end point.

Ferrari M, Kruzliak P, Spiliopoulos K. An insight into short- and long-term mechanical circulatory support systems. *Clin Res Cardiol*. 2015;104:95–111.

A.15. What are the physiologic considerations in patients requiring a VAD?

The left ventricle is the most commonly supported ventricle. The LVAD will replace some or all of the LV function in supplying systemic perfusion. This will leave the right ventricle unassisted and susceptible to failure from the increased preload (the effect

of LVAD). At the same time, pulmonary hypertension from any cause will increase RV afterload which may cause RV ischemia and will further decrease RV performance. In a similar fashion, an RVAD may increase the preload of the left ventricle and precipitate LV failure. The most common scenario is for a patient with cardiogenic shock or acute decompensated heart failure to be supported with an LVAD or ECMO.

Dalia AA, Cronin B, Stone ME, et al. Anesthetic management of patients with continuous-flow left ventricular assist devices undergoing noncardiac surgery: an update for anesthesiologists. *J Cardiothorac Vasc Anesth*. 2018;32(2):1001–1012.

A.16. What are the reasons for suboptimal VAD support?

The performance of a VAD (its systemic output) may decrease from hypovolemia, bleeding, RV failure, cardiac tamponade, and increased left-sided afterload. Relative or absolute hypovolemia reduces VAD output by causing a "suction event" where the interventricular septum gets "sucked into" the outflow cannula causing decreased VAD filling and device "stroke volume." Increased afterload increases the resistance to pump outflow and will likewise decrease cardiac output from the VAD. Additionally, a long-term complication causing decreased VAD function is VAD thrombosis, described in the following text.

Nicolosi AC, Pagel PS. Perioperative considerations in the patient with a left ventricular assist device. *Anesthesiology*. 2003;98:565–570.

Sen A, Larson JS, Kashani KB, et al. Mechanical circulatory assist devices: a primer for critical care and emergency physicians. *Crit Care*. 2016;20(1):153.

A.17. What are common complications from VAD?

VAD thrombosis, reported in 2% to 4% of patients, is defined as clot formation in the VAD. It is often ascribed to noncompliance, inadequate response to anticoagulation therapy, an inherited hypercoagulable state, atrial fibrillation, and

infection. Inflow cannula malposition and low pump flow have also been associated with VAD thrombosis. Clinically, VAD thrombosis manifests as occult cardiogenic shock, hemolysis with increasing lactate dehydrogenase levels (LDH) above 500 IU per L and increasing LVAD pump power. A “ramp study” can be performed to further support the diagnosis of VAD thrombosis. In this study, increasing pump speed should normally produce an increasingly empty left ventricle, a decrease in LV end-diastolic diameter, and a loss of aortic valve opening. When the left ventricle does not decompress (measured by end-diastolic diameter), VAD thrombosis is increasingly suspected.

Surgical treatment (i.e., pump exchange or heart transplantation) of the thrombosed VAD is considered far more effective than medical treatment in HeartMate® II devices. The mortality rate with medical treatment is reported as 48.2%, and the mortality after surgical treatment at 6 months is similar to those patients who did not experience VAD thrombosis. Medical treatment focuses on anticoagulation and antiplatelet therapies.

Right heart failure occurs in 20% to 50% of patients who receive LVAD support. Those patients who have significant right heart dysfunction should be carefully evaluated before LVAD placement.

Bleeding accounts for 9% of the mortality observed in LVAD patients. It is thought to be due to an acquired von Willebrand syndrome secondary to polymer degradation by the VAD impeller.

Sepsis and systemic infections affect nearly 1 in 3 patients with an LVAD and may necessitate evaluation for endocarditis and device removal.

Birati E, Rame E. Left ventricular assist device management and complications. *Crit Care Clin*. 2014;30(3):607–627.

Oleyar M, Stone M, Neustein SM. Perioperative management of a patient with a nonpulsatile left ventricular-assist device presenting for noncardiac surgery. *J Cardiothorac Vasc Anesth*. 2010;24(5):820–823.

A.18. How long can VADs remain in the patient?

VADs can remain in patients until there are complications that necessitate exchange or removal. Myocardial recovery is also an indication for VAD explanation. Current survival for continuous-flow LVADs is 81% at 1 year and 59% at 3 years.

Kanwar M, Bailey S, Murali S. Challenges and future directions in left ventricular assist device therapy. *Crit Care Clin*. 2018;34(3):479–492.

Nguyen AB, Uriel N, Adatya S. New challenges in the treatment of patients with left ventricular support: LVAD thrombosis. *Curr Heart Fail Rep*. 2016;13(6):302–309.

Sladen RN. New innovations in circulatory support with ventricular assist device and extracorporeal membrane oxygenation therapy. *Anesth Analg*. 2017;124(4):1071–1086.

B. Preoperative Evaluation and Preparation

B.1. What is the focus of the preoperative assessment of an LVAD patient?

The number of patients with LVADs are increasing mainly due to their success as a destination therapy in advanced heart failure. Therefore, these patients are increasingly encountered for noncardiac surgical procedures. Commonly encountered procedures include upper and lower GI procedures for bleeding due to arteriovenous malformation or larger and more extensive surgical procedures.

The preoperative evaluation should include a standard evaluation assessing the patient's current state of health and changes in exercise tolerance to screen for symptoms of acute heart failure. Careful physical examination should be performed to determine fluid status, right heart function, and signs of worsening heart failure. Medications, recent cardiology notes,

and laboratory results should be reviewed.

The medications list should be examined for diuretics, inotropes, anticoagulants, and anti-arrhythmic therapies. Laboratory results should be reviewed for baseline renal function, coagulation panel (as all of these patients should be on anticoagulation), and hepatic function (which may indicate worsening right heart function). VAD patients often have renal impairment and renal precautions should be taken during surgery.

Coagulation status should be carefully assessed. The risk of bleeding versus VAD thrombosis should be assessed for each individual procedure to determine whether or not to stop or bridge anticoagulation perioperatively.

The most recent cardiology note should be reviewed for the type of VAD, indication for device placement, VAD settings (including flow rate, device alarms, power elevations, and backup battery life), and any other device interrogations (i.e., pacemakers and implantable cardioverter-defibrillators [ICDs]). Many VAD patients have implanted defibrillators. Depending on the procedure, the tachyarrhythmia therapies may need to be disabled, and the pacemaker function may need to be switched to asynchronous mode if electrocautery interference is anticipated.

The most recent echocardiogram should be reviewed for inflow cannula position, outflow graft patency, and, most importantly, RV function and tricuspid regurgitation. The most common valvular pathologies present in patients with an LVAD are aortic stenosis and insufficiency as well as tricuspid insufficiency.

Patients with VADs should ideally be cared for at a facility that has a support team dedicated to caring for these patients perioperatively. Members of this team should include a cardiologist, a VAD coordinator, cardiac surgeons, cardiac

anesthesiologists, and perfusionists. The team should be notified in advance, if possible, that the patient with a VAD will be presenting for surgery.

VAD patients require extensive support services, and there is frequently 24-hour coverage by a specialized nurse or physician assistant, specifically assigned to the hospital VAD program. These specialists often accompany VAD patients to the operating room and are very facile in the intricacies of individual VADs. In addition, device manufacturers have 24-hour support services and are a source of useful clinical information.

Dalia AA, Cronin B, Stone ME, et al. Anesthetic management of patients with continuous-flow left ventricular assist devices undergoing noncardiac surgery: an update for anesthesiologists. *J Cardiothorac Vasc Anesth*. 2018;32(2):1001–1012.

Nicolosi AC, Pagel PS. Perioperative considerations in the patient with a left ventricular assist device. *Anesthesiology*. 2003;98:565–570.

C. Intraoperative Management

C.1. Detail the anesthetic management for a patient undergoing LVAD placement.

The management of patients requiring LVAD placement can be divided into the preoperative, intraoperative, and post-CPB periods.

Preoperatively, a patient requiring an LVAD will, by definition, have severely reduced LV function. They may require mechanical ventilation, multiple inotropes, vasopressors, and/or an IABP. Due to chronic heart failure and its treatment, such a patient may have profoundly abnormal electrolytes, liver, renal, and coagulation function tests. Preoperative echocardiography demonstrating the presence of pulmonary hypertension, impaired RV function, or tricuspid regurgitation is

particularly important because these findings indicate the possible need for RV support or even placement of an RVAD as well. Severe irreversible pulmonary hypertension, severe tricuspid regurgitation, and severe RV dysfunction may be a contraindication for an LVAD or indicate the need for a BiVAD.

An arterial line is placed prior to the induction of anesthesia. No matter what the anesthetic induction is, myocardial depression or rapid changes in systemic vascular resistance must be avoided. Given the patient's slow circulation time, the preemptive administration of vasopressors is prudent to offset the unwanted side effects of induction agents. To avoid possible acute RV dysfunction due to hypoxia and hypercarbia, ventilation and intubation should be accomplished as expeditiously as possible. Early administration of muscle relaxants and controlled lung ventilation with low inspiratory airway pressure is suggested to avoid increases in intrathoracic pressure that may have deleterious effect on the right heart. Once the patient is successfully induced, ICDs must be deactivated and the pacing mode changed to allow the use of intraoperative electrocautery. Large-bore peripheral and central intravenous access and a pulmonary artery catheter should be placed. Large-bore venous access is especially important in the case of patients who have had prior cardiac surgery because the risk of adhesions and massive hemorrhage is a major concern. Blood and blood products should be available in case of major bleeding.

Intraoperatively, the anesthetic goals are to avoid deterioration of the existing cardiac function, to avoid hypovolemia and anemia, and to optimize the cardiovascular status while the LVAD is implanted under CPB. Because the primary concern in a patient undergoing an LVAD is RV failure, real-time monitoring of central venous pressure (and its association with pulmonary pressures) is crucial. TEE is

invaluable in patients undergoing LVAD placement, and a complete echocardiographic assessment should be performed on every patient. The focus of the transesophageal echocardiographic examination is the presence of (1) atrial septal defects, which may predispose to hypoxemia due to right-to-left shunting post-VAD placement as left atrial pressures are decreased; (2) aortic regurgitation, which will cause a "recycling" of the blood from the aorta back to the left ventricle; (3) tricuspid regurgitation, which may cause or exacerbate RV failure; (4) mitral stenosis, which may decrease filling of the left ventricle and therefore the "preload" to the LVAD; (5) an intracardiac LV thrombus; and (6) preexisting RV dysfunction.

Following the LVAD implantation, the focus is on maintaining euvolemia, treating coagulation abnormalities, and supporting the RV function as needed. A variety of vasoactive medications and inotropes are infused, and frequently inhaled nitric oxide (NO) or prostacyclin is administered to ameliorate any pulmonary hypertension. Those patients treated with pulmonary vasodilators early after LVAD had a decreased incidence of RV failure in observational studies, notably. The VAD patients require long-term anticoagulation.

Critoph C, Green G, Hayes H, et al. Clinical outcomes of patients treated with pulmonary vasodilators early and in high dose after left ventricular assist device implantation. *Artif Organs*. 2016;40(1):106–114.

Dalia AA, Cronin B, Stone ME, et al. Anesthetic management of patients with continuous-flow left ventricular assist devices undergoing noncardiac surgery: an update for anesthesiologists. *J Cardiothorac Vasc Anesth*. 2018;32(2):1001–1012.

Nicolosi AC, Pagel PS. Perioperative considerations in the patient with a left ventricular assist device. *Anesthesiology*. 2003;98:565–570.

Sparrow CT, LaRue SJ, Schilling JD. Intersection of pulmonary hypertension and right ventricular dysfunction in patients on left ventricular assist device support: is there a role for pulmonary vasodilators? *Circ Heart Fail*. 2018;11(1):e004255.

C.2. How is a VAD patient monitored during a general anesthetic?

Standard American Society of Anesthesiologists (ASA) monitoring is used at a minimum. Due to the continuous flow of the newer VADs, noninvasive blood pressure cuffs and pulse oximeters may not function reliably in all patients. Nevertheless, the mean arterial blood pressure should be monitored with noninvasive or direct measurements, and oxygenation may be determined by arterial blood gas measurement and continuously by cerebral oxygenation monitors. When arterial line placement is necessary, ultrasound may prove useful to locate the vessel as the systemic pulse may be weak or nonpalpable. The monitoring of central venous pressure or placement of pulmonary artery catheters must be individualized based on the procedure and the patient's underlying RV function. In patients with impaired RV function or for procedures involving large fluid shifts, intraoperative TEE is recommended if available.

No consensus guidelines currently exist to recommend whether these patients should be cared for by a cardiac or general anesthesiologist in the setting of noncardiac surgery. It is generally agreed on that the anesthesiologist should be familiar with LVAD settings and specific alarms. Increasingly, these patients are being cared for safely by general anesthesiologists.

Invasive arterial blood pressure monitoring is recommended for major surgery given its accuracy, reliability, and the ability to obtain blood gasses. Mean arterial pressure (MAP) should generally be kept less than 85 mmHg given concern for reduced LVAD flows, pump stasis, and an association with stroke at higher MAPs.

Common VAD settings: *Pulsatility index* (*PI*) is a dimensionless measure of LV pulsatility, ranging from 1 to 10 with an average of 5 for the HeartMate® LVADs. It is increased in the setting of adequate LV preload and suggests LV systolic

augmentation, and a low PI represents low preload or contractility. Increasing pump speed, by decompressing the left ventricle, will typically decrease PI and vice versa. Once a normal PI range is determined for a patient, it should not vary significantly. *Pump speed* is determined to allow adequate LV preload for intermittent LV ejection and avoid suction events. A low speed may cause pump stasis and thrombosis, and a high speed may cause hemolysis, excessive LV decompression, and suction events as well as RV dysfunction. *Pump power*, which typically correlates directly with pump speed, may be reduced secondary to inflow cannula obstruction or reduced LV preload. An increase in pump power without increased pump flow should raise suspicion for pump thrombosis.

In the event of periprocedural cardiac arrest, standard advanced cardiac life support (ACLS) should be employed with the exception of external chest compressions. Chest compressions are contraindicated because they may disrupt or dislodge VAD cannulas.

Dalia AA, Cronin B, Stone ME, et al. Anesthetic management of patients with continuous-flow left ventricular assist devices undergoing noncardiac surgery: an update for anesthesiologists. *J Cardiothorac Vasc Anesth*. 2018;32(2):1001–1012.

Nicolosi AC, Pagel PS. Perioperative considerations in the patient with a left ventricular assist device. *Anesthesiology*. 2003;98:565–570.

Stone M, Hinchey J, Sattler C, et al. Trends in the management of patients with left ventricular assist devices presenting for noncardiac surgery: a 10-year institutional experience. *Semin Cardiothorac Vasc Anesth*. 2016;20(3):197–204.

C.3. Prescribe an anesthetic for a VAD patient.

No specific type of anesthetic is recommended for patients with mechanical circulatory support. The presence of chronic anticoagulation and the acute decrease in systemic vascular resistance following neuraxial anesthesia make spinal or

epidural anesthesia undesirable. Patients with fully implantable VADs should be considered as having a "full stomach" and be treated accordingly. Decreased rates of gastric emptying and deaths from aspiration of gastric contents have been reported in patients with VADs.

Regardless of the anesthetic technique chosen, physiologic derangements that increase pulmonary and systemic vascular resistance must be avoided because they negatively impact RV function and VAD performance. Hypoxemia, acidosis, and hypercarbia all contribute to RV failure and must be avoided at all costs. Adequate preload must be maintained to promote adequate VAD flows. Rapid changes in venous capacitance due to vasodilating medications (propofol) and patient positioning (i.e., reverse Trendelenburg) are poorly tolerated because decreased venous return will reduce LVAD flow. Intravascular volume must be administered carefully to avoid a rapid increase in central venous pressure and possible RV failure in those patients with impaired RV function.

Many, if not all, VAD patients have an implanted defibrillator/pacemaker, and the anesthesiologist should be aware of potential interference from the electrical cautery. Standard of care should be followed with these devices; if the patient is pacemaker dependent, the device should be programmed to an asynchronous mode because a magnet will likely only turn off the tachyarrhythmia therapy. The electrophysiology team should also be consulted to turn off tachyarrhythmia therapy if necessary and external defibrillator pads should be placed after it is switched off. After the surgery, the tachyarrhythmia therapy should be reinstated.

Dalia AA, Cronin B, Stone ME, et al. Anesthetic management of patients with continuous-flow left ventricular assist devices undergoing noncardiac surgery: an update for anesthesiologists. *J Cardiothorac Vasc Anesth*. 2018;32(2):1001–1012.

Hwang K, Hwang N. Facilitating noncardiac surgery for the patient with left ventricular assist device: a guide for the anesthesiologist. *Ann Card Anaesth*. 2018;21(4):351–362.

Suarez J, Yang D. Gastrointestinal symptoms from left-ventricular assist device external compression of the gastric lumen. *ACG Case Rep J*. 2016;3(4):e180.

C.4. What is ECMO? What are the indications for ECMO? What are the different types of ECMO?

ECMO is the mechanical support of the heart, lungs, or both using a modified heart–lung bypass machine. It usually consists of a centrifugal pump, a heat exchanger, and a membrane oxygenator. Venous blood is aspirated from the right atrium into a centrifugal pump through a long cannula inserted into the right atrium via the femoral vein or jugular vein, sent to the membrane oxygenator, and returned to the circulation via an outflow cannula into the descending aorta from the femoral artery.

Although ECMO can provide up to 4.0 L per minute of support and reduce LV preload, it also increases LV afterload and may increase myocardial oxygen demand.

Although originally used for short-term therapy (days), the development of improved oxygenators and circuits have allowed patients to be supported on ECMO for weeks, as in the case of patients with respiratory failure due to novel influenza type A (H1N1). There are two basic types of ECMO: VA-ECMO and venovenous (VV-ECMO). The terms illustrate the location of the cannulas. In each case, a modified CPB circuit is used that is composed of (1) the cannulas and tubing to drain and return the blood, (2) oxygenator/heat exchanger, and (3) pump.

VV-ECMO is primarily used for severe acute respiratory distress syndrome (ARDS) or as a bridge to lung transplantation but may also be used during surgical procedures on the lungs or airway. In VV-ECMO, an oxygenator is placed in series

between an *outflow* cannula (usually internal jugular vein) and a venous *inflow* cannula (usually femoral vein). However, using a dual-lumen cannula eliminates the need for separate in/outflow cannulae. There is no pump, and the patient's native cardiac output supplies the driving pressure that creates flow across the oxygenator, where gas exchange occurs. Once deoxygenated venous blood has passed through the oxygenator, it is returned to the patient where it mixes with systemic venous blood and is returned via the pulmonary circulation to the left side of the heart and to systemic circulation. As such, there is no cardiac support provided by VV-ECMO. This allows patients on VV-ECMO the opportunity to ambulate or perform physical therapy as well as making the VV-ECMO circuit simpler. TEE is especially useful in directing placement of caval cannulas and diagnosing cannula malposition, obstructed flow, and LV dilatation.

VV-ECMO is often instituted by upper body venovenous cannulation, which uses a bicaval dual-lumen cannula to drain venous return from the superior and inferior vena cava and return oxygenated blood into the right atrium.

VA-ECMO is akin to conventional CPB, in which blood is drained via a cannula placed in the vena cava, routed to a blood pump and an oxygenator/heat exchanger, and returned via the aorta or a large artery. As a result, both cardiac and pulmonary support is achieved. The indications for VA-ECMO include (1) reversible postcardiotomy shock/failure to wean from CPB, (2) bridge to transplantation, and (3) recently as an adjunct to advanced life support for cardiac arrest (i.e., extracorporeal cardiopulmonary bypass [ECPB]). There has been a steep increase in the number of patients placed on ECMO. Although ECMO can provide up to 4.0 L per minute of support and reduce LV preload, it also increases LV afterload and may increase myocardial oxygen demand.

The main advantages of ECMO are quick and easy percutaneous insertion of inflow and outflow cannulas, full circulatory support with up to 4.0 L per minute, and the ability to rapidly improve tissue oxygenation in situations of cardiogenic shock combined with severe pulmonary edema. Due to these reasons, ECMO use is increasing popular and has potential for wider clinical use. The main disadvantage is that it does not reduce LV afterload.

Lafç G, Budak AB, Yener AÜ, et al. Use of extracorporeal membrane oxygenation in adults. *Heart Lung Circ*. 2014;23:10–23.

Shekar K, Mullany DV, Thomson B, et al. Extracorporeal life support devices and strategies for management of acute cardiorespiratory failure in adult patients: a comprehensive review. *Crit Care*. 2014;18:219.

Werdan K, Gielen S, Ebelt H, et al. Mechanical circulatory support in cardiogenic shock. *Eur Heart J*. 2014;35:156–167.

C.5. What are the contraindications of ECMO?

The most universally agreed on contraindications to ECMO support are the absence of a reversible etiology, perceived short life expectancy due to malignancy or other terminal disease, and ongoing bleeding. Other increasingly debated contraindications include advancing age, obesity, sepsis, end-stage renal disease, end-stage hepatic disease, and coagulopathy.

C.6. What are the main complications of ECMO?

Similar to other types of percutaneous VAD support, the most common complications of ECMO are systemic inflammation, renal failure, limb ischemia, and bleeding.

C.7. What are the necessary equipment and teams required to place ECMO? What are the pros and cons of different venoatrial ECMO (VA-ECMO) cannula placement?

The basic ECMO circuit includes a blood pump, oxygenator,

heat exchanger, and the venous and arterial cannulae. A manual pump is also necessary in the event of power outage. Typically, a cardiothoracic surgeon, an intensive care team, and perfusion teams are needed to initiate and manage ECMO support.

Peripheral VA-ECMO cannulation most often uses femoral venous and femoral arterial sites for venous and arterial cannulation. As a result, retrograde flow from the arterial cannula up the aorta can compete with the native antegrade flow through the aorta. To demonstrate oxygenation from native pulsatile flow of the heart that is perfusing the right upper extremity and the right common carotid artery, it is imperative to perform arterial blood gas sampling from the right upper extremity. Peripheral cannulation is associated with an increased risk of limb ischemia.

Central VA-ECMO cannulation (most often after failure to wean from CPB) is associated with an increased risk of infection, less risk of right upper extremity and right cerebral ischemia, and less risk of limb ischemia. It may "rest" the heart better than peripheral cannulation because of improved LV emptying and decreased afterload.

C.8. How are patients monitored and managed while on ECMO?

All patients on ECMO require anticoagulation due to the thrombotic nature of the circuit and oxygenator. Heparin is administered with a goal activated clotting time (ACT) of 1.5 to 2.0 times normal. In VA-ECMO, the circuit flow is titrated to mean arterial pressure and the oxygen saturation of blood in the drainage cannula (S_{DO_2}). On VV-ECMO, flow is titrated to Sa_{O_2} and S_{DO_2}. Because VV-ECMO is primarily used in respiratory failure, once adequate oxygen saturation is achieved, mechanical ventilation is reduced and the lungs are "rested." This is achieved by the use of protective lung ventilation strategies,

including low respiratory rate, low tidal volumes, limited peak inflation pressures, and the use of positive end-expiratory pressure.

Lafç G, Budak AB, Yener AÜ, et al. Use of extracorporeal membrane oxygenation in adults. *Heart Lung Circ*. 2014;23:10–23.

C.9. What are the complications of ECMO?

Complications of ECMO can be either patient or circuit related. Blood clots are the most feared circuit-related complications and may develop in any part of the ECMO circuit, including the pump, oxygenator, or tubing. Signs of clot formation include rising plasma-free hemoglobin or D-dimers, an increasing pressure gradient across the oxygenator, and a fall in post-oxygenator Sa_{O_2}.

Patient-related complications include cannula site and coagulopathic bleeding, hemodynamic instability, sepsis, and intracerebral hemorrhage. In VA-ECMO, hypotension, as evidenced by low mean arterial pressure in the presence of adequate ECMO flow, indicates reduced vascular tone. This can be treated with vasopressors such as norepinephrine or vasopressin. In a patient supported by VA-ECMO, low pump output and "line chatter" (visible oscillations of the circuit tubing) are signs of hypovolemia. Because VV-ECMO has no effect on cardiac function, hypotension in a patient supported by VV-ECMO may be caused by hypovolemia, reduced vascular tone, or myocardial dysfunction. In each case, the treatment must be tailored to the specific cause or causes. This includes the administration of volume and the use of inotropes/vasopressors.

Lafç G, Budak AB, Yener AÜ, et al. Use of extracorporeal membrane oxygenation in adults. *Heart Lung Circ*. 2014;23:10–23.

C.10. How frequently is VA-ECMO being used and how

effective is it in cardiogenic shock?

Due to technologic advances and improvements in ECMO circuit components, ECMO use has increased by over fourfold from 2006 to 2011. As per a January 2018 extracorporeal life support organization (ELSO) report, there were 15,201 adult patients with cardiogenic shock treated with VA-ECMO in 2017 and survival to hospital discharge was 41%. Those patients on VA-ECMO for myocarditis and post–heart transplantation graft failure have a survival of greater than 70%.

Chakaramakkil M, Sivathasan C. ECMO and short-term support for cardiogenic shock. *Curr Cardiol Rep*. 2018;20(10):87.

D. Postoperative Management

D.1. When and how is a patient weaned off IABP support?

Weaning from IABP support is initiated once the patient's requirement for inotropic support is reduced. IABP weaning is done in conjunction with vasoactive support; so, if cardiac output or overall hemodynamics worsen, inotropic support may be increased. Weaning is gradually undertaken over the course of 6 to 12 hours while the ratio of augmented to nonaugmented beats is decreased gradually from 1:1 to 1:2 to 1:3 if the patient maintains hemodynamic stability. If there are any hemodynamic derangements, the weaning process is halted and vasoactive medications are titrated to achieve an adequate cardiac output (or mixed venous oxygen saturation). Following a successful weaning period, the IABP device is removed.

Klopman MA, Chen EP, Sniecinski RM. Positioning an intraaortic balloon pump using intraoperative transesophageal echocardiogram guidance. *Anesth Analg*. 2011;113(1):40–43.

D.2. How is weaning from ECMO accomplished?

Weaning from VA-ECMO follows a similar sequence of actions as weaning from CPB. It is important that the underlying cause requiring ECMO placement has resolved or improved. The patient should be optimized both from a hemodynamic standpoint (titrating vasopressors and inotropes) and from a volume perspective (have low filling pressures). Respiratory status should be optimized as hypercarbia and hypoxia will impair RV function. Inotropic support is usually increased several hours before the planned weaning. Using echocardiography (transthoracic or transesophageal) and a pulmonary artery catheter to guide therapy, ECMO circuit flows are slowly reduced over the course of several hours. With a combination of inotropes for contractility, vasopressors for tone, volume/red blood cells for preload and optimal tissue oxygen delivery, and blood products to treat coagulopathy, the patient is weaned to minimal circuit flows. If the patient remains stable, the circuit is clamped and the cannulas are removed. The presence of pulsatility on the arterial waveform at full ECMO flows indicates myocardial recovery and is a promising sign for a successful wean. If there are declining hemodynamics and/or evidence of poor tissue perfusion (decreasing mixed venous saturation/low cardiac output/low MAPs), then the ECMO flows are increased and the weaning is postponed.
Echocardiographically, it is important that the interventricular septum remains midline; shifting of the septum to the left and dilation of the right ventricle, as well as the presence of increased tricuspid regurgitation indicates impending right heart failure, and weaning should be discontinued. Increased dilation of the left ventricle and presence of increasing functional mitral regurgitation similarly indicates impending LV failure. There is some evidence that TEE-measured systolic velocities on tissue Doppler imaging at the lateral mitral annulus and aortic valve velocity time integrals at minimal ECMO support may correlate

with successful weaning from ECMO.

Weaning from VV-ECMO requires recovery of adequate lung function and may take weeks or longer to occur. Signs that a patient can be weaned include improvements in chest radiograph, improved lung compliance, as well as an increasing Sa_{O_2} for a given circuit flow.

Aissaoui N, Guerot E, Combes A, et al. Two-dimensional strain rate and Doppler tissue myocardial velocities: analysis by echocardiography of hemodynamic and functional changes of the failed left ventricle during different degrees of extracorporeal life support. *J Am Soc Echocardiogr*. 2012;25(6):632–640.

Kaushal M, Schwartz J, Gupta N, et al. Patient demographics and extracorporeal membranous oxygenation (ECMO)-related complications associated with survival to discharge or 30-day survival in adult patients receiving venoarterial (VA) and venovenous (VV) ECMO in a quaternary care urban center. *J Cardiothorac Vasc Anesth*. 2019;33(4):918–919.

Napp L, Kuhn C, Hoeper M, et al. Cannulation strategies for percutaneous extracorporeal membrane oxygenation in adults. *Clin Res Cardiol*. 2016;105:283–296.

Pappalardo F, Pieri M, Arnaez Corada B, et al. Timing and strategy for weaning from venoarterial ECMO are complex issues. *J Cardiothorac Vasc Anesth*. 2015;29:906–911.

Platts DG, Sedgwick JF, Burstow DJ, et al. The role of echocardiography in the management of patients supported by extracorporeal membrane oxygenation. *J Am Soc Echocardiogr*. 2012;25:131–141.

Rihal CS, Naidu SS, Givertz MM, et al. 2015 SCAI/ACC/HFSA/STS clinical expert consensus statement on the use of percutaneous mechanical circulatory support devices in cardiovascular care: endorsed by the American Heart Association, the Cardiological Society of India, and Sociedad Latino Americana de Cardiologia Intervencion; affirmation of value by the Canadian Association of Interventional Cardiology-Association Canadienne de Cardiologie d'intervention. *J Am Coll Cardiol*. 2015;65(19):e7–e26.

Ventetuolo C, Muratore C. Extracorporeal life support in critically ill adults. *Am J Respir Crit Care Med*. 2014;190(5):497–508.

7 Valvular Heart Disease

Meghann M. Fitzgerald and
Natalia S. Ivascu

A 78-year-old man was admitted with increasing shortness of breath. He had chest pain in the past but was able to continue with normal activities. In the past year, he experienced two episodes of syncope. On physical examination, a loud systolic murmur could be heard at the left sternal border radiating to the neck. His vital signs were blood pressure 150/90 mmHg and heart rate 88 beats per minute and irregular. The electrocardiogram (ECG) showed sinus rhythm with atrial premature contractions and left ventricular hypertrophy (LVH) with strain. A transthoracic echocardiogram (TTE) showed a hypertrophied left ventricle (LV), and Doppler examination demonstrated severe aortic stenosis (AS) with a pressure gradient of 64 mmHg, mild aortic insufficiency (AI), and moderate mitral regurgitation (MR). He was scheduled for an aortic valve (AV) replacement and a possible mitral valve (MV) repair or replacement.

A. Medical Disease and Differential Diagnosis

1. What are the major etiologies of AS, AI, mitral stenosis (MS), and MR?
2. What are the major changes in the loading conditions of the LV that result from the four different lesions? Why do they occur? What changes result from them?

3. What are pressure–volume (P–V) loops? What do the different inflection points represent?
4. What are representative P–V loops for the four valvular lesions?
5. Draw the pressure/time curves for the LV, left atrium, pulmonary artery, and aorta for a normal patient and for patients with each of the four valvular lesions.
6. What are the basic principles of echocardiography? What are M-mode, B-mode, and Doppler color modalities? How do TTE and transesophageal echocardiography (TEE) differ?
7. What are the three TEE vantage points for the comprehensive imaging of the LV? How are pressure gradients measured by echocardiography? How do the pressure gradients derived from Doppler echocardiography differ from those obtained in the catheterization laboratory by direct pressure measurement?
8. What is the role for three-dimensional (3D) echocardiography in the operating room?
9. What are the echocardiographic and cardiac catheterization criteria for the four valvular lesions?

B. Preoperative Evaluation and Preparation

1. What are the presenting signs and symptoms of the four valvular lesions listed previously?
2. What is the New York Heart Association classification of heart failure?
3. Discuss the role of premedication for patients with the four different valvular lesions.
4. How would you premedicate the patient with severe AS and MR?

C. Intraoperative Management

1. Outline the hemodynamic management goals for each of the four valvular lesions. What are the anesthetic goals with respect to heart rate and rhythm, preload, afterload, and

contractility?

2. What are the hemodynamic goals for this patient with the combination of severe AS and MR?
3. How would you monitor this patient with severe AS and MR?
4. Should the patient have a pulmonary artery catheter placed before induction?
5. Is a pulmonary artery catheter with pacing capabilities indicated?
6. What anesthetic technique would you employ? Why?
7. What muscle relaxant would you use for this patient?
8. What are the usual TEE findings in a patient with AS or MR? How do you grade the severity of AS by TEE? How do you quantify the severity of MR? What is the impact of AS on the severity of MR?
9. What special considerations particular to cardiopulmonary bypass (CPB) operations do you have for each of the four lesions? Focus on these concerns with respect to the induction and prebypass, bypass, and postbypass periods.
10. The patient cannot be weaned from CPB following an AV replacement and MV replacement. What are the possible causes?
11. How would you diagnose right-sided heart failure and pulmonary hypertension? How would you treat it?
12. How does an intra-aortic balloon pump (IABP) work to benefit the failing heart?
13. What role does the IABP have in this setting?
14. What role does TEE play in the placement, timing, and demonstration of efficacy of an IABP?
15. How would you properly time the IABP cycle?
16. What are the contraindications to the use of an IABP?
17. What is the role for ventricular assist devices?

D. Postoperative Management

1. In the intensive care unit (ICU) 4 hours later, the patient became hypotensive with a low cardiac output. How could you distinguish between cardiac tamponade and pump failure? How would the TEE images differ?
2. Would you extubate this patient early in the ICU? Why?
3. What are the advantages and disadvantages of early extubation?

E. Alternative Treatments

1. What are the percutaneous options for MV repair?
2. How is percutaneous MV repair performed?
3. What are the percutaneous options for AV repair and replacement?
4. How is percutaneous AV replacement performed?
5. What anesthetic techniques and monitors are used?
6. What is minimally invasive cardiac valve surgery?

A. Medical Disease and Differential Diagnosis

A.1. What are the major etiologies of AS, AI, mitral stenosis (MS), and MR?

AS occurs as a congenital lesion but more commonly as an acquired disease. Stenosis may develop on a previously normal AV following rheumatic fever or from progressive calcification. Congenitally bicuspid AVs are also prone to calcification with eventual stenosis. Calcification of the AV leaflets can result in incomplete closure of the valve with associated insufficiency.

AI is usually an acquired disease. The most common causes include bacterial endocarditis and rheumatic heart disease. Annular dilation with resultant AI may result from diseases, such as cystic medial necrosis and collagen disorders, or following aortic dissection.

MS is almost always caused by rheumatic fever, although

only half of patients will have a history of an acute febrile illness. The inflammatory process of rheumatic fever results in thickening of the leaflets and fusion of the commissures. Other rare causes include congenital stenosis and other systemic diseases, such as systemic lupus erythematosus and carcinoid. Pathophysiology similar to that seen with valvular MS can occur with obstructing left atrial tumors and cor triatriatum. MS commonly occurs in conjunction with other valvular heart disease; only 25% of patients present with isolated MS, and approximately 40% have combined MS and MR.

MR can result from defects in the leaflets, the annular ring, or the supporting chords or papillary muscles or any combination of these. Primary leaflet dysfunction occurs with rheumatic fever but can also follow bacterial endocarditis, connective tissue disorders, and congenital malformations. Annular dilation can follow left ventricular dysfunction and dilation. MV prolapse and rupture of papillary muscles result in incomplete leaflet closure or coaptation with resultant MR. Left ventricular ischemia can affect papillary muscle contraction and is the cause of functional MR.

Czarny MJ, Resar JR. Diagnosis and management of valvular aortic stenosis. *Clin Med Insights Cardiol*. 2014;8(suppl 1):15–24.

Iung B, Vahanian A. Epidemiology of acquired valvular heart disease. *Can J Cardiol*. 2014;30(9):962–970.

Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2017;135(25):e1159–e1195.

A.2. What are the major changes in the loading conditions of the LV that result from the four different lesions? Why do they occur? What changes result from them?

AS represents a chronic systolic pressure load on the LV. This

increases the wall tension (stress) in accordance with Laplace's law:

$$\text{Wall tension} = \frac{(\text{Pressure} \times \text{Radius})}{(2 \times \text{Wall thickness})}$$

The LV undergoes parallel duplication of muscle fibers in an attempt to compensate, and this results in increased wall thickness or concentric hypertrophy and some decrease in radius, thereby normalizing wall stress. If the MV remains competent, little change occurs in the other cardiac chambers.

AI causes left ventricular diastolic volume overload due to the additional volume flowing retrograde into the LV across the incompetent AV during diastole. This results in eccentric hypertrophy and left ventricular dilation (increased muscle mass and chamber radius). However, AI decreases the aortic diastolic pressure, which is the pressure that must be exceeded by the contracting LV to open the AV and result in left ventricular systolic ejection. Therefore, left ventricular work is performed against a lower outflow impedance (aortic diastolic pressure). Stroke volume and ejection fraction may be preserved until late in the disease process. As with AS, the presence of a competent MV confines the changes to the LV. However, the left ventricular dilation that follows chronic AI may result in mitral annular dilation or alteration in the papillary muscle orientations with resultant MR. Left atrial enlargement secondary to MR, or left atrial pressure overload as left ventricular end-diastolic pressure (LVEDP) rises in the course of AI, can occur.

MS results in a chronically underfilled LV because of progressive obstruction to left atrial emptying. This chronic underloading condition can result in diminished contractile function (a "disuse atrophy" of sort). In addition, if the cause of the MS is rheumatic, myofibril damage may also occur.

Contrary to the left ventricular pressure and volume *under*loading, the left atrium is both pressure and volume *over*loaded in order to maintain flow across the progressively narrowing mitral orifice. According to Gorlin's equation for pressure gradient:

$$\text{Pressure gradient (mmHg)} = \left\{ \frac{\text{Valve flow rate (mL/s)}}{[\text{K} \times \text{valve area (cm}^2)]} \right\}^2$$

It would predict that the pressure gradient increases by the square of any increase in flow rate or decrease in valve area. The elevated left atrial pressure leads to hypertrophy and eventually dilation that predisposes to premature atrial contractions and subsequent atrial fibrillation. The loss of atrial contraction will further diminish the flow across the stenotic MV. At the same time, the elevated left atrial pressure hinders pulmonary venous flow with consequent pulmonary vascular engorgement. This will lead to intimal hypertrophy that induces irreversible elevations in pulmonary vascular resistance. As a consequence of pulmonary hypertension, the right ventricular (RV) systolic pressure increases and right ventricle dilates, and these may lead to RV failure and tricuspid regurgitation.

MR results in volume overload of the LV. In MR, the LV ejects into both systemic circulation (across the AV; high afterload and low compliance) and retrograde to the left atrium (low afterload and high compliance) across the incompetent MV. This "back and forth" of the regurgitant volume results in left ventricular volume overload. However, this work is performed at a low pressure; therefore, left ventricular wall tension is minimally increased initially. As with AI, the volume overload results in marked left ventricular dilation and eccentric hypertrophy. At the same time, the left atrium is also volume overloaded and undergoes dilation. When the volume overload

occurs slowly, the pulmonary pressures increase minimally despite large regurgitant volumes. In contrast, acute MR, for example, following an acute myocardial infarction with papillary muscle rupture, presents a sudden volume overload to the left atrium. Without the time to dilate, the left atrial pressure rapidly rises, limiting pulmonary drainage with resultant pulmonary engorgement and acute increase in pulmonary pressures.

Frogel J, Galusca D. Anesthetic considerations for patients with advanced valvular heart disease undergoing noncardiac surgery. *Anesthesiol Clin*. 2010;28:67–85.

Schoen FJ. Cardiac valves and valvular pathology: update on function, disease, repair, and replacement. *Cardiovasc Pathol*. 2005;14:189–194.

Zipes DP, Libby P, Bonow RO, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 11th ed. Philadelphia, PA: Elsevier; 2019:1383–1445.

A.3. What are pressure–volume (P–V) loops? What do the different inflection points represent?

The P–V loop analysis (**Fig. 7.1**) depicts the relation between left ventricular volume and pressure during a single cardiac cycle. Opening and closing of the MV and AV are represented by the inflection points A, B, C, and D, respectively (**Fig. 7.1**). Moving from points A to D, AB depicts left ventricular filling, BC depicts isovolumetric contraction, CD shows left ventricular ejection, and DA shows isovolumetric relaxation. Point A coincides with opening of the MV and represents left ventricular end-systolic volume and early diastolic pressure. Point B is closure of the MV and the relationship of end-diastolic pressure (LVEDP) and volume (left ventricular end-diastolic volume [LVEDV]). Point C represents the opening of the AV and coincides with systemic, aortic diastolic pressure. Finally, point D is the closure of the AV and represents left ventricular end-systolic pressure (LVESP) and volume (LVESV), coinciding

with the dicrotic notch in the aortic pressure tracing (**Fig. 7.1**). Left ventricular compliance is the relation between pressure and volume and is defined by the slope of the filling phase (segment AB). Preload is the P–V relation before the onset of contraction (LVEDP). Contractility may be illustrated by the slope of a line termed the *end-systolic pressure–volume relation* (ESPVR). The ESPVR slope is created by connecting multiple points (D) from multiple P–V loops generated by changing the filling volume to the LV (**Fig. 7.2**). Increased contractility results in a steeper line, whereas diminished contractility results in a flatter line. The P–V loop analysis permits illustration of stroke volume and ejection fraction. Stroke volume is defined as difference in volume from the end of filling to the end of ejection (EDV–ESV), whereas the ejection fraction is the ratio of stroke volume to total volume in the heart at peak filling (SV/EDV). Therefore, the P–V loop analysis permits illustration of the volume–pressure relations and their changes with each of the four valvular lesions.

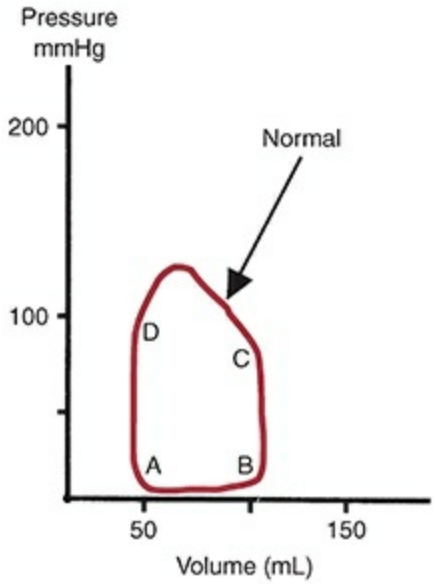


FIGURE 7.1. Normal P–V loop and valve positions. A, mitral valve (MV) opening; AB, left ventricular filling; B, MV closure; BC, isovolumetric contraction; C, aortic valve (AV) opening; CD, ejection; D, AV closure; DA, isovolumetric relaxation.

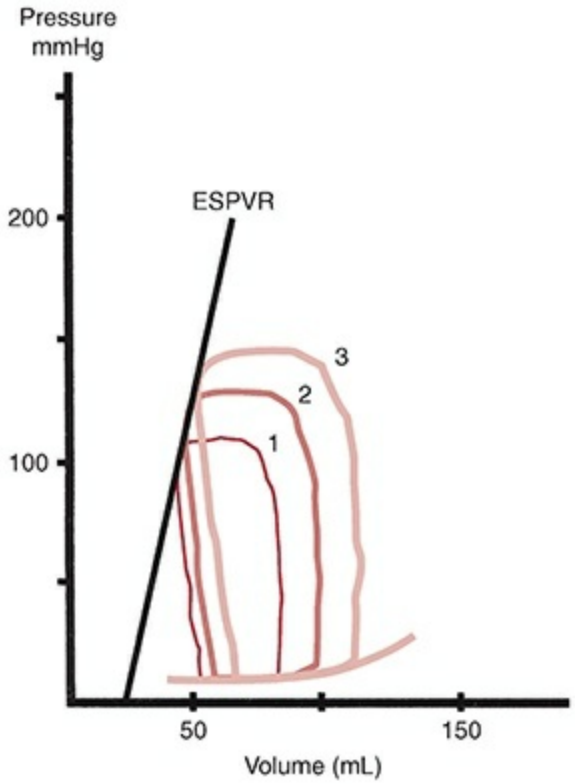


FIGURE 7.2. Contractility. ESPVR, end-systolic pressure–volume relation.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:277–300.

Carabello BA. Volume overload. *Heart Fail Clin*. 2012;8(1):33–42.

Kohil K, Kovacs SJ. The quest for load-independent left ventricular chamber properties: exploring the normalized pressure-volume loop. *Physiol Rep*. 2017;5(6):e13160.

Mérillon JP, Ennezat PV, Guiomard A, et al. Left ventricular performance is closely related to the physical properties of the arterial system: landmark clinical investigations in the 1970s and 1980s. *Arch Cardiovasc Dis*. 2014;107(10):554–562.

A.4. What are representative P–V loops for the four valvular lesions?

The hallmarks of AS, illustrated by the P–V loop analysis, are an increased left ventricular systolic pressure and an upward and counterclockwise rotation in the end-diastolic P–V relation (AB) indicative of decreased chamber compliance (**Fig. 7.3**). Stroke volume and ejection fraction are well preserved, but the ejection

phase of the loop occurs at much higher pressures. This is accomplished by an increase in contractility (counterclockwise rotation of the ESPVR line).

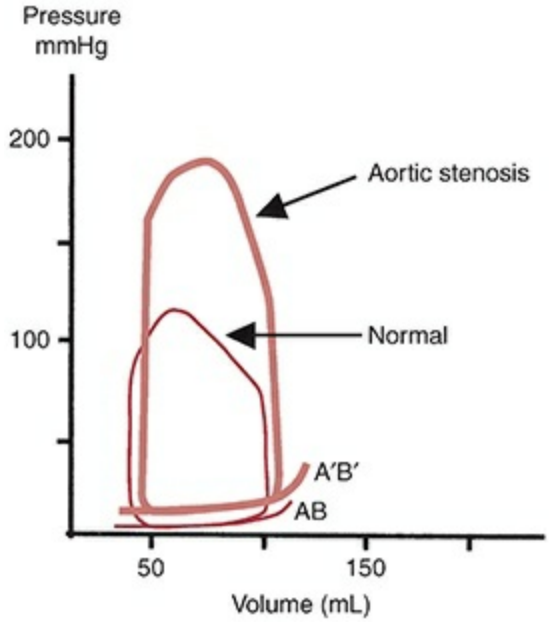


FIGURE 7.3. P–V loop of AS.

The schematic P–V loop for chronic AI depicts an enlarged LV. The minimal change in LVEDP despite the large volume overload is seen by the shift in the diastolic P–V curve to the right (A″B″) (**Fig. 7.4**). Low systemic diastolic pressures result in a brief isovolumetric phase (B″C″) and early complete ejection. The isovolumetric relaxation phase is absent because the incompetent valve permits regurgitant filling of the LV from the aorta during diastole even before opening of the MV. In contrast, when acute AI occurs, the left ventricular compliance is unchanged. Rapid increases in LVEDP from volume overload along the unshifted left ventricular diastolic P–V curve (A′B′) rapidly lead to increased left atrial pressure and pulmonary congestion.

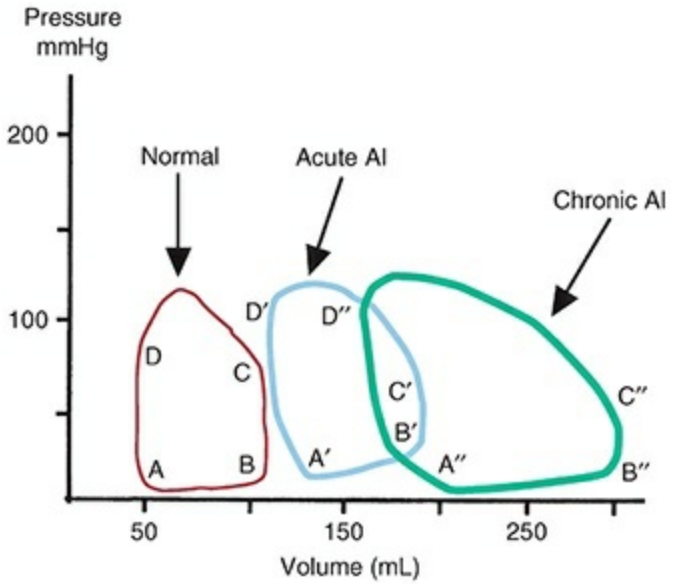


FIGURE 7.4. **P–V loops of acute and chronic aortic insufficiency (AI).**

The P–V loop of MS illustrates hypovolemia, the cause of which cannot be determined from the loop alone (**Fig. 7.5**). Because the predominant impact of MS occurs proximal to the LV, the P–V analysis format is less useful.

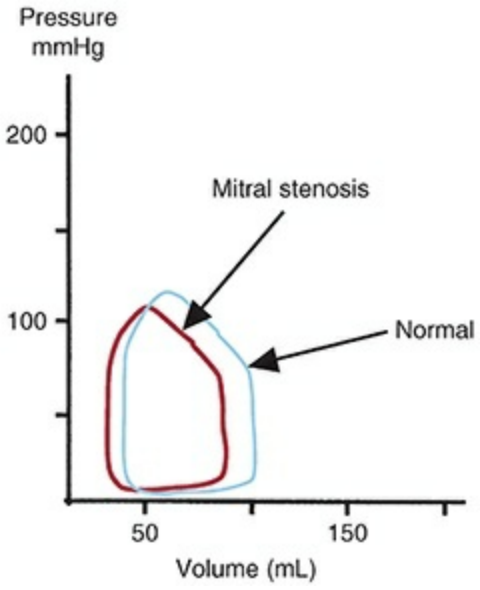


FIGURE 7.5. **P–V loops of MS.**

In MR, the diastolic P–V relation (line AB) is shifted to the right, as it is in chronic AI, consistent with a marked increase in compliance (**Fig. 7.6**). The isovolumetric phase (BC) is nearly

absent because the left atrium generally serves as a low-pressure/high-compliance route for ejection through an incompetent MV. Decreases in contractility are depicted by a decrease in the slope of the end-systolic-PV line (line through D).

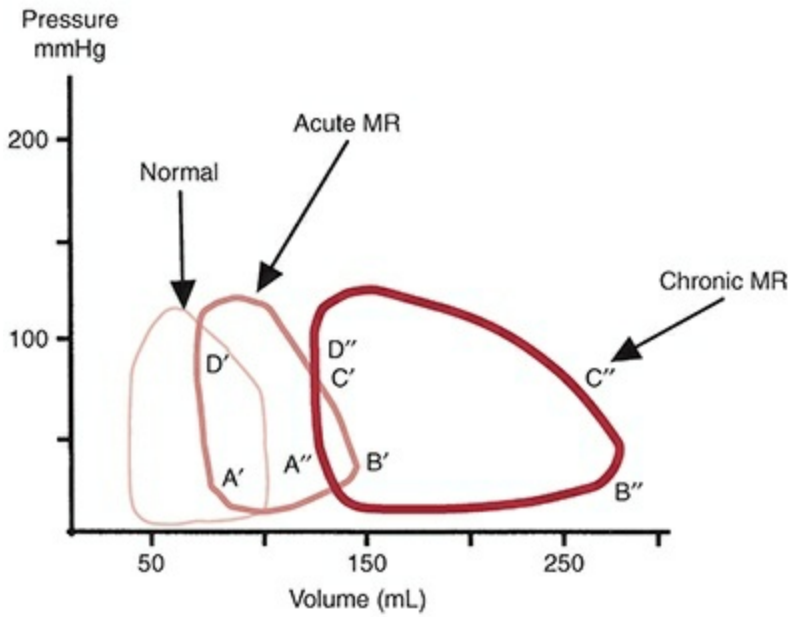


FIGURE 7.6. P–V loop of acute and chronic mitral regurgitation (MR).

Carabello BA, Zile MR, Tanaka R, et al. Left ventricular hypertrophy due to volume overload versus pressure overload. *Am J Physiol*. 1992;263(4 pt 2):H1137–H1144.

Kohil K, Kovacs SJ. The quest for load-independent left ventricular chamber properties: exploring the normalized pressure-volume loop. *Physiol Rep*. 2017;5(6):e13160.

Nishimura RA, Carabello BA. Hemodynamics in the cardiac catheterization laboratory of the 21st century. *Circulation*. 2012;125(17):2138–2150.

A.5. Draw the pressure/time curves for the LV, left atrium, pulmonary artery, and aorta for a normal patient and for patients with each of the four valvular lesions.

Normal curves are shown in **Figure 7.7**. The points A, B, C, and D correspond to the same points in the P–V loops.

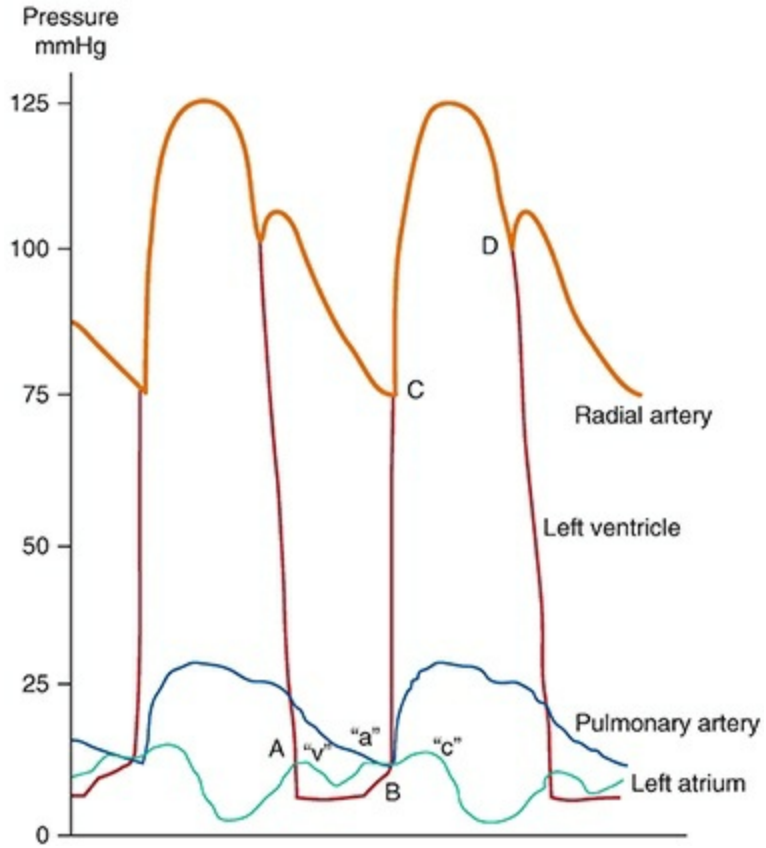


FIGURE 7.7. Pressure curves for the LV, left atrium, pulmonary artery, and aorta in a healthy individual.

Aortic Stenosis

The additional systolic pressure work of AS can be seen in the left ventricular pressure tracing (**Fig. 7.8**). Elevations in LVEDP (point B) can be seen to diminish the perfusion gradient for coronary flow to the LV. The augmentation in left ventricular filling late in diastole secondary to atrial contraction (left atrial "kick" from sinus rhythm) is highlighted in the inset. Rising left ventricular diastolic pressures secondary to decreased compliance necessitate elevations in left atrial pressures to permit complete left ventricular volume loading. Atrial systole provides this elevation in left atrial pressure synchronous with elevations in LVEDP while keeping left atrial pressures relatively low during the remaining cardiac cycle facilitating pulmonary venous drainage.

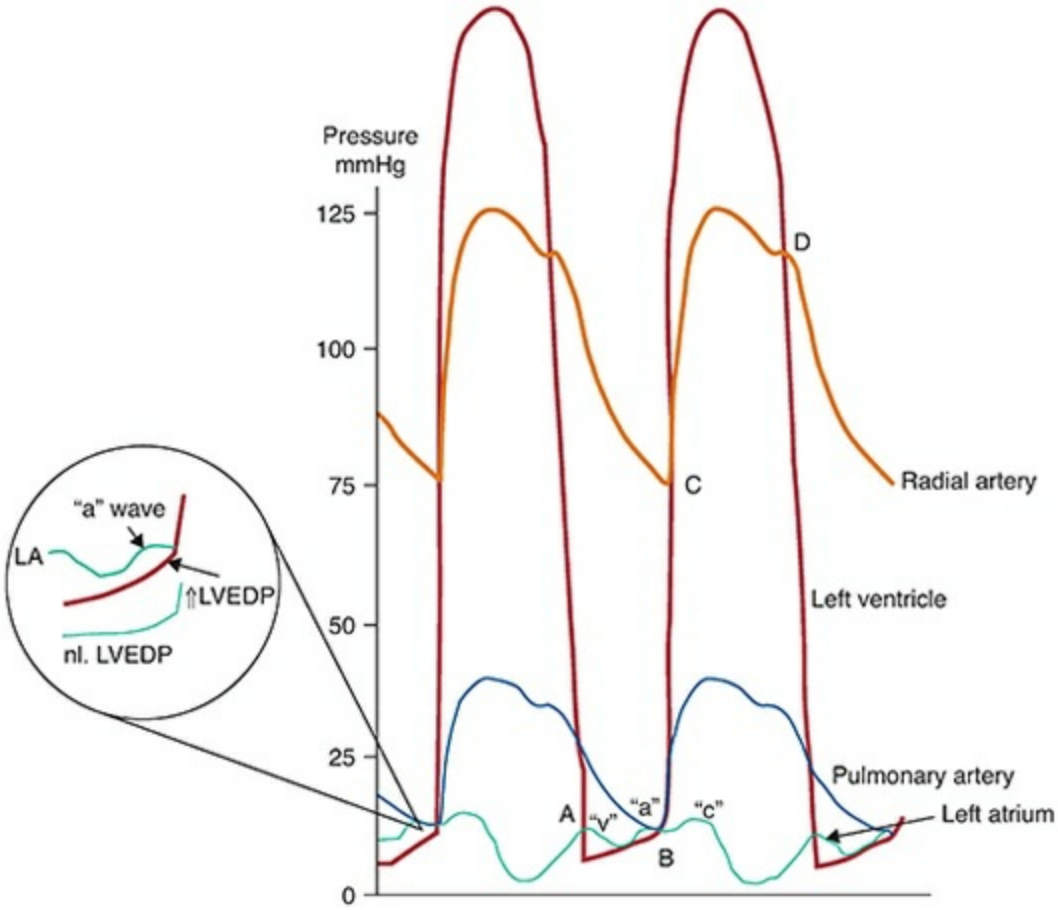


FIGURE 7.8. Pressure curves for the LV, left atrium (LA), pulmonary artery, and aorta in patients with AS. LVEDP, left ventricular end-diastolic pressure.

Aortic Insufficiency

The rapid upstroke and rapid decline of arterial pressure indicate absence of AV closure and low end-diastolic aortic pressure (**Fig. 7.9**). Elevations in LVEDV and LVEDP are typical of AI. The early increase in LVEDP can result in left ventricular pressures exceeding those of the left atrium during diastole, with resultant premature closure of the MV.

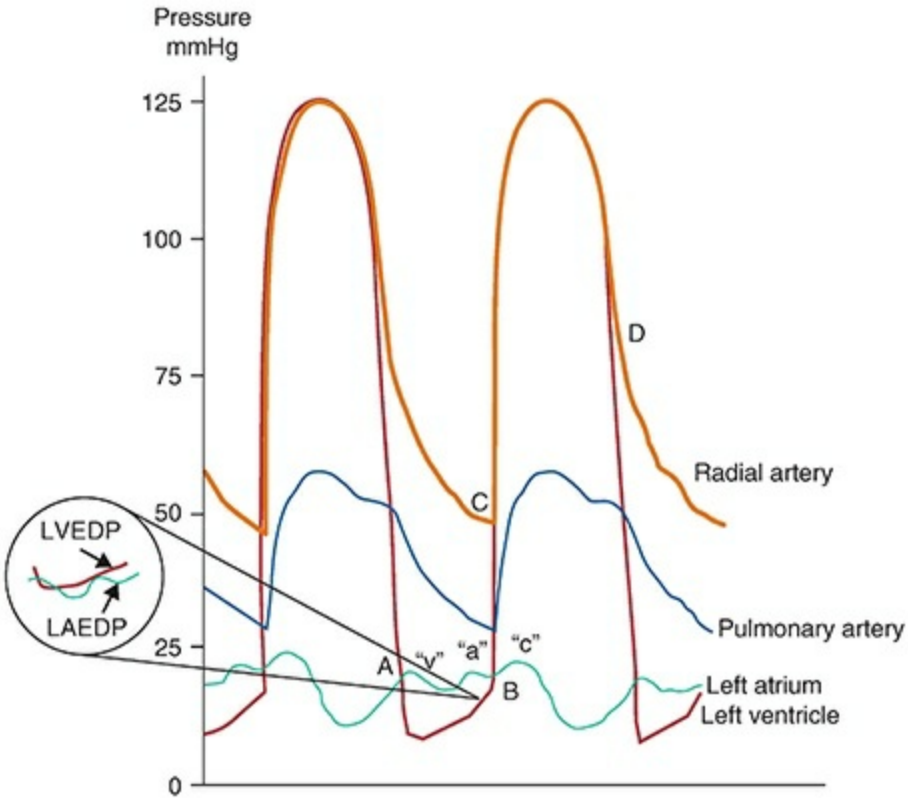


FIGURE 7.9. Pressure curves for the LV, left atrium, pulmonary artery, and aorta in patients with aortic regurgitation. LAEDP, left atrium end-diastolic pressure; LVEDP, left ventricular end-diastolic pressure.

Mitral Stenosis

Elevations in pressure are seen in both the left atrial and pulmonary artery tracing with MS (**Fig. 7.10**). The large gradient between left atrial and left ventricular pressures is highlighted in the inset. Chronic elevation in pulmonary volume induces changes the pulmonary arterial vascular bed and results in pulmonary hypertension.

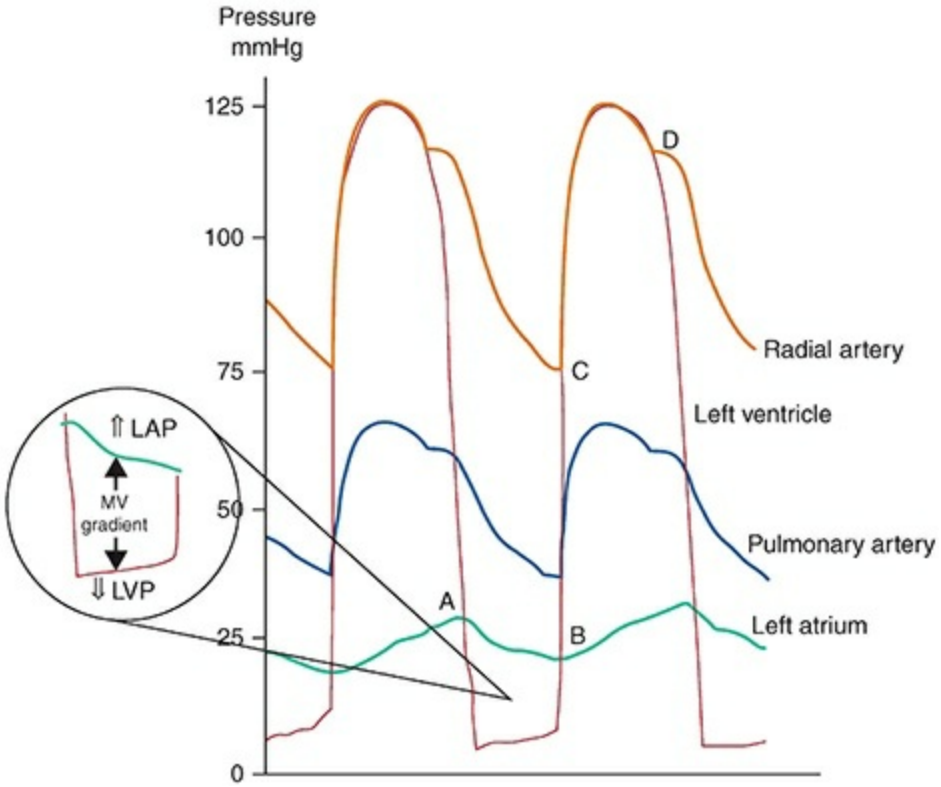


FIGURE 7.10. Pressure curves for the LV, left atrium, pulmonary artery, and aorta in patients with MS. LAP, left atrial pressure; LVP, left ventricular pressure; MV, mitral valve.

Mitral Regurgitation

The hallmark of MR is the marked elevations of left atrial pressure during systole and the occurrence of a giant "cv" wave and elevated pulmonary artery pressures (**Fig. 7.11**).

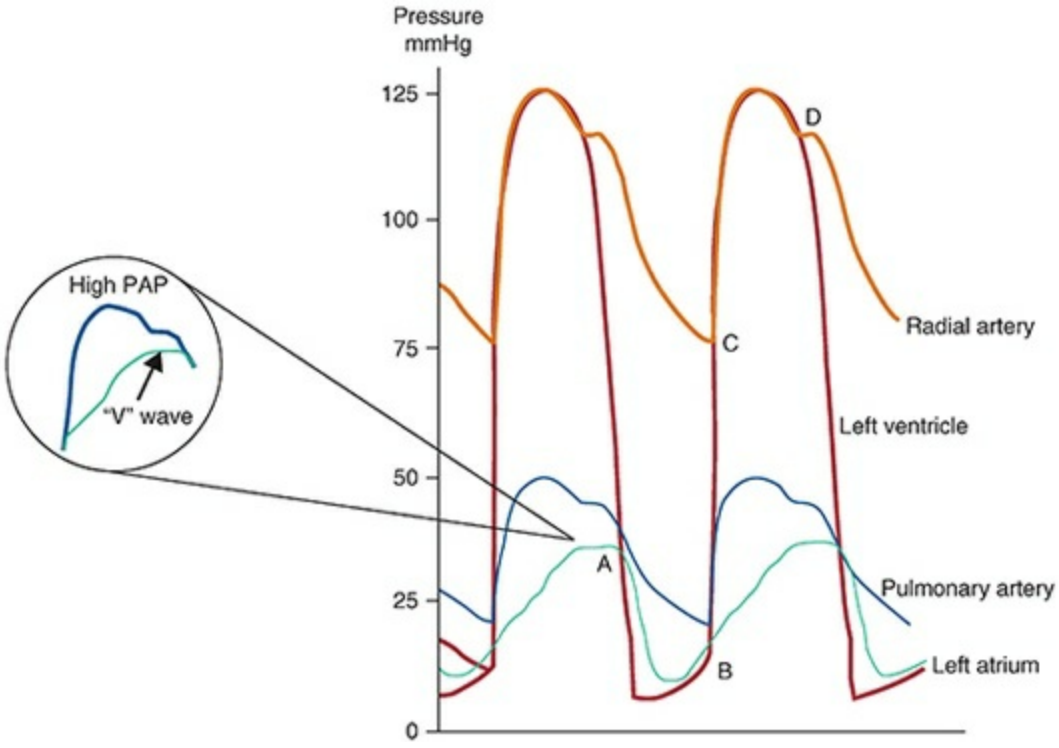


FIGURE 7.11. Pressure curves for the LV, left atrium, pulmonary artery, and aorta in patients with MR. PAP, pulmonary artery pressure.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:277–300.

A.6. What are the basic principles of echocardiography? What are M-mode, B-mode, and Doppler color modalities? How do TTE and transesophageal echocardiography (TEE) differ?

Echocardiography is the use of sound waves to image structures and blood flow within the heart and great vessels. To image tissue, sound waves are emitted from a transducer at known speeds and constant intervals. The sound packets bounce off structures in their path, and the reflected sound waves are received by the transducer during its "listening" mode. The time it takes for the reflected waves to return to the crystal is measured, and because the velocity of sound in tissues is relatively constant (1,540 m per second), solving for distance can be easily accomplished:

$$\text{Distance} = \tfrac{1}{2}\,(\text{velocity} \times \text{time})$$

(½ because the distance is traversed twice, once to the object and again on returning).

In this manner, the spatial orientation of cardiac structures can be determined. The strength of the returning signal can be quantified as an amplitude, thus "A" or amplitude mode (**Fig. 7.12B**). The echocardiographic system codes this amplitude on a black and white scale, thereby converting the amplitude to brightness or B-mode scanning (**Fig. 7.12C**). **Figure 7.12D** shows this "ice-pick" view through the LV of the heart. Each change in tissue density results in some sound waves being reflected and hence an interface. In this example, bold lines are seen at the epicardial, the endocardial–chamber, the chamber–endocardial, and the epicardial borders. If these amplitude bars are displayed in real time, a motion or M-mode display results (**Fig. 7.12E**). These images were difficult to reliably obtain and interpret because the views represent a linear slice without surrounding structural images for referencing. If the probe is moved in a sweeping mode, back and forth repetitively, multiple M-mode images can be obtained in a given instant and a two-dimensional (2D) image formed. This rapid back and forth sweep of the ultrasound beam is performed electronically in a phased array transducer. The images derived in this manner appear as a cineradiographic display of myocardial movement. Echocardiography can provide information about the size, shape, location, and movement of myocardial structures.

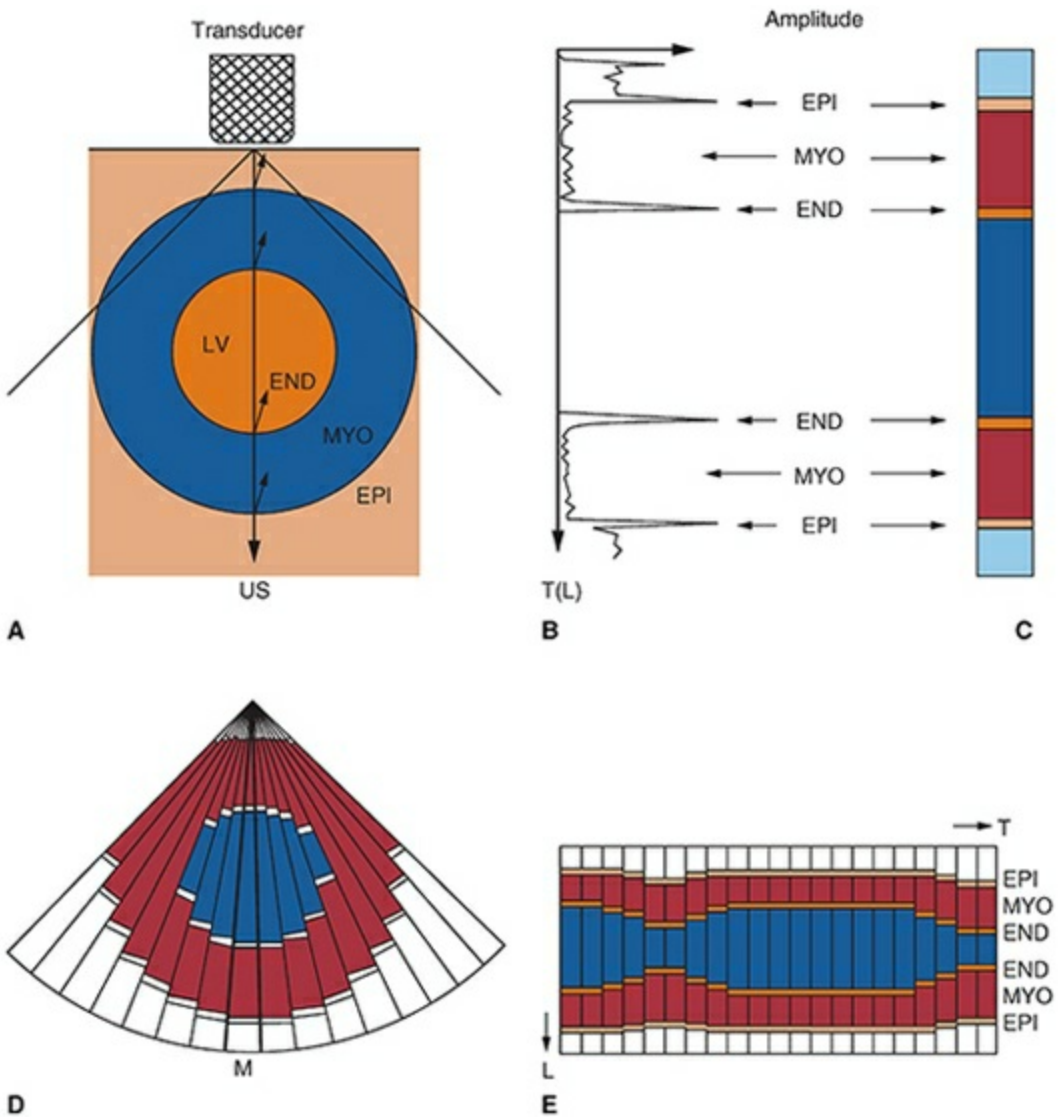


FIGURE 7.12. The process of producing the B-mode and M-mode images. A. A pulse of ultrasound is emitted into the object, and the backscattered echo is received by the same transducer. **B.** The received acoustic signal is converted to the electric signal (A-mode). **C.** The amplitude is modulated into brightness (B-mode). **D.** As subsequent pulses of ultrasound are emitted with the sequentially changing angles and the obtained one-dimensional (1D) B-mode images are compounded according to the direction of each ultrasound emission, the first frame of the sector-shaped image is formed. **E.** When the ultrasound is repeatedly transmitted in one direction, a series of 1D B-mode images is obtained. As these are arranged against time, an M-mode image is obtained. END, endocardium; EPI, epicardium; L, length; LV, left ventricle; M, motion; MYO, myocardium; T, time; US, ultrasound. (*Reprinted with permission from Oka Y, Goldiner PL, eds.* Transesophageal Echocardiography. *Philadelphia, PA: JB Lippincott; 1992:12.*)

In addition to determining how long it takes for a given sound wave to return and thereby deriving the distance from the transducer, contact of the sound wave packet with the reflecting

object (tissue, blood cells, air) will alter the wavelength of the sound packet according to the Doppler principle. When the object coming in contact with the sound wave is moving toward the source of the ultrasound, the reflected ultrasound wavelengths are compressed (shorter). The opposite occurs when the contacted object is moving away from the sound source. These shifts in frequency (ΔF) are proportional to the velocity of the contacted structure, and thereby, the velocity and direction of the encountered object (usually of blood flow) can be calculated. With Doppler ultrasound, only the component of blood flow parallel to the Doppler beam will be analyzed because the Doppler equation velocity = $c\ (\Delta F) / 2\ F_T\ (\cos \theta)$ contains the cosine of the angle of incidence between the ultrasound beam and the moving object (F_T is the transmitted frequency). Because the cosine of 90 degrees is zero, blood flow that is perpendicular to the ultrasound beam will not cause any Doppler shift and, therefore, cannot be measured. For this reason, it is important to choose an ultrasound "window" in which the expected blood flow direction is most parallel to the ultrasound. This velocity information can be displayed on a color map (Doppler color flow) or on a time/velocity scale (spectral Doppler display). Doppler-derived blood flow velocity information can determine laminar and turbulent flow patterns, regurgitant or stenotic lesions, and congenital anomalies and can permit quantification of pressure gradients.

Pressure gradients (ΔP) can be estimated from the measured blood flow velocity using the modified Bernoulli equation ($\Delta P = 4 \times \text{velocity}^2$). Simply, the greater the velocity of blood flow, the higher is the ΔP. TTE uses imaging points or "acoustic windows" obtained with the transducer handheld on the chest wall. TTE is simple and noninvasive. Most standard echocardiograms are obtained from this position. During cardiac

surgery, the chest wall is in the sterile field and therefore unavailable. The esophagus lies immediately adjacent to the heart outside of the operative field and affords an excellent imaging vantage point. In 1976, Yasu Oka from the Albert Einstein College of Medicine developed a practical method of intraoperative imaging. She mounted an ultrasound crystal on the end of a gastroscope and, thereby, obtained images of the heart during surgery. This has been refined considerably since. TEE has become the standard of care for heart surgery at many institutions. The close proximity of the probe to the heart affords excellent resolution. The probe is not in the operative field, so surgery is unhindered and sterility is not an issue. Although mildly invasive, the risk for esophageal injury in the anesthetized state is very low.

Intraoperative TEE is beneficial for quantification of cardiac contractility, for determination of the severity of regurgitant and stenotic valvular disease, for detection of intracardiac shunts and the occurrence of dissections, and as a guide for catheter placement.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:731–766.

Savage RM, Aronson S, Shernan SK, eds. *Comprehensive Textbook of Intraoperative Transesophageal Echocardiography*. 2nd ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2011:3–41.

A.7. What are the three TEE vantage points for the comprehensive imaging of the LV? How are pressure gradients measured by echocardiography? How do the pressure gradients derived from Doppler echocardiography differ from those obtained in the catheterization laboratory by direct pressure measurement?

The heart has two main axes: the longitudinal axis running from

the base to the apex and the short axis perpendicular to that. Multiple scan planes are required to completely image a 3D structure, such as the heart. The LV is divided into 17 segments: 6 at the basal level, 6 at the midpapillary level, 4 at the apical level, and 1 apical cap (**Fig. 7.13**). By moving the TEE probe in the esophagus and rotating the crystal within the transducer tip, the LV can be imaged from three acoustic windows. These are the midesophageal four-chamber, the transgastric short axis, and the transgastric two-chamber view. Normal ventricular motion requires that each wall segment thickens and moves toward the left ventricular cavity at systole. Segmental wall function is usually quantified as normal, hypokinesis, akinesis, and dyskinesis.

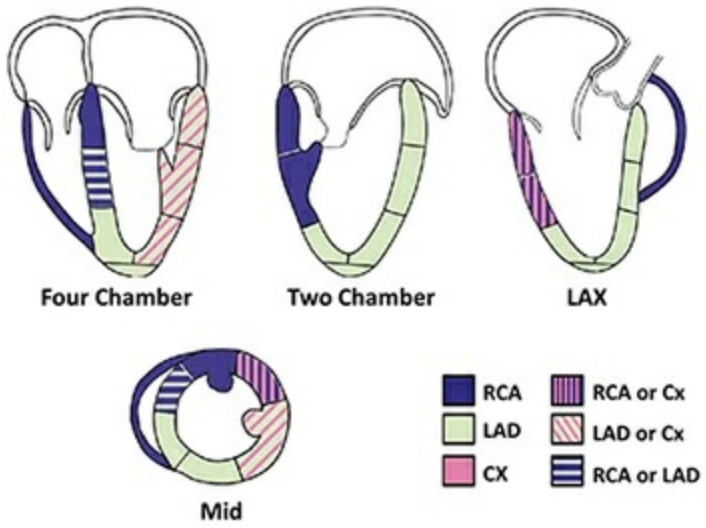


FIGURE 7.13. Wall segments of the LV. CX, circumflex; LAD, left anterior descending; LAX, long axis; RCA, right coronary artery. (*Reprinted from Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology.* J Am Soc Echocardiogr. *2005;18[12]:1440–1463. Copyright © 2005 American Society of Echocardiography. With permission.*)

In addition to function, TEE permits the determination of wall thickness and chamber size—important parameters in understanding the pathophysiology of valvular heart disease.

As mentioned previously, pressure gradients are derived through analysis of the Doppler profiles of blood flow. A commonly determined echocardiography gradient is that which is present from the LV to the aorta in the setting of AS. To obtain the change in blood flow velocity across the AV with TEE, the probe is advanced far into the stomach and sharply anteflexed and left deflected to obtain the window from the apex of the heart (deep transgastric long axis) and align the ultrasound beam most parallel to the path of blood flow. From this window, the continuous-wave Doppler cursor is directed across the left ventricular outflow tract and AV. An example of such a spectral Doppler display is seen in **Figure 7.14**. The large increase in blood flow velocity in this display occurs at the narrowest point along its path, which, in this case, is the stenosed orifice of the AV. Using the modified Bernoulli equation mentioned previously, a gradient is calculated (100 mmHg in the example). This represents the maximum instantaneous systolic pressure difference between the LV and the aorta. AS is also quantified at the time of catheterization by measuring the pressures from within the LV and the aorta as a rapid response pressure transducer catheter is withdrawn from the LV back to the aorta across the stenotic valve. The standard reported pressure gradient is the difference between the maximum LV and aorta pressures. **Figure 7.15** illustrates that these peaks are not simultaneous events. Therefore, Doppler-derived AS gradients are usually higher than those derived at the time of left heart catheterization.

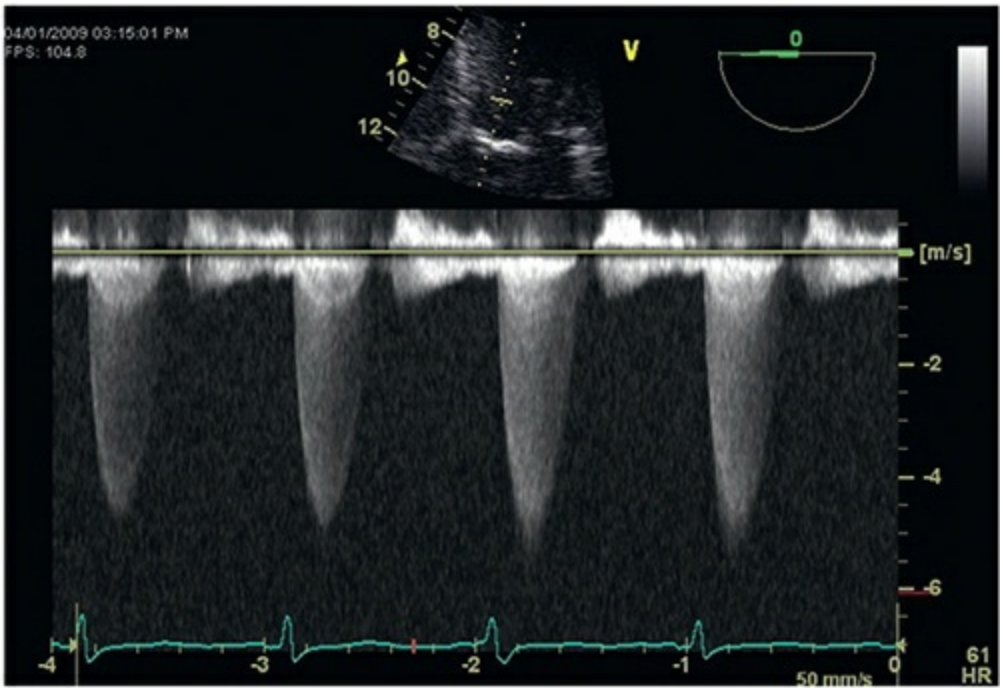


FIGURE 7.14. Continuous-wave Doppler across the AV in the deep transgastric apical view from a patient with severe AS.

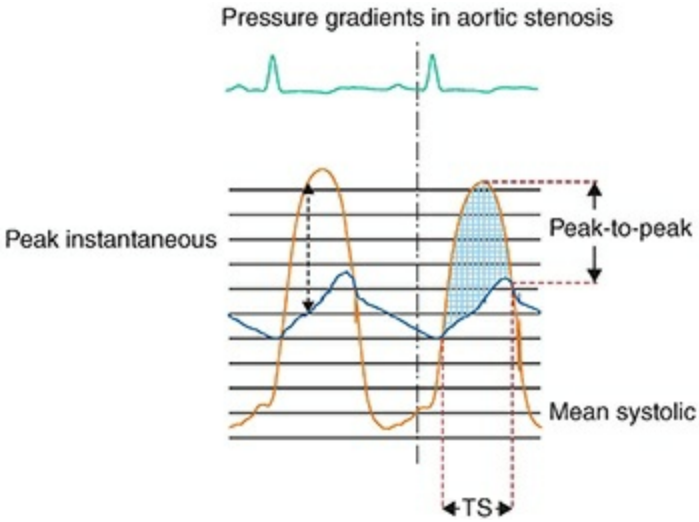


FIGURE 7.15. Pressure gradients in severe AS are measured during systole as the difference between aortic and left ventricular pressures displayed using a scale of 0 to 20 mmHg. The peak instantaneous gradient is the maximum gradient noted; the peak-to-peak gradient is the difference between peak left ventricular and aortic pressures. The mean systolic gradient is the average of all systolic pressure gradients noted during systolic ejection (TS). (*Adapted with permission from Nanda NC, ed.* Doppler Echocardiography. *Philadelphia, PA: Lea & Febiger; 1993:130.*)

Hahn RT, Abraham T, Adams MS, et al. Guidelines for performing a comprehensive transesophageal echocardiographic examination: recommendations from the American Society of Echocardiography and the

Society of Cardiovascular Anesthesiologists. *J Am Soc Echocardiogr*. 2013;26(9):921–964.

Reeves ST, Finley AC, Skubas NJ, et al. Basic perioperative transesophageal echocardiography examination: a consensus statement of the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists. *J Am Soc Echocardiogr*. 2013;26(5):443–456.

Savage RM, Aronson S, Shernan SK, eds. *Comprehensive Textbook of Intraoperative Transesophageal Echocardiography*. 2nd ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2011:406–425.

A.8. What is the role for three-dimensional (3D) echocardiography in the operating room?

Modern TEE technology has progressed from 2D multiplane images to real-time 3D displays of the heart. The 3D probes are etched in such a way to allow for a pyramidal scanning sector (volume). There are different 3D imaging modalities used to assess cardiac anatomy (real-time, zoom, and full-volume, usually gated to ECG signal). The 3D images can be further modified by cropping in any plane to investigate details in morphology. Studies have shown that intraoperative assessment of the MV with 3D TEE examinations have decreased interobserver variability and provided better correlation with surgical findings.

Left ventricular assessments including volume and wall motion can easily be done in the operating room. After identification of the left ventricular walls and apex from two orthogonal 2D views, a 3D model of the heart is created using endocardial border tracking. Stroke volume and ejection fraction can be automatically calculated. However, 3D echocardiography can only be combined with color, not spectral, Doppler ultrasound and is prone to all limitations related to 2D echocardiography.

Jungwirth B, Mackensen GB. Real-time 3-dimensional echocardiography in the operating room. *Semin Cardiothorac Vasc Anesth*. 2008;12:248–264.

Kapoor PM, Muralidhar K, Nanda NC, et al. An update on transesophageal

echocardiography views 2016: 2D versus 3D tee views. *Ann Card Anaesth*. 2016;19(suppl):S56–S72.

Vegas A, Meineri M. Core review: three-dimensional transesophageal echocardiography is a major advance for intraoperative clinical management of patients undergoing cardiac surgery: a core review. *Anesth Analg*. 2010;110: 1548–1573.

A.9. What are the echocardiographic and cardiac catheterization criteria for the four valvular lesions?

The TEE severity scales of the various valvular lesions are summarized in **Table 7.1**.

TABLE 7.1 Transesophageal Echocardiography Severity Scales of Valvular Lesions

	Severity Scale			
Measurement	**Normal**	**Mild**	**Moderate**	**Severe**
MS				
MVA (cm^2)	4.0–6.0	>1.5	1.0–1.5	<1.0
Mean pressure gradient (mmHg)	<2.0	<5.0	5.0–10.0	>10.0
AS				
AVA (cm^2)	2.5–3.5	>1.5	1.0–1.5	<1.0
Mean pressure gradient (mmHg)	<5	<20	20–40	>40
MR				
Jet area/LA area	0	<20%	20%–40%	>40%
Jet area (cm^2)	0	<4.0	4.0–10.0	>10.0
Pulmonary vein Doppler	S wave » D wave	S > D	S < D	Systolic flow reversal
AI				
Jet width/LVOT width	0	<25%	25%–60%	>60%

AI, aortic insufficiency; AS, aortic stenosis; AVA, aortic valve area; LA, left atrium; LVOT, left ventricular outflow tract; MR, mitral regurgitation; MS, mitral stenosis; MVA, mitral valve area.

Aortic Stenosis

Echocardiographic criteria for AS include 2D imaging demonstrating limited AV cusp motion, small orifice, and left

ventricular concentric hypertrophy (**Fig. 7.16**, **Video 7.1**). Doppler examination will reveal a turbulent, high-velocity jet across the AV, and color flow Doppler will demonstrate a turbulent, mosaic-appearing color map. The gradient across the AV measured at cardiac catheterization is different from that measured by echocardiography as mentioned previously. Quantification of the Doppler-derived AS pressure gradient relies on the modified Bernoulli equation.

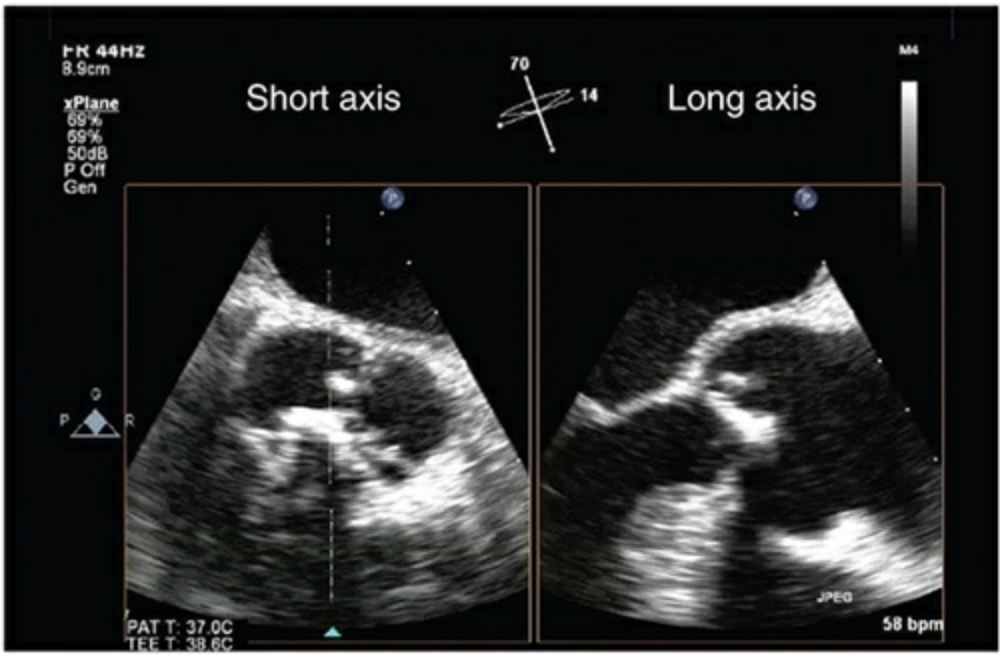


FIGURE 7.16. Transesophageal echocardiographic findings of moderate AS (midesophageal AV short-axis view [left] and long-axis view [right]). The AV cusps are calcified and demonstrate limited systolic excursion.

$$\text{Pressure gradient (mmHg)} = 4\ (\text{transaortic valve velocity, m/s})^2$$

Because flow is an important determinant of pressure gradients, both the catheterization and Doppler-derived values must be interpreted along with cardiac output. Calculations permit the determination of a valve area. Severe AS is present when the mean pressure gradient exceeds 40 mmHg or the valve area is less than 1.0 cm^2.

Aortic Insufficiency

Catheterization criteria for AI rely on the qualitative estimation of the regurgitation volume and an estimation of left ventricular size and ejection fraction. Similar quantification can be made from Doppler color echocardiography–derived data. A commonly used echocardiographic criterion compares the width of the regurgitant jet at the level of the AV to the width of the left ventricular outflow tract. A ratio of greater than 0.6 corresponds with severe AI (**Fig. 7.17**, **Video 7.2**). Another sign of severe AI can be observed in the spectral Doppler display of blood velocity in the descending thoracic aorta. The TEE probe is advanced to the level of the descending thoracic aorta and rotated to 90 degrees to obtain a long axis view. Under normal conditions, flow remains forward (to distal beds) during diastole. In severe AI, regurgitation of blood back into the ventricle decreases proximal pressure in the aorta, and thus, the spectral display of blood velocities will demonstrate a reversal of blood flow during diastole back toward the aortic root.

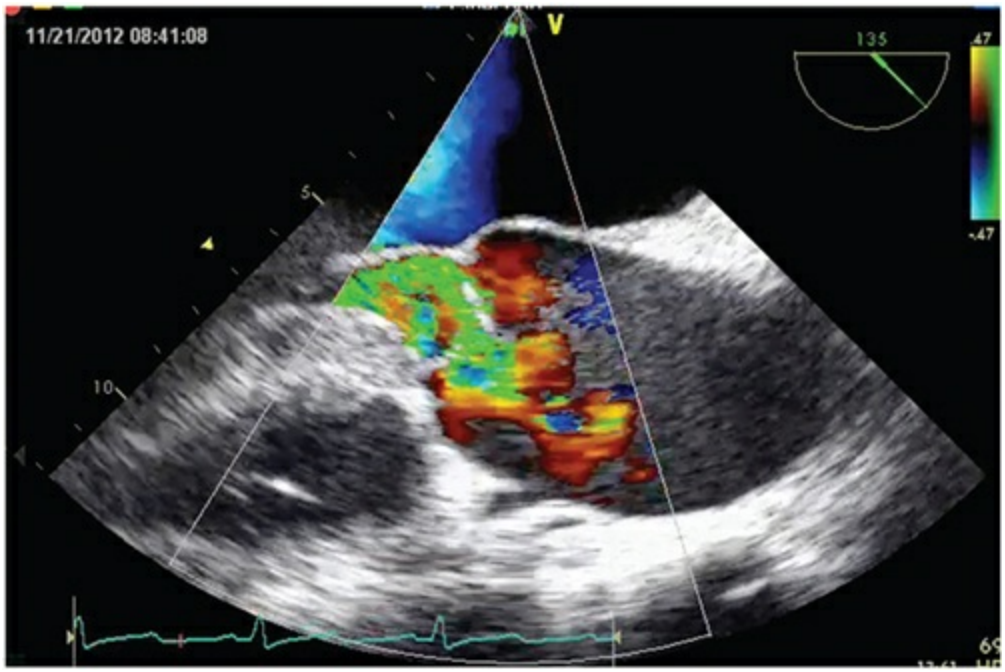


FIGURE 7.17. Transesophageal echocardiographic findings of moderate aortic regurgitation (midesophageal AV long-axis view; color flow Doppler).

Mitral Stenosis

The severity of MS can be obtained by the direct measurement of a diastolic gradient between the left atrium and ventricle at the time of cardiac catheterization. This requires a transatrial puncture, a procedure largely replaced by echocardiographic techniques. Echocardiographic diagnosis is based on gradient estimation by Doppler and by measuring the rate of decay in the pressure with the time spent in diastole (pressure halftime). The MV area (cm^2) can be derived from an empirical formula wherein the MV area equals 220 divided by this pressure halftime. Severe MS is present when the mean diastolic gradient exceeds 10 mmHg, corresponding to a valve area of less than 1.0 cm^2 (**Fig. 7.18**, **Video 7.3**).

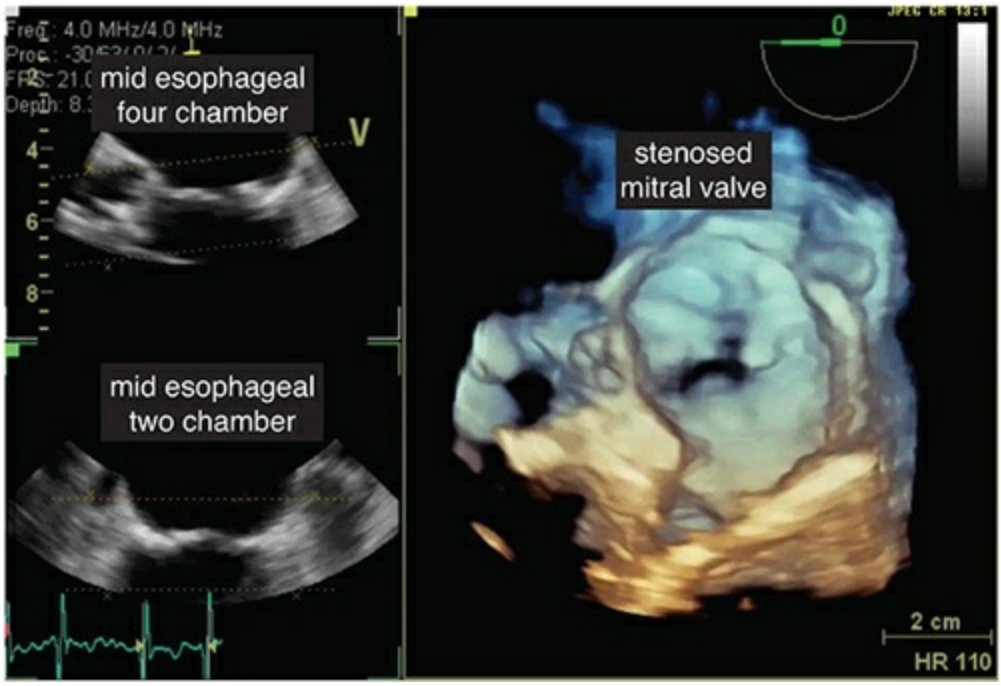


FIGURE 7.18. Transesophageal echocardiographic findings of severe MS with 2D view (left) and 3D view (right).

Mitral Regurgitation

In the presence of MR, ventriculography will demonstrate the reflux of dye from the LV into the left atrium. Severe MR is

diagnosed when dye refluxes into the pulmonary veins. Color Doppler echocardiography permits similar quantification. Estimation relies on an estimation of regurgitant jet area as compared with the left atrium area and through analysis of pulmonary venous flow profiles (**Fig. 7.19**, **Video 7.4**).

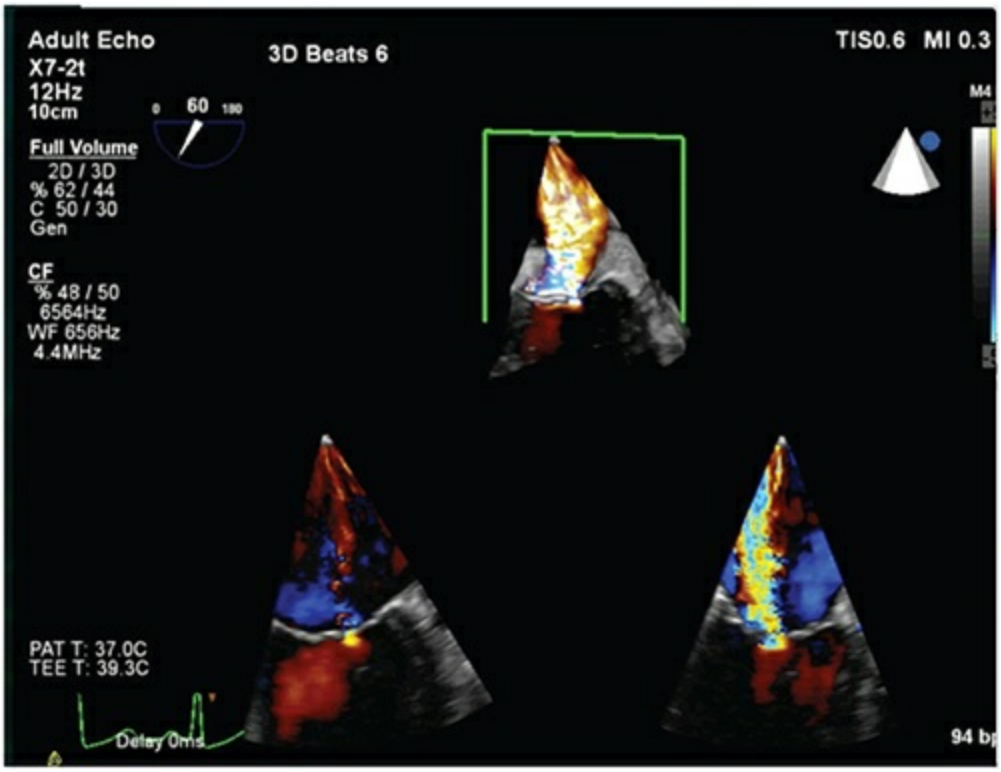


FIGURE 7.19. Transesophageal echocardiographic findings of moderate MR (color flow Doppler) with 3D view (top) and 2D view (bottom).

In every case, color Doppler echocardiography is often useful in identifying the cause of the valvular lesion, its extent of involvement within and around the valve, and the associated hemodynamic changes. Therefore, for many valvular lesions, it may be sufficient for the diagnosis. Catheterization, however, is often performed to assess the presence of concomitant coronary artery disease, especially in patients of advanced age.

Baumgartner H, Hung J, Bermejo J, et al. Recommendations on the echocardiographic assessment of aortic valve stenosis: a focused update from the European Association of Cardiovascular Imaging and the American

Society of Echocardiography. *J Am Soc Echocardiogr*. 2017;30(4):372–392.

Lancellotti P, Tribouilloy C, Hagendorff A, et al. Recommendations for the echocardiographic assessment of native valvular regurgitation: an executive summary from the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging*. 2013;14(7):611–644.

Quiñones M, Otto C, Stoddard M, et al. Recommendations for quantification of Doppler echocardiography: a report from the Doppler Quantification Task Force of the Nomenclature and Standards Committee of the American Society of Echocardiography. *J Am Soc Echocardiogr*. 2002;15:167–184.

B. Preoperative Evaluation and Preparation

B.1. What are the presenting signs and symptoms of the four valvular lesions listed previously?

See **Table 7.2**.

TABLE 7.2 The Signs and Symptoms for the Various Valvular Lesions

Lesion	Signs and Symptoms
AS	Angina, syncope, dyspnea/CHF
AI	
Chronic	Fatigability, dyspnea
Acute	Severe pulmonary edema, CHF
MS	Pulmonary congestion, AFib
MR	
Chronic	DOE, PND, AFib
Acute	Severe pulmonary edema, CHF

AFib, atrial fibrillation; AI, aortic insufficiency; AS, aortic stenosis; CHF, congestive heart failure; DOE, dyspnea on exertion; MR, mitral regurgitation; MS, mitral stenosis; PND, paroxysmal nocturnal dyspnea.

Aortic Stenosis

The triad of angina, syncope, and congestive heart failure represents the progression of symptoms associated with AS. These symptoms correlate directly with mortality; the 50% survival data for these symptoms are 5, 3, and 2 years from the onset of these symptoms, respectively. Angina results from both

increased demand for and a decrease in supply of coronary blood flow. Increased muscle mass from left ventricular hypertrophy and the high energy requirements to generate increased (high) systolic pressure combine to increase demands for coronary blood flow. In addition, insufficient supply secondary to decreased perfusion gradients and a decrease in coronary vasculature relative to the increased myocardial mass add up to diminish relative myocardial blood supply. Therefore, up to one-third of patients with AS can have angina in the absence of significant coronary artery disease.

Aortic Insufficiency

Patients with AI have variable clinical presentations based primarily on the rapidity with which the left ventricular volume overload develops. When the volume increase occurs gradually as in chronic AI, there is usually a long asymptomatic period. The onset of fatigue and dyspnea signals either reduced cardiac output or increased LVEDP, indicative of impairment of left ventricular contractile function. When AI occurs acutely, the ventricular compliance is unchanged; increased left ventricular diastolic volumes from regurgitant flow, therefore, lead to rapid rises in LVEDP and the clinical picture of congestive failure.

Mitral Stenosis

In MS, the slow and progressive obstruction to flow across the MV leads to gradual increase in left atrial pressure and volume. Symptoms of pulmonary congestion result from elevations in left atrial pressures and *not* from poor left ventricular systolic function. Atrial fibrillation develops secondary to atrial dilation.

Mitral Regurgitation

The time course for the development of MR determines the severity of the symptoms. When the volume of regurgitant flow from the LV to the left atrium increases gradually, the left

atrium compensates by gradual dilation. In contrast, the onset of acute MR can lead to rapid increases in left atrial pressures, severe pulmonary congestion, and congestive heart failure.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1077–1111.

Frogel J, Galusca D. Anesthetic considerations for patients with advanced valvular heart disease undergoing noncardiac surgery. *Anesthesiol Clin*. 2010;28:67–85.

Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2017;135(25):e1159–e1195.

Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;63(22):e57–e185.

B.2. What is the New York Heart Association classification of heart failure?

The New York Heart Association heart failure classification is based on the severity of symptoms, specifically dyspnea and fatigue. The classes are the following:

Class I—no symptoms (fatigue, palpitations, dyspnea, or angina) during ordinary physical activity; no limitations of physical activity

Class II—symptoms with ordinary activity but comfortable at rest; slight limitation of physical activity

Class III—symptoms with less than ordinary activity but comfortable at rest; marked limitation of physical activity

Class IV—symptoms at rest; inability to carry on any physical activity without discomfort

Raphael C, Briscoe C, Davies J, et al. Limitations of the New York Heart Association functional classification system and self-reported walking distances in chronic heart failure. *Heart*. 2007;93(4):476–482.

B.3. Discuss the role of premedication for patients with the four different valvular lesions.

The role of premedication is to allay the anxiety of the impending surgical procedure, thereby controlling the sympathetic outflow that may accompany the stress response. Acute changes in heart rate, venous return, and systemic resistance can have particularly profound effects on patients with valvular heart disease.

Patients with AS may benefit from premedication to prevent unnecessary increases in heart rate. Concern must be taken to ensure adequate venous return and preservation of sinus rhythm (see later discussion).

Patients with AI can similarly benefit from premedication because any increases in afterload, which may accompany sympathetic stimulation, can increase regurgitant volume. Drug doses should be adjusted based on the severity of debilitation and degree of systemic hypoperfusion.

Patients with MS should be premedicated with caution. Elevations in carbon dioxide resulting from opioid-induced hypoventilation can dramatically elevate pulmonary pressures, further compromising right ventricle output. Equally important, venodilation may excessively diminish filling pressures.

Patients with MR can respond similarly to those with MS, particularly when pulmonary hypertension is present. However, elevations in systemic pressure from stress can also compromise forward left ventricular output. Proper premedication can be delivered by careful dose selection and the provision of supplemental oxygen.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1077–1111.

B.4. How would you premedicate the patient with severe AS and MR?

Premedication of a patient with severe AS and MR must be approached with caution. The patient should receive supplemental oxygen. A light premedication could be provided with small doses of benzodiazepines by mouth. However, it would preferable to titrate in small intravenous doses of sedation (e.g., midazolam 0.5 mg) while the patient is closely monitored in the operating room or holding area with oxygen supplementation. It is important to remember that there may be significant delay in the onset of sedation secondary to pooling in the pulmonary circulation, and adequate waiting periods must be observed to avoid inadvertent overdose, which may herald respiratory depression, pulmonary hypertension, and systemic hypotension. In the elderly, use of benzodiazepines has been linked to postoperative delirium, which can be quite severe and difficult to treat increasing their length of stay and resource utilization.

C. Intraoperative Management

C.1. Outline the hemodynamic management goals for each of the four valvular lesions. What are the anesthetic goals with respect to heart rate and rhythm, preload, afterload, and contractility?

Table 7.3 summarizes the hemodynamic goals with respect to heart rate and rhythm, preload, afterload, and contractility.

TABLE 7.3 Hemodynamic Goals for the Various Valvular Lesions

		Hemodynamic Goals		
Lesions	**HR and Rhythm**	**Preload**	**Afterload**	**Contractility**
AS	60–70, sinus	Full	Maintain	—
AI	80–90	Maintain	Lower	May need support
MS	60–70	Full	—	—
MR	80–90, sinus if possible	Maintain	Lower	May need support

AI, aortic insufficiency; AS, aortic stenosis; HR, heart rate (beats per minute); MR, mitral regurgitation; MS, mitral stenosis.

Aortic Stenosis

Patients with AS depend on left ventricular filling occurring through a well-timed atrial contraction. Similarly, left ventricular hypertrophy renders the LV stiff, and adequate preload is required. The stenotic AV is a fixed lesion that will not respond to pharmacologic intervention. Reducing vascular tone will only lower diastolic coronary perfusion gradients and should be avoided. Patients with AS experiencing angina may require the administration of an α-agonist such as phenylephrine rather than nitroglycerin to increase coronary perfusion pressure.

Aortic Insufficiency

The severity of AI is determined by the size of the regurgitant orifice, the diastolic pressure gradient between the aorta and LV, and the duration of diastole. Elevated heart rates decrease the time spent in diastole and can lead to a decrease in heart size. Afterload reduction can lessen the regurgitant driving forces, but therapeutic maneuvers to accomplish this may be limited by resulting systemic hypotension.

Mitral Stenosis

Slower heart rates permit adequate time for transfer of blood from the left atrium to the LV across the stenotic MV to occur. In addition, the pressure gradient across the MV is also reduced, thereby lowering left atrial pressure and diminishing pulmonary congestion. Patients with MS can swiftly deteriorate in the setting of rapid heart rates. The decreased filling time exacerbates the marked elevation of left atrial pressures, and pulmonary edema can rapidly ensue. Whereas left ventricular contractility is generally preserved in MS, use of β-blockade does result in decreased RV contractility, which in the setting of

pulmonary hypertension can further compromise the cardiac output and systemic blood pressure. However, the loss in RV contractility is more than offset by the beneficial effects of the reduction of heart rate. Because there is some variability in the individual response, the use of short-acting β-blockers, such as esmolol, is prudent because an adverse response could be catastrophic.

Mitral Regurgitation

Patients with MR can rapidly deteriorate with marked increases in systemic blood pressure, so afterload reduction is recommended. As with AI, slightly increased heart rates (80 to 90 beats per minute) should result in smaller left ventricular volumes. However, tachycardia should be avoided in patients with ischemic (functional) MR.

Frogel J, Galusca D. Anesthetic considerations for patients with advanced valvular heart disease undergoing noncardiac surgery. *Anesthesiol Clin*. 2010;28:67–85.

C.2. What are the hemodynamic goals for this patient with the combination of severe AS and MR?

In this patient with combined AS and MR, therapy benefiting AS may exacerbate the severity of the MR. A good rule of thumb is to prioritize the management based on the character of the paramount symptoms. Patients with AS and MR who present with syncope or angina are best managed for their AS, whereas patients with dyspnea and pulmonary edema are best managed for their congestive symptoms. Preoperative echo and ECG findings can also be used to determine the predominant lesion. It is prudent to maintain the patient's own usual hemodynamics. Early aggressive intervention is the key to these combined lesions. A lower margin for error usually exists because minor hemodynamic aberrations can rapidly lead to cardiac collapse. TEE evaluation of left ventricular performance can be helpful in

separating pulmonary congestion secondary to left heart failure from that due to decreased diastolic left ventricular compliance from AS.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1077–1111.

Frogel J, Galusca D. Anesthetic considerations for patients with advanced valvular heart disease undergoing noncardiac surgery. *Anesthesiol Clin*. 2010;28:67–85.

Silbiger, JJ. Pathophysiology and echocardiographic diagnosis of left ventricular diastolic dysfunction. *J Am Soc Echocardiogr*. 2019;32:216–232.

C.3. How would you monitor this patient with severe AS and MR?

In addition to the standard American Society of Anesthesiologists–recommended monitors, the patient should have a radial artery and a pulmonary artery catheter. Following induction of anesthesia and endotracheal intubation, a TEE probe would be inserted to confirm the valvular pathology and to assess ventricular function. Following valve replacement, the TEE probe would be used to check for adequacy of valvular function and the absence of paravalvular leaks and to assess postbypass ventricular function.

American Society of Anesthesiologists and Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. Practice guidelines for perioperative transesophageal echocardiography. An updated report by the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. *Anesthesiology*. 2010;112(5):1084–1096.

C.4. Should the patient have a pulmonary artery catheter placed before induction?

Volume status may be particularly difficult to assess in patients with valvular heart disease and yet of critical importance in the management of these patients. Patients with stenotic lesions depend on adequate filling pressures for diastolic filling of the

ventricle. Patients with the volume overload lesions of AI and MR can benefit from the careful reductions in pulmonary pressure guided by the simultaneous assessment of cardiac performance. In these capacities, the pulmonary artery catheter is useful. Patients with current hemodynamic stability, without severe respiratory distress, can be safely anesthetized before placement of the pulmonary artery catheter. Overall, there is no evidence that use of the pulmonary artery catheter improves outcome in the setting of surgery.

American Society of Anesthesiologists and Society of Cardiovascular Anesthesiologists Task Force on Pulmonary Artery Catheterization. Practice guidelines for pulmonary artery catheterization: an updated report by the American Society of Anesthesiologists Task Force on Pulmonary Artery Catheterization. *Anesthesiology*. 2003;99(4):988–1014.

C.5. Is a pulmonary artery catheter with pacing capabilities indicated?

Patients with AS can become severely compromised with the loss of atrial kick or the presence of slow junctional rhythms. Patients with AI or MR can experience left ventricular dilation in the setting of slow heart rates. In such cases, a pulmonary artery catheter with atrial and ventricular pacing capacity can be useful. In patients with intact conduction systems, rate manipulation can often be achieved pharmacologically. Transesophageal atrial pacing is another option. Transthoracic pacing elicits a ventricular response only and does not permit atrial stimulation. Transcutaneous pacing is indicated when the ability to rapidly open the pericardium and obtain epicardial pacing is limited. This occurs in the setting of reoperations or in patients with a history of inflammatory pericardial disease. Pacing will be limited to capture of the ventricle alone. The loss of atrial contraction can lead to underfilling and hemodynamic compromise in patients dependent on the added volume from atrial systole. One of the other pacing modalities is best in this

setting.

Raiten JM, Ghadimi K. Atrial fibrillation after cardiac surgery: clinical update on mechanisms and prophylactic strategies. *J Cardiothorac Vasc Anesth*. 2015;29(3):806–816.

C.6. What anesthetic technique would you employ? Why?

For the patient undergoing CPB and AV replacement, general anesthesia with endotracheal intubation is the obvious choice. Both narcotics and inhalation anesthetics can be safely administered. The modern anesthetic technique for cardiac surgery has focused on the use of techniques permitting earlier tracheal extubation. Anesthetic combinations, using smaller total narcotic doses, inhalation anesthetics, and short-acting intravenous sedatives such as propofol, are gaining popularity. For uncomplicated valve replacements with good ventricular function, the advantages of early tracheal extubation can be safely achieved. In complicated cases with longer bypass periods, poor ventricular function, or postbypass bleeding, the hemodynamic stability of a high-dose narcotic technique may be advantageous.

Barry AE, Chaney MA, London MJ. Anesthetic management during cardiopulmonary bypass: a systematic review. *Anesth Analg*. 2015;120(4):749–769.

De Hert SG, Van der Linden PJ, Cromheecke S, et al. Choice of primary anesthetic regimen can influence intensive care unit length of stay after coronary surgery with cardiopulmonary bypass. *Anesthesiology*. 2004;101(1):9–20.

Fleming IO, Garratt C, Guha R, et al. Aggregation of marginal gains in cardiac surgery: feasibility of a perioperative enhanced recovery in cardiac surgical patients. *J Cardiothorac Vasc Anesth*. 2016;30(3):665–670.

C.7. What muscle relaxant would you use for this patient?

The use of high-dose narcotics results in bradycardia secondary to the vagotonic actions. Although slowing of heart rates usually benefits the patient with angina, it may have severe

consequences in patients with valvular heart disease. If a high-dose narcotic technique is employed, muscle relaxants, such as pancuronium, may be chosen to beneficially counteract the resultant bradycardia via histamine-mediated tachycardia. With a limited narcotic technique, hemodynamically "neutral" relaxants such as vecuronium, rocuronium, or cisatracurium are now commonly used with attention to redosing at key points in the procedure.

It is important to choose a combination of agents that will promote hemodynamic stability in a particular patient with his or her unique hemodynamic presentation. In this patient, the judicious use of any muscle relaxant would be indicated.

Hemmerling TM, Russo G, Bracco D. Neuromuscular blockade in cardiac surgery: an update for clinicians. *Ann Card Anaesth*. 2008;11(2):80–90.

Roy M, Morissette N. Postoperative awake paralysis in the intensive care unit after cardiac surgery due to residual neuromuscular blockade: a case report and prospective observational study. *Can J Anaesth*. 2016;63(6):725–730.

C.8. What are the usual TEE findings in a patient with AS or MR? How do you grade the severity of AS by TEE? How do you quantify the severity of MR? What is the impact of AS on the severity of MR?

The *echocardiographic* severity of AS is usually determined by AV area and transaortic valve pressure gradient. Normal AV area is 2.5 to 3.5 cm^2. Moderate stenosis is when the AV area is within the range of 1.0 to 1.5 cm^2 and severe AS when the AV area is less than 1.0 cm^2. A patient with a large mean pressure gradient (usually more than 40 mmHg) in the absence of excessively high cardiac output is usually considered to have severe AS as well. In the setting of low cardiac outputs, the pressure gradient may not be as great, and additional investigation may be necessary. The *clinical* severity of AS is determined by a combination of echocardiographic and clinical

factors. Even a patient with less than severely stenosed AV may be considered to have severe AS if his or her daily activities of life are reduced, he or she experiences symptoms, or left ventricular systolic dysfunction is present.

MR is graded by the amount of blood regurgitated backward into the left atrium during systole. Doppler color flow permits the estimation of this flow. Common methods for MR quantification include calculation of the area of the regurgitant orifice (effective orifice area) or the width of the MR jet (vena contracta) and by analysis of pulmonary vein flow profiles. It is important to remember that the amount of regurgitant blood flow in the setting of MR is determined by the amount of time spent in systole, the size of the MV defect, and the pressure gradient across the defect. Therefore, MR severity by Doppler color flow is load dependent. Lower systemic pressure or relative hypovolemia due to the anesthetic state can often mask more severe degrees of MR, which are found in the awake state.

Left ventricular pressures are increased in the setting of AS. Therefore, the gradient across the MV is increased often leading to more severe MR. Following replacement of the stenotic AV and elimination of the obstruction to systolic flow, left ventricular pressures are markedly reduced. In cases of functional MR without major structural defects in the MV apparatus, the MR will be less severe following replacement of AV.

Mahmood F, Matyal R. A quantitative approach to the intraoperative echocardiographic assessment of the mitral valve for repair. *Anesth Analg*. 2015;121(1):34–58.

Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;63(22):e57–e185.

C.9. What special considerations particular to

cardiopulmonary bypass (CPB) operations do you have for each of the four lesions? Focus on these concerns with respect to the induction and prebypass, bypass, and postbypass periods.

Aortic Stenosis

Critical to the management of a patient with AS is the avoidance of hypotension. Low blood pressure can initiate a cascade of events leading to cardiac arrest. Hypotension decreases the gradient for coronary perfusion with resultant ischemia. Ischemia leads to diminished cardiac output and decreased blood pressure further compromising coronary perfusion. The occurrence of cardiac arrest in a patient with AS is particularly catastrophic because closed-chest cardiac massage will provide little gradient for blood flow across a stenotic AV.

Patients with AS are particularly dependent on their atrial kick for adequate ventricular filling volume and can rapidly become hypotensive and ischemic following the onset of supraventricular tachycardia or atrial fibrillation. These rhythms are not uncommon during atrial cannulation. Therefore, it is of particular importance that every preparation for the initiation of CPB be made before atrial manipulation. The increased muscle mass of ventricular hypertrophy can be more difficult to adequately protect with cardioplegia. Careful attention to surface cooling, myocardial temperature measurement, and the use of retrograde cardioplegia can be helpful. Following AV replacement, hypertension from left ventricular output now unopposed by any valvular lesion can result in stress on suture lines and excessive bleeding. It is important to remember that the compliance of the LV is unchanged by surgery and still critically dependent on adequate preload and sinus rhythm. Hypertension is best managed with an afterload-reducing agent, such as nicardipine, versus a preload-reducing agent, such as

nitroglycerin.

Aortic Insufficiency

Patients undergoing AV replacement for AI can often present difficult management decisions. The usual treatment measures for hypotension (α-agonist) may have deleterious effects by increasing regurgitant volume. The use of combined α- and β-agonists (ephedrine, epinephrine, or infusions of dopamine or dobutamine) may be required. Although it would serve to lessen regurgitant volume, afterload reduction is beneficial in only a subset of patients with AI. Those patients with elevated LVEDP, reduced ejection fraction, diminished cardiac output, and systemic hypertension usually benefit from afterload reduction. In contrast, those patients without the previously mentioned constellation may experience a decrease in forward cardiac output secondary to diminished preload from reduced venous return. Systemic hypotension usually limits the utility in the acute setting. The presence of AI makes initiation of CPB a critical period. Periods of bradycardia or ventricular fibrillation can lead to rapid volume overload of the LV through the incompetent AV. Pacing, electrical defibrillation, and/or cross-clamping should be performed to prevent ventricular distention. Similarly, myocardial protection is compromised by AI. Generation of adequate root pressures is usually not obtainable; hence, delivery of cardioplegia requires aortotomy and cannulation of the coronary ostia. Use of retrograde cardioplegia is advantageous. Following AV replacement, the ventricle no longer has the lower pressure/impedance outflow afforded by the low aortic diastolic pressure. Inotropic support is often required. As with AS, the presence of an aortic suture line necessitates rapid response to hypertension to avoid bleeding and dissection.

Mitral Stenosis

Patients undergoing MV replacement for MS are particularly challenging. Marked elevations in pulmonary vascular resistance can be present with associated right-sided heart failure. Stasis in the left atrium necessitates careful echocardiographic examination for the presence of atrial thrombi. Manipulation of the heart before cross-clamping should be avoided. Following replacement, the chronically underfilled, underworked LV may be unable to handle the new volume load. Inotropic support is often required for RV failure and occasionally to improve left ventricular function. Afterload reduction and improved systemic perfusion using an IABP may be beneficial.

Mitral Regurgitation

Similarly, patients with MR may have pulmonary hypertension and right-sided heart failure. In contrast to AI, almost all patients with MR can be greatly benefited by afterload reduction, both pharmacologically and through an IABP. Diminution of left ventricular systolic pressure through afterload reduction decreases the pressure gradient from the LV to the left atrium during systole, with a resultant decrease in regurgitant volume.

Prebypass assessment can be misleading. Preserved ejection fractions and elevated stroke volumes may mask marked left ventricular systolic dysfunction. It should be remembered that much of the left ventricular volume is ejected into the low-pressure/impedance outflow path of the left atrium. This route is no longer available after valve replacement. Following MV replacement, dysfunctional ventricles may be unable to provide adequate forward flow into the systemic circuit with its elevated vascular resistance, which usually necessitates the use of inotropic support.

Patients previously in atrial fibrillation without marked atrial enlargement often revert to or can be converted to sinus rhythm following valve replacement. When the diameter of the atrium is

more than 5 cm, the likelihood of maintaining sinus rhythm dramatically decreases.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1077–1111.

C.10. The patient cannot be weaned from CPB following an AV replacement and MV replacement. What are the possible causes?

The adequacy of myocardial preservation should be considered. Left ventricular hypertrophy without or with accompanying coronary artery disease increases myocardial oxygen demands. The prolonged cross-clamp time necessitated by dual valve replacement can lead to inadequate and/or nonhomogeneous myocardial protection. In addition, there may be residual effects from the cardioplegia solution. Therefore, some degree of postbypass left ventricular dysfunction can be anticipated. Inotropic support may be required. It is important to remember that although the obstruction to left ventricular ejection is acutely relieved by replacement of the stenotic valve, left ventricular compliance is largely unchanged. Adequate preload still depends on sinus rhythm and sufficient left ventricular filling pressures (pulmonary artery occlusion pressure [PAOP] or LVEDP). Elevations in pulmonary vascular resistance may render estimation of left atrial pressure through the pulmonary artery catheter inaccurate. In this setting, placement of a left atrial catheter is indicated. TEE may prove invaluable in identifying surgically correctable causes for inability to wean from CPB. Evaluation of left ventricular filling and contractility can help resolve the situation of low cardiac output and high filling pressures. A small underfilled LV with hyperdynamic contractility and a dilated, overfilled, hypokinetic LV can both give the same hemodynamic parameters but obviously require different pharmacologic interventions. Abnormal valve seating

may compromise flow into the coronary ostia and return to bypass with valve repositioning or coronary artery bypass grafting may be indicated. Similarly, paravalvular leaks or aortic dissections can be readily identified. Iatrogenic injury to the circumflex artery, although rare, can occur during MV annuloplasty or replacement. The course of the circumflex artery along the posterior path of the MV annulus makes it a potential target for errant valve stitches. New regional wall motion abnormalities in the inferior-lateral territory may help make this unusual diagnosis or influence the decision to pursue diagnostic testing, such as emergent cardiac catheterization. The coronary sinus can also be damaged during MV repair and replacement because the suture line is placed in the lateral mitral annulus. TEE may demonstrate abnormal echodensities in the area of the atrioventricular groove, and color flow Doppler can demonstrate high-velocity flow jets from the chambers to the sinus.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1077–1111.

Ender J, Selbach M, Borger MA, et al. Echocardiographic identification of iatrogenic injury of the circumflex artery during minimally invasive mitral valve repair. *Ann Thorac Surg*. 2010;89:1866–1872.

C.11. How would you diagnose right-sided heart failure and pulmonary hypertension? How would you treat it?

Right-sided heart failure is diagnosed by elevations in right-sided filling pressures, specifically central venous pressure. Careful examination is required to rule out tricuspid insufficiency as the cause of the central venous pressure elevation. A high central venous pressure indicates the inability of the right heart to adequately propel the venous return volume into the pulmonary circulation. Elevation in pulmonary artery pressures is indicative of pulmonary hypertension. The

combination of high central venous pressure and high pulmonary artery pressures indicates severe right-sided heart failure. This scenario can be difficult to manage. Attempts to elevate systemic perfusion pressure with α-agonists can worsen pulmonary hypertension. Administration of vasodilators to lower pulmonary pressures results in systemic hypotension. In this setting, it is often prudent to return to CPB, relieve ventricular distention, and improve myocardial perfusion. During this "rest period," adjustments in inotropic therapy, ventilation, and cardiac rhythm can be instituted. Optimization of acid–base status and hemoglobin concentration should also be performed. Separation from bypass can then be reattempted.

Typical inotropic agents effective in this setting are those with high degrees of β-adrenergic potency and potent vasodilation in the pulmonary vasculature. Commonly employed agents include dobutamine, epinephrine, prostaglandin E_1, and the phosphodiesterase-III (PDE-III) inhibitors amrinone and milrinone. It is not uncommon to require the administration of α-agonists to counteract the systemic vasodilating effects of prostaglandin E_1 and the PDE-III inhibitors. Some selective pulmonary vasodilating action and systemic vasoconstricting effects can often be achieved by administering pulmonary vasodilating agents such as prostaglandin E_1 through the right-sided access (central venous pressure or pulmonary artery catheter) and infusing the α-agonists through the left arterial line, thereby minimizing vasoconstriction of the pulmonary arterial bed. Vasopressin can also be used for systemic vasoconstriction and has little effect on the pulmonary vasculature.

Nitric oxide is a potent, inhaled pulmonary vasodilator. Its half-life in the systemic circulation is extremely short, permitting its administration to the pulmonary vasculature with

minimal systemic hypotensive effects. Nitric oxide can selectively and effectively dilate the pulmonary vasculature. The exact method of delivery, scavenging of waste gases, and high cost remain as obstacles to its clinical application.

Galiè N, Humbert M, Vachiery JL, et al. 2015 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension: the Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). *Eur Heart J*. 2016;37(1):67–119.

Haddad F, Elmi-Sarabi M, Fader E, et al. Pearls and pitfalls in managing right heart failure in cardiac surgery. *Curr Opin Anaesthesiol*. 2016;29(1):68–79.

Savage RM, Aronson S, Shernan SK, eds. *Comprehensive Textbook of Intraoperative Transesophageal Echocardiography*. 2nd ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2011:156–167.

C.12. How does an intra-aortic balloon pump (IABP) work to benefit the failing heart?

An IABP is a catheter with a large balloon (40 to 60 mL) at its tip. It is positioned in the thoracic aorta distal to the left subclavian artery origin and proximal to the takeoff of the renal vessels. It is timed to inflate during diastole to increase diastolic perfusion pressure to the coronary arteries, great vessels, and major abdominal organs and to deflate just before systole, creating a void in volume within the aorta and thus a low pressure with a resultant decrease in afterload. The decreased afterload increases stroke volume and hence forward cardiac output. It is a unique modality that can improve coronary perfusion pressures while reducing myocardial oxygen demand.

Baskett RJ, Ghali WA, Maitland A, et al. The intraaortic balloon pump in cardiac surgery. *Ann Thorac Surg*. 2002;74:1276–1287.

Kucuker A, Cetin L, Kucuker SA, et al. Single-centre experience with perioperative use of intraaortic balloon pump in cardiac surgery. *Heart Lung Circ*. 2014;23(5):475–481.

C.13. What role does the IABP have in this setting?

An IABP may be useful because unlike any pharmacologic maneuver, it is capable of increasing mean pressure during diastole critical for coronary perfusion while lowering afterload to systolic left ventricular ejection. Myocardial dysfunction secondary to inadequate protection during bypass can be reduced by decreased afterload and augmentation of diastolic pressures through IABP counterpulsation. Studies have shown superior survival among patients with isolated cardiac artery bypass graft (CABG) treated with IABP compared with patients undergoing non-CABG cardiac surgeries. The IABP can only aid patients in whom ventricular function can recover in a relatively short time. Outside of this population, ventricular assist devices may be more appropriate.

Baskett RJ, Ghali WA, Maitland A, et al. The intraaortic balloon pump in cardiac surgery. *Ann Thorac Surg*. 2002;74:1276–1287.

C.14. What role does TEE play in the placement, timing, and demonstration of efficacy of an IABP?

The thoracic aorta and aortic arch can be clearly imaged by TEE. Imaging of the takeoff of the left subclavian artery facilitates optimal positioning of the IABP. In addition, before insertion, the aorta can be evaluated for dissection or the presence of severe atheromatous disease; both are contraindications to IABP insertion. TEE can demonstrate the efficacy of an IABP by showing enhanced ventricular emptying during systole and filling during diastole.

Klopman MA, Chen EP, Sniecinski RM. Positioning an intraaortic balloon pump using intraoperative transesophageal echocardiogram guidance. *Anesth Analg*. 2011;113(1):40–43.

C.15. How would you properly time the IABP cycle?

Inflation should occur just following the dicrotic notch and

deflation before the upstroke in the aortic pressure curve. Augmentation in pressures during diastole and mean pressures should occur. Diastolic pressure (the lowest pressure in the cardiac cycle) should in fact fall. Peak pressure generated by the left ventricular or systolic pressure should fall while the balloon-generated pressure during ventricular diastole (augmented pressure) should increase.

Baskett RJ, Ghali WA, Maitland A, et al. The intraaortic balloon pump in cardiac surgery. *Ann Thorac Surg*. 2002;74:1276–1287.

Cheung AT, Savino JS, Weiss SJ. Beat-to-beat augmentation of left ventricular function by intraaortic counterpulsation. *Anesthesiology*. 1996;84:545–554.

C.16. What are the contraindications to the use of an IABP?

The most common contraindications are severe AI and severe aortic disease, atheromatous, aneurysmal, or a dissection. Although often listed as absolute contraindications, there are reports of the effective use of the IABP in these settings. TEE can be helpful in evaluating the effect of an IABP on overall ventricular function. End-systolic areas should decrease, and end-diastolic areas should at least not increase but may decrease as well.

White JM, Ruygrok PN. Intra-aortic balloon counterpulsation in contemporary practice—where are we? *Heart Lung Circ*. 2015;24(4):335–341.

C.17. What is the role for ventricular assist devices?

Ventricular assist devices are used in the management of chronic heart failure after exhausting medical therapy. These devices can be used as a bridge to transplantation or as a destination therapy in those who do not qualify for transplantation. The short-term use of ventricular assist devices includes patients with refractory heart failure in the immediate postoperative setting. Historically, the operative mortality associated with postcardiotomy assist

devices was very high. Newer machines utilize smaller cannulas and have smaller, more efficient pumps. The magnetically suspended centrifugal pumps are associated with minimal trauma to red blood cells or pump failures. The use of these devices is rapidly expanding, and early indications show a decreased mortality for patients experiencing postcardiotomy shock with recoverable myocardium. Ventricular assist devices are used for right, left, and biventricular support.

Bhama JK, Kormos RL, Toyoda Y, et al. Clinical experience using the Levitronix Centrimag System for temporary right ventricular mechanical circulatory support. *J Heart Lung Transpl*. 2009;28:971–976.

De Robertis F, Birks EJ, Rogers P, et al. Clinical performance with the Levitronix Centrimag short-term ventricular assist device. *J Heart Lung Transplant*. 2006;25:181–186.

Ziemba EA, John R. Mechanical circulatory support for bridge to decision: which device and when to decide. *J Card Surg*. 2010;25(4):425–433.

D. Postoperative Management

D.1. In the intensive care unit (ICU) 4 hours later, the patient became hypotensive with a low cardiac output. How could you distinguish between cardiac tamponade and pump failure? How would the TEE images differ?

The differentiation between cardiac tamponade and primary pump failure in the immediate postbypass-ICU setting can be difficult. Elevations in filling pressures, systemic hypotension, and low cardiac output are consistent with both diagnoses. The classic teaching of equalization of cardiac pressures seen in a "fluid" tamponade may not be present because areas of focal compression from clot can markedly reduce filling of only one chamber in the absence of an intact pericardium. Echocardiography can be beneficial in this setting by permitting

visualization of chamber volume and function. The TEE approach has particular advantage over TTE in the postoperative setting in which the usual transthoracic window may be obscured by dressings and drainage tubing. Focal compression of the cardiac chambers from a clot or pericardial effusion can readily be distinguished from a volume-overloaded, failing heart with poor myocardial contractility. When the diagnosis is not clear, however, surgical reexploration may be indicated. (See Chapter 12, Cardiac Tamponade.)

Flynn BC, Spellman J, Bodian C, et al. Inadequate visualization and reporting of ventricular function from transthoracic echocardiography after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2010;24:280–284.

Leiva EH, Carreño M, Bucheli FR, et al. Factors associated with delayed cardiac tamponade after cardiac surgery. *Ann Card Anaesth*. 2018;21(2):158–166.

Society of Thoracic Surgeons Task Force on Resuscitation After Cardiac Surgery. The Society of Thoracic Surgeons expert consensus for the resuscitation of patients who arrest after cardiac surgery. *Ann Thorac Surg*. 2017;103(3):1005–1020.

D.2. Would you extubate this patient early in the ICU? Why?

No. This patient has undergone a double valve replacement. In this more complex procedure, coagulopathy and postoperative bleeding, hypothermia from incomplete and nonuniform rewarming, and pulmonary hypertension are not uncommon occurrences in the immediate postoperative period. Sedation, paralysis, and mechanical ventilation can reduce the oxygen requirements during this early phase of recovery, minimize pulmonary hypertension secondary to hypercarbia, and permit reestablishment of core temperatures.

Cheng DC. Pro: early extubation after cardiac surgery decreases intensive care unit stay and cost. *J Cardiothorac Vasc Anesth*. 1995;9:460–464.

Guenther CR. Con: early extubation after cardiac surgery decreases intensive

care unit stay and cost. *J Cardiothorac Vasc Anesth*. 1995;9:465–467.

D.3. What are the advantages and disadvantages of early extubation?

The advantages of early extubation are both medical and financial. Early extubation can lessen the adverse sequelae from prolonged endotracheal intubation, including epithelial damage, decreased ciliary motility, and diminished mobilization of secretions. Positive pressure ventilation can have adverse effects on venous return. Nevertheless, the overwhelming drive toward early extubation is cost and patient comfort. Early extubation can decrease cost by decreasing ICU staff requirements, decreasing the cost of sedatives, lessening the duration of ICU stays, and improving operating room use by lessening cancellation of cases secondary to blocked ICU beds.

The potential advantages of early extubation, both financial and physiologic, must be weighed against the potential disadvantages of early extubation. The potential for respiratory compromise leading to hypoxemia, hypercarbia, ischemia, and the potential for infarction and neurologic injury is real. Any savings realized from early extubation can be rapidly lost by one adverse event. Success relies on careful integration of all players in the care of the patient undergoing cardiac surgery, from the management of intraoperative anesthetic techniques to the organization of the ICU and staff and the provision of postoperative analgesia. Equally important to the success of an early extubation program is appropriate patient selection.

Fitch ZW, Debesa O, Ohkuma R, et al. A protocol-driven approach to early extubation after heart surgery. *J Thorac Cardiovasc Surg*. 2014;147(4):1344–1350.

Richey M, Mann A, He J, et al. Implementation of an early extubation protocol in cardiac surgical patients decreased ventilator time but not intensive care unit of hospital length of stay. *J Cardiothorac Vasc Anesth*. 2018;32(2):739–744.

Subramaniam K, DeAndrade DS, Mandell DR, et al. Predictors of operating room extubation in adult cardiac surgery. 2017;154(5):1656–1665.

E. Alternative Treatments

E.1. What are the percutaneous options for MV repair?

In 1991, a surgical correction of MR was described using a technique of suturing the middle portions of the two mitral leaflets together. The resultant double orifice valve is an adequate solution for many MV lesions. Based on this principle, a percutaneous treatment for MR has emerged. The safety and efficacy of various transcatheter MVs for mitral replacement are currently underway.

Sherlock KE, Muthuswamy G, Basu R, et al. The Alfieri stitch: the advantages for mitral valve repair in difficult circumstances. *J Card Surg*. 2011;26(5):475–477.

E.2. How is percutaneous MV repair performed?

The MitraClip is a small, polyester fabric-covered cobalt-chromium clip that is applied to the mitral leaflets to mimic the surgical procedure described earlier. The device is delivered percutaneously via a transfemoral venous approach and a transseptal puncture, and favorable results are associated with a reduction of MR to less than moderate. General anesthesia is typically used.

Buzzatti N, Taramasso M, Latib A, et al. Transcatheter mitral repair and replacement: state of the art and future directions. *J Heart Valve Dis*. 2014;23(4):492–505.

Feldman T, Kar S, Elmariah S, et al. Randomized comparison of percutaneous repair and surgery for mitral regurgitation: 5-year results of EVEREST II. *J Am Coll Cardiol*. 2015;66(25):2844–2854.

Guarracino F, Baldassarri R, Ferro B, et al. Transesophageal echocardiography during MitraClip® procedure. *Anesth Analg*. 2014;118(6):1188–1196.

E.3. What are the percutaneous options for AV repair and replacement?

Aortic balloon valvuloplasty has been a nonsurgical option since the 1980s. Although it is far less invasive than surgery, high complication rates and in-hospital mortality have reserved this treatment for a select population. In addition, high restenosis rates make this a short-lived solution. Surgical valve replacement was previously the treatment of choice for severe AS. Alternative treatment options are now becoming available to patients at high and intermediate risk for surgery.

Arora S, Misenheimer JA, Ramaraj R. Transcatheter aortic valve replacement: comprehensive review and present status. *Tex Heart Inst J*. 2017;44(1):29–38.

E.4. How is percutaneous AV replacement performed?

Currently, two prosthetic devices are used in the United States. The percutaneous devices are bioprosthetic valves mounted in nitinol stents. The valves may be delivered by retrograde (femoral artery, axillary artery, or directly in the aorta) or antegrade (transapical) approaches. After balloon valvuloplasty, the valve stent is deployed. Rapid ventricular pacing is used to decrease cardiac translation and minimize ejection pressure during deployment. TEE and fluoroscopic guidance are used. The most frequent complications are cerebral embolism, coronary obstruction, conduction abnormalities, and paravalvular leaks.

Arora S, Misenheimer JA, Ramaraj R. Transcatheter aortic valve replacement: comprehensive review and present status. *Tex Heart Inst J*. 2017;44(1):29–38.

E.5. What anesthetic techniques and monitors are used?

Intravenous sedation with local infiltration can be used in carefully selected patients. Those patients with a nonreassuring airway, severe gastroesophageal reflux disease (GERD), anxiety, low ejection fraction, and pulmonary hypertension are

not typically good candidates for sedation. General anesthesia facilitates simultaneous TEE examination and access to alternate approaches if surgical challenges are encountered. Large-bore central venous access is necessary in the event of vascular injury or to administer vasoactive medications. Pulmonary artery catheters may be indicated in patients with RV dysfunction with or without pulmonary hypertension and in those with reduced ejection fraction. In sedation cases, TTE examination is performed for evaluation at the conclusion of the procedure. Radial artery catheters are placed before induction for continuous monitoring and for arterial blood gases analysis.

Neuberger PJ, Patel PA. Anesthetic techniques in transcatheter aortic valve replacement and the evolving role of the anesthesiologist. *J Cardiothorac Vasc Anesth*. 2017;31(6):2175–2182.

E.6. What is minimally invasive cardiac valve surgery?

The Society of Thoracic Surgeons database considers "any procedure not performed with a full sternotomy and CPB support" a minimally invasive procedure. The practical applications of "mini-valve surgery" include partial sternotomy, thoracotomy, and video-assisted and robot-assisted procedures. The downside to minimally invasive approaches includes difficulty converting to a sternotomy in the case of cannula displacement or aortic dissection and complications of femoral artery cannulation (including arterial dissection, infection, and hematoma). The anesthetic management varies from standard sternotomy cases, including single-lung ventilation for thoracotomy approaches and transjugular coronary sinus catheters to provide retrograde cardioplegia. Intraoperative TEE is especially critical in these cases to monitor for cardiac distention, removal of air, and cannula placement. There is clearly a significant learning curve to provide an equivalent surgical outcome with a "mini" versus traditional strategy. In

successful procedures, patients enjoy improved cosmesis and decreased bleeding, wound infection, pain, and hospital length of stay. Unfortunately, in high-risk patients, the increased time of aortic cross-clamping and CPB may be deleterious. Also, complications are extremely morbid, including aortic dissection and death. Mini-valve surgery is limited to patients with an isolated valve disease.

Langer NB, Argenziano M. Minimally invasive cardiovascular surgery: incisions and approaches. *Methodist Debakey Cardiovasc J*. 2016;12(1):4–9.

8 Pacemakers, Implantable Cardioverter-Defibrillators, and Cardiac Resynchronization Therapy Devices

Alan Cheng and Fun-Sun F. Yao

A 63-year-old woman was scheduled for urgent open cholecystectomy. She underwent a dual-chamber permanent pacemaker (PPM) implantation 10 years ago for sick sinus syndrome and intermittent heart block. Over time, she developed systolic heart failure from greater amounts of ventricular pacing that resulted in an upgrade to a cardiac resynchronization therapy-defibrillator (CRT-D) 9 months ago. Her blood pressure was 110/68 mmHg, and her heart rate was regular at 60 beats per minute. An electrocardiogram (ECG) obtained on admission demonstrated atrioventricular (AV) sequential pacing.

A. Medical Disease and Differential Diagnosis

1. What are the indications for PPMs?
2. What is sick sinus syndrome? What is chronotropic incompetence?
3. How would you diagnose first-, second-, and third-degree AV block; bifascicular block (right bundle branch block [RBBB] with left anterior fascicular hemiblock or left posterior fascicular hemiblock); and trifascicular block?
4. Is it necessary to insert a temporary pacemaker before general anesthesia for an asymptomatic patient with bifascicular or trifascicular block?
5. What are the three-letter and five-letter identification codes of the North American Society of Pacing and Electrophysiology (NASPE) and British Pacing and Electrophysiology Group (BPEG) generic (NBG) code for pacemaker classification?
6. How many modes of pacing are available in modern PPMs? How do they work? What is the difference between DDD pacing and DDI pacing?
7. The patient was mechanically hyperventilated during surgery, and her pacemaker gradually increased her heart rate. What feature of the PPM is accounting for this?
8. What are the advantages and disadvantages of atrial pacing only? What are the disadvantages of right ventricular pacing only?
9. What are the indications for and complications associated with AV sequential PPMs?
10. How would you know if the patient's PPM was atrially, ventricularly, or atrioventricularly sequentially pacing?
11. What is a biventricular PPM or CRT device? What are the indications for such a device?
12. What are the usual lifespans of PPMs and implantable cardioverter-defibrillators (ICDs)?
13. What is an ICD? How does it work? What is a subcutaneous ICD?

14. What are the indications for ICDs?
15. What is the NASPE and BPEG generic defibrillator (NBD) code?

B. Preoperative Evaluation and Preparation

1. How would you preoperatively evaluate the patient described earlier?
2. How do you determine whether the patient has a cardiac implantable electronic device (CIED) and define what type of CIED?
3. How do you determine whether the patient is dependent on the pacing from the CIED?
4. How do you know if the implanted PPM or ICD is working?
5. What information would you like to obtain from interrogating this device?
6. How do you preoperatively prepare the patient for surgery and anesthesia?
7. Would you recommend reprogramming this device to asynchronously pace before surgery? What would you recommend regarding the ICD functions of the device?
8. The patient requires an abdominal magnetic resonance imaging (MRI) prior to the surgery. What considerations should you make regarding her CIED?

C. Intraoperative Management

1. How would you monitor this patient?
2. What drugs and equipment would you like to have on hand in the operating room?
3. How would you set up the transcutaneous external pacer and defibrillator?
4. Had this patient's ICD been implanted the day before surgery, would you consider avoiding certain inhalational gases for anesthesia?
5. Electromagnetic interference (EMI) from electrocautery results

in significant noise on your cardiac monitor. You recall that EMI also can inhibit pacing function from the PPM. In this pacemaker-dependent patient, how can you determine whether inappropriate inhibition of the PPM is occurring?

6. What are the potential responses of pacemakers and ICDs to electrocautery?
7. How would you prevent the effects of EMI on the pacemaker or ICD from the electrocautery?
8. What are the effects of a magnet on pacemakers and ICDs?
9. In the middle of surgery, the patient developed ventricular tachycardia. What would you do?
10. What precautions should be taken when a patient with a CIED is undergoing extracorporeal shock wave lithotripsy (ESWL)?
11. Is electroconvulsive therapy (ECT) contraindicated in patients with pacemakers or ICDs?
12. What precautions should be taken during radiofrequency ablation for a patient with a CIED?
13. During surgery, the patient developed frequent premature ventricular complexes and some of these resulted in rapid ventricular pacing (see **Fig. 8.8**). What is accounting for the pacemaker's behavior?

D. Postoperative Management

1. How would you monitor this patient in the postanesthesia care unit?
2. How would you confirm that the CIED is functioning properly after surgery?

A. Medical Disease and Differential Diagnosis

A.1. What are the indications for PPMs?

Artificial pacing is generally indicated for the treatment of symptomatic bradycardia or abnormalities in AV conduction

that suggest a high risk for progression to complete heart block. The two main indications for permanent pacing are failure of impulse formation and failure of cardiac conduction. Clinically, sick sinus syndrome and complete heart block are the most common indications for pacemakers. The following conditions are class I and IIa indications for a PPM:

- Sinus node dysfunction with documented symptomatic bradycardia, symptomatic chronotropic incompetence, or symptomatic sinus bradycardia secondary to required drug therapy for medical conditions
- Sinus node dysfunction for heart rates less than 40 beats per minute when a clear association between symptoms consistent with bradycardia and the actual presence of bradycardia has not been documented
- Recurrent syncope caused by spontaneous carotid sinus hypersensitivity or greater than 3-second episode of ventricular asystole induced with carotid sinus pressure
- Third-degree or advanced second-degree AV block associated with bradycardia with symptoms or ventricular arrhythmias presumed secondary to AV block
- Asymptomatic third-degree or advanced second-degree AV block in patients with sinus rhythm and documented periods of asystole greater than 3 seconds, escape rate less than 40 beats per minute, or an escape rhythm that is below the AV node (as suggested by a wide QRS complex)
- Ventricular pauses of greater than 5 seconds in patients with persistent atrial fibrillation
- Third-degree or advanced second-degree AV block resulting from catheter ablation or cardiac surgery
- First- or second-degree AV block associated with symptoms similar to those of pacemaker syndrome or hemodynamic compromise
- Chronic bifascicular block with advanced second-degree AV

block or intermittent third-degree AV block

- Chronic bifascicular block with alternating left bundle branch block (LBBB) and RBBB conduction
- High-risk patients with congenital long QT syndrome or those with documented sustained pause-dependent ventricular tachycardia
- New York Heart Association (NYHA) class III or class IV heart failure symptoms despite optimal medical therapy in patients with dilated cardiomyopathy (ejection fraction [EF] less than 35%), QRS duration greater than 120 milliseconds, and sinus rhythm (e.g., biventricular pacing)

Zipes DP, Libby P, Bonow RO, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 11th ed. Philadelphia, PA: Elsevier; 2019:780–806.

A.2. What is sick sinus syndrome? What is chronotropic incompetence?

Sick sinus syndrome describes an array of clinical disorders resulting from irreversible sinus node dysfunction. This may be manifested by episodes of sinus arrest, sinus pause, or bradycardia secondary to inadequate sinus node automaticity. When the sinus node fails to adequately generate an electrical impulse, ectopic atrial foci fire and at times can result in episodes of atrial tachyarrhythmias. The diagnosis is made when a correlation is made between a patient's symptoms and electrocardiographic evidence of bradycardia. Hence, extended ambulatory cardiac telemetry such as 24-/48-hour Holter, event monitoring, or implantable loop monitors may be helpful to make a diagnosis. When episodes of tachycardia and bradycardia coexist, it is often referred to as *tachy-brady* syndrome. This is one of the most common indications for pacemakers and is characterized by the following:

- Unexpected persistent symptomatic sinus bradycardia

- Episodes of sinus arrest or sinoatrial exit block
- Episodes of atrial fibrillation, atrial tachycardia, or atrial flutter
- Slow return to sinus rhythm following cardioversion (prolonged sinus node recovery time)

Chronotropic incompetence is loosely defined as the inability to achieve at least 80% to 85% of an individual's maximum predicted heart rate (MPHR) at peak exercise. Use of medications including β-blockers, calcium channel blockers, and antiarrhythmic medications can confound this diagnosis. In the presence of these medications, some people have used a modified definition of failure to achieve at least 62% of the MPHR. Chronotropic incompetence has been shown to increase mortality and morbidity especially in those with heart failure. Rate-adaptive pacing is often used in these instances and has been shown to increase peak oxygen consumption during exercise. It is important to point out that not all patients with sick sinus syndrome have chronotropic incompetence and not all patients with chronotropic incompetence have sick sinus syndrome.

Dobrzynski H, Boyett MR, Anderson RH. New insights into pacemaker activity: promoting understanding of sick sinus syndrome. *Circulation*. 2007;115:1921–1932.

John RM, Kumar S. Sinus node and atrial arrhythmias. *Circulation*. 2016;133:1892–1900.

Zipes DP, Libby P, Bonow RO, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 11th ed. Philadelphia, PA: Elsevier; 2019:772–779.

A.3. How would you diagnose first-, second-, and third-degree AV block; bifascicular block (right bundle branch block [RBBB] with left anterior fascicular hemiblock or left posterior fascicular hemiblock);

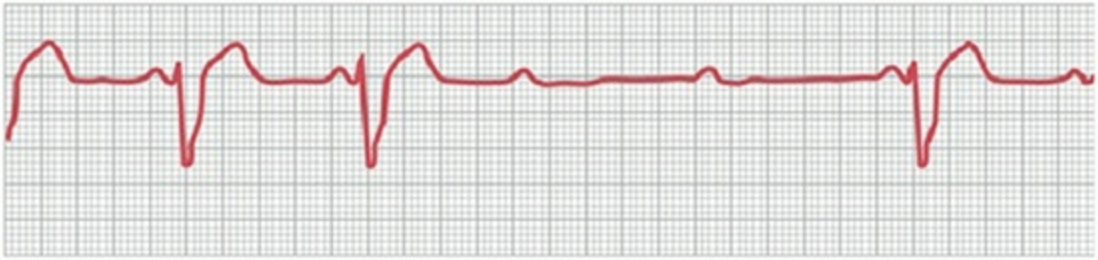
and trifascicular block?

First-degree AV block (some refer to as “delay” rather than “block” because the impulse is still being conducted) is characterized by a PR interval of greater than 0.20 seconds during normal sinus rhythm (**Fig. 8.1**). Second-degree AV block is subdivided into two types, Mobitz type I and Mobitz type II. Mobitz type I, or Wenckebach block, is characterized by a progressively lengthening PR interval, which occurs until a P wave is not conducted down the AV node and a QRS complex is dropped. The PR interval of the first beat after the blocked P wave is almost always shorter than the PR interval of the beat prior to being blocked. The site of block is usually in the AV node, and the natural history of Mobitz type I may or may not involve progression toward complete heart block. Mobitz type II block is characterized by a loss of AV conduction with no progressive lengthening of the PR interval before the sudden dropping of one or more QRS complexes. Additionally, the PR interval of the first beat after the blocked P wave is usually the same (<25 milliseconds) as the PR interval of the beat prior to the blocked P wave. The site of block is typically below the AV node and within the His bundle or in the Purkinje system. The natural history of Mobitz type II block is often progression toward complete heart block over time. Third-degree AV block, also called *complete heart block*, occurs when all electrical activity from the atrium fails to conduct to the ventricle. The site of block can lie in either the AV node or the His-Purkinje system. The atrial and ventricular contractions have no relation with each other, with the atrial rate almost always faster than the ventricular rate. As a result, the QRS complexes seen result from an ectopic focus either from the ventricular myocardium (wide QRS complex) or in an area of the AV node/His-Purkinje system below the site of block (narrow QRS complex). The typical rate of these ventricular escape beats range between 40

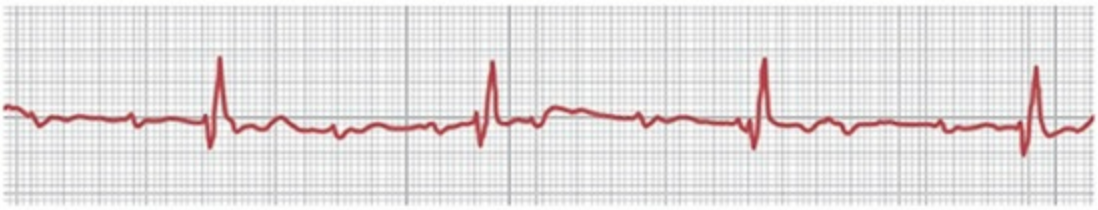
and 60 beats per minute.

First-degree heart block. Sustained prolongation of the PR interval with no dropped QRS complexes.

Second-degree heart block, Mobitz type I. Also referred to as Wenckebach block, there is progressive prolongation of the PR interval before the dropped QRS complex. The PR interval of the first return QRS complex has normalized compared to the PR interval of the QRS complex of the last beat before dropping. This behavior suggests that the location of block occurs in the AV node.



Second-degree heart block, Mobitz type II. There is no progressive increase in the PR interval before the dropped QRS complex. This suggests that the location of the block occurs below the AV node. Note also the QRS morphology during conducted beats. The wide QRS complex suggests the presence of fascicular disease, which is often seen in the presence of Mobitz type II heart block.



Third-degree heart block. The P waves march through with no communication with the ventricular beats.

FIGURE 8.1. Atrioventricular heart block.

The term *bifascicular block* often refers to block in the right bundle and one of the two major fascicles of the left bundle. RBBB with left anterior hemiblock is present when the ECG shows an RBBB with a left axis deviation (usually greater than −60 degrees) in the absence of an inferior myocardial infarction.

Complete RBBB with right axis deviation (greater than 90 degrees) is indicative of RBBB and left posterior hemiblock in the absence of a lateral myocardial infarction or evidence of right-sided heart failure. The term *trifascicular block* is used to describe first-degree AV block in the presence of bifascicular block.

Zipes DP, Libby P, Bonow RO, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 11th ed. Philadelphia, PA: Elsevier; 2019:772–779.

A.4. Is it necessary to insert a temporary pacemaker before general anesthesia for an asymptomatic patient with bifascicular or trifascicular block?

The risk for progression to complete heart block in asymptomatic patients with bifascicular block is low. Furthermore, no clinical characteristics have been identified that accurately predict the risk of development of complete heart block. Therefore, routine PPM implantation in patients with asymptomatic bifascicular block is not recommended. Observations made in the perioperative period have suggested that development of complete heart block during general anesthesia is also rare; therefore, it is generally not recommended that patients undergo temporary pacemaker insertion before general anesthesia. However, it is advisable to have an external pacemaker available in the operating room. The term *trifascicular block* is somewhat of a misnomer because, in truth, if all three fascicles (i.e., right bundle, left anterior fascicle, and left posterior fascicle) were blocked, the patient would be in complete heart block. Although it is generally agreed that individuals with trifascicular block have a higher risk for sudden death, there is no single clinical variable that predicts a higher risk for complete heart block during surgery. Small case series have shown that the development of

intraoperative complete heart block in asymptomatic patients with trifascicular block is uncommon. Therefore, routine temporary pacemaker insertion before general anesthesia in these patients is not recommended.

Gauss A, Hübner C, Radermacher P, et al. Perioperative risk of bradyarrhythmias in patients with asymptomatic chronic bifascicular block or left bundle branch block: does an additional first-degree atrioventricular block make any difference? *Anesthesiology*. 1998;88:679–687.

Zipes DP, Libby P, Bonow RO, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 11th ed. Philadelphia, PA: Elsevier; 2019:780–799.

A.5. What are the three-letter and five-letter identification codes of the North American Society of Pacing and Electrophysiology (NASPE) and British Pacing and Electrophysiology Group (BPEG) generic (NBG) code for pacemaker classification?

Given the complexity of current pacemaker systems, the Intersociety Commission for Heart Disease Resources established a classification code in the 1970s that is still used widely. The original nomenclature involved a three-letter identification code, as shown in the first three columns of **Table 8.1**. In 1980, this code was extended to five letters; the last two letters are omitted when not applicable. In 1987, this five-letter coding system become known as the NBG pacemaker code after being adopted by both the NASPE (now known as the *Heart Rhythm Society*) and BPEG (now referred to as the *British Heart Rhythm Society*). The first letter describes the chamber(s) that the pacemaker can pace, the second letter describes the chamber(s) that it senses, and the third letter describes the response of the pacemaker to sensed intrinsic activity. The last two letters describe additional features such as rate responsiveness that are commonly omitted when not used. For example, a VVI pacing mode paces in the ventricle, can sense

intrinsic activity in the ventricle, and inhibits pacing when it senses intrinsic activity. A VOO pacing mode paces in the ventricle but does not sense intrinsic activity nor does it inhibit pacing—it simply paces regardless of the heart's intrinsic electrical activity.

TABLE 8.1 NASPE/BPEG Generic Pacemaker Identification Code[a]

Letter I	Letter II	Letter III	Letter IV	Letter V
Chamber(s) Paced	Chamber(s) Sensed	Mode of Response	Programmability Rate Modulation	Antitachyarrhythmi Function(s)
O = None	O = None	O = None	O = None	O = None
A = Atrium	A = Atrium	T = Triggered	P = Single programmable	P = Pacing
V = Ventricle	V = Ventricle	I = Inhibited	M = Multiprogrammable	S = Shock
D = Dual (A + V)	D = Dual (A + V)	D = Dual (T + I)	C = Communicating	D = Dual (P + S)
			R = Rate modulation	

[a]Although the pacemaker identification coding involved the use of five letters, few modern pacemakers have antitachyarrhythmia functions. Therefore, most pacemakers are currently described by the first four letters of the coding system.
BPEG, British Pacing and Electrophysiology Group; NASPE, North American Society of Pacing and Electrophysiology.

American Society of Anesthesiologists. Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices. *Anesthesiology*. 2011;114:247–261.

Zipes DP, Libby P, Bonow RO, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 11th ed. Philadelphia, PA: Elsevier; 2019:780–799.

A.6. How many modes of pacing are available in modern PPMs? How do they work? What is the difference between DDD pacing and DDI pacing?

Modern pacemakers are programmable into one of three modes of pacing: asynchronous pacing, single-chamber demand pacing, and dual-chamber AV sequential demand pacing. Asynchronous or fixed-rate (e.g., AOO, VOO, DOO [see section A.5 for details]) modes pace at a programmable preset rate that is independent of the heart's intrinsic activity. They can be atrial, ventricular, or dual-chamber. When pacing occurs without coordinating with the heart's intrinsic electrical activity, this can result in pacing competition, pacemaker syndrome, and rarely induction of ventricular arrhythmias. Ventricular tachyarrhythmias in those with structural heart disease can theoretically occur because the pacing spike can potentially be delivered during a time when the myocardium is vulnerable to arrhythmogenesis, but this is extremely rare.

Single-chamber demand pacing (e.g., AAI, VVI) paces at a preset rate only when the spontaneous heart rate drops below the programmed preset rate. For example, if this patient's device was programmed to VVI 70, the device would pace in the ventricle only when the native ventricular rate fell below 70 beats per minute. Once the native ventricular rate resumed above 70 beats per minute, the device would sense this activity and inhibit further pacing. Single-chamber demand pacing in the atrium functions in a similar way but is rarely used alone in the United States.

Dual-chamber AV sequential pacing requires two pacemaker leads: one in the right atrium and one in the right ventricle. The atrium is stimulated to contract first; then, after an adjustable PR interval (also referred to as the *AV interval*), the ventricle is stimulated to contract if no intrinsic ventricular activity is sensed by the ventricular pacing lead. For example, if this patient's device was programmed to DDD 70 with an AV interval of 200 milliseconds, the device would begin pacing the atrium first if the intrinsic sinus rate fell below 70 beats per minute. After the

atrium has been paced, the device will wait for 200 milliseconds to sense intrinsic ventricular activity that presumably would have been conducted down the AV node. If it does not see intrinsic activity within 200 milliseconds, it will then pace in the ventricle as well. DDD pacemakers can also pace in the ventricle in response to intrinsic atrial activity. For example, if the intrinsic atrial rate was 80 beats per minute, the device would inhibit pacing in the atrium because the base rate was set to 70 beats per minute. But because it is a dual-chamber device programmed to inhibit and trigger pacing in both chambers (i.e., the third "D" in the coding sequence), it will wait 200 milliseconds from the time of the intrinsic atrial activity and watch for intrinsic ventricular activity. If it sees intrinsic ventricular activity (i.e., the atrial signal conducted down the AV node and to the ventricle), it will inhibit ventricular pacing. If it does not see intrinsic ventricular activity occurring within 200 milliseconds from the intrinsic atrial activity, the pacemaker will then "trigger" the ventricular pacing lead to pace the ventricle. Dual-chamber pacemakers programmed to DDI differ slightly from devices programmed to DDD, and the main difference is that AV sequential pacing occurs only when atrial pacing is present. This is in contrast to DDD pacing in which AV sequential pacing is preserved regardless of whether atrial pacing or atrial sensing is occurring. Suppose we have a dual-chamber pacemaker programmed to DDI 70 with an AV interval of 200 milliseconds. If the sinus rate fell below 70 beats per minute, the atrial pacing lead would pace the atrium. After a 200 millisecond interval, if intrinsic ventricular activity was seen by the ventricular lead the ventricular lead would be inhibited from pacing the ventricle. If ventricular activity was not seen after 200 milliseconds, the ventricular lead would pace the ventricle. Suppose now that the sinus rate is 80 beats per minute. Because the DDI pacemaker is programmed to 70 beats per minute, no

atrial pacing is occurring. Because DDI pacemakers do not track atrial sensed events, ventricular pacing would not be "triggered" after 200 milliseconds by these atrial sensed events and ventricular pacing would only occur if the *ventricular* rate fell below the preset rate of 70 beats per minute.

Zipes DP, Libby P, Bonow RO, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 11th ed. Philadelphia, PA: Elsevier; 2019:780–799.

A.7. The patient was mechanically hyperventilated during surgery, and her pacemaker gradually increased her heart rate. What feature of the PPM is accounting for this?

All modern pacemakers have the ability to adjust the pacing rate according to the patient's level of activity in an effort to obtain a more physiologic response to exercise. This is known as *rate-response* (adaptive) pacing and is denoted by an "R" in the fourth position of the NBG coding schema. This is often applied in patients with chronotropic incompetence or those with permanent atrial fibrillation who have undergone AV node ablation. Various activity-detecting systems have been developed to create a reliable rate-responsive pacemaker (e.g., muscle movement, respiratory rate, minute ventilation, central venous temperature, QT interval, myocardial contractility [dP/dt], oxygen saturation and pH in mixed venous blood, and ventricular depolarization gradient), but currently PPMs used in the United States rely on sensors of motion or changes in minute ventilation through measurements of intrathoracic impedance. Because of the latter phenomenon, patients undergoing general anesthesia who are subjected to mechanical hyperventilation (e.g., neurosurgery) can experience an increase in the rate of pacing. Although it is generally not required to disable rate-responsive features before surgery, pacemaker-induced changes

in heart rate resulting from intraoperative hyperventilation or significant motion may sometimes be mistaken for inadequate anesthesia. Hence, it is important that the anesthesia team be aware of the programmed settings of the pacemaker. If reprogramming the device to disable rate-responsive features is not readily available, a magnet may be placed over the pacemaker site to temporarily convert it to asynchronous pacing. Although the response to a magnet may be programmed off in some pacemakers, all properly functioning pacemakers within the United States have magnet-responsive features activated as a default.

Ellenbogen KA, Wilkoff B, Kay GN, et al, eds. *Clinical Cardiac Pacing, Defibrillation and Resynchronization Therapy*. 5th ed. Philadelphia, PA: Elsevier; 2016:168–189.

Zipes DP, Libby P, Bonow RO, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 11th ed. Philadelphia, PA: Elsevier; 2019:780–799.

A.8. What are the advantages and disadvantages of atrial pacing only? What are the disadvantages of right ventricular pacing only?

Atrial pacing only increases cardiac output by 26% over the cardiac output of ventricular pacing only because atrial contraction contributes to approximately 15% to 25% of the diastolic filling of the ventricle in normal hearts. It has been shown that coronary blood flow increases and coronary resistance decreases during atrial pacing only. Atrial pacing has also been associated with a reduction in the incidence of atrial fibrillation. Atrial pacing only is seldom used in the United States and often is implanted with the addition of a ventricular pacing lead in the event AV block develops over time.

Ventricular pacing, occurring individually or sequentially with atrial pacing, has been shown to result in dyssynchronous

left ventricular electrical activation and mechanical contraction. Under normal circumstances, electrical activation along the His-Purkinje system results in a near simultaneous activation of the entire left ventricle. This allows for efficient contraction and is said to be synchronous. When right ventricular pacing is introduced (the lead often at the right ventricular septum or apex), this results in activation of the right ventricular septum first, followed by passive activation of the left ventricle toward the free wall. This form of contraction is said to be dyssynchronous and has been shown to potentially worsen congestive heart failure and the left ventricular EF. Prior studies have shown that individuals at greatest risk for developing reductions in EF from right ventricular pacing are those who exhibit ventricular pacing greater than 40% of the time. Studies have shown that individuals requiring ventricular pacing for AV block with an EF less than 50% have a 56% risk for developing a composite end point of death, urgent visit for heart failure, or left ventricular dilatation over an average of 37 months. As a result, this has led to increased interest in finding alternative, more physiologic ways of pacing the heart. These include directly pacing the His-Purkinje system (e.g., His bundle pacing, peri-left bundle branch pacing) or application of resynchronization therapy. In fact, the patient in this case likely developed heart failure as a result of right ventricular pacing and underwent upgrade to a resynchronization system to help restore left ventricular synchrony.

Curtis AB, Worley SJ, Adamson PB, et al. Biventricular pacing for atrioventricular block and systolic dysfunction. *N Engl J Med*. 2013;368:1585–1593.

Healey JS, Toff WD, Lamas GA, et al. Cardiovascular outcomes with atrial-based pacing compared with ventricular pacing: meta-analysis of randomized trials, using individual patient data. *Circulation*. 2006;114:11–17.

Vijayaraman P, Bordachar P, Ellenbogen KA. The continued search for physiological pacing: where are we now? *J Am Coll Cardiol*. 2017;69:3099–

3114.

A.9. What are the indications for and complications associated with AV sequential PPMs?

When ventricular pacing alone cannot maintain adequate cardiac output and atrial pacing alone is not justified, as in complete AV block, AV sequential pacing is indicated. Because of the success of transvenous leads, bioengineering advances such as thinner polyurethane insulation and improved device programmability, the indications for dual-chamber pacing, have broadened. It can be used for sick sinus syndrome and all degrees of heart block. PPMs programmed to DDD pacing are the ultimate form of physiologic pacing. Programmable features include the mode of pacing, the AV delay, the maximum atrial rate that the ventricle will follow (atrial tracking), and the minimum atrial rate for sensing at which atrial pacing commences. The major advantage of such pacing is the ability to significantly increase the cardiac output under extreme stress and a reduced incidence of atrial fibrillation development. Historically, the major disadvantage of DDD pacing has been the possibility of pacemaker-mediated tachycardia (see section C.13). Another disadvantage recognized has been the development of ventricular dyssynchrony (see section A.8) as a result of right ventricular only pacing. Long-term follow-up of patients with dual-chamber pacemakers demonstrated reductions in left ventricular EFs when compared to atrial pacing alone, especially in the setting of preexisting left ventricular dysfunction.

Zipes DP, Libby P, Bonow RO, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 11th ed. Philadelphia, PA: Elsevier; 2019:780–799.

A.10. How would you know if the patient's PPM was atrially, ventricularly, or atrioventricularly sequentially pacing?

Modern-day cardiac monitors are equipped with filters that can accentuate and highlight artificial pacing potentials. In atrial pacing, an electrical spike often appears before the P wave and the QRS complex is usually normal, provided there is normal intrinsic AV conduction. One may need to adjust the monitor so that pacing spikes are accentuated and can readily be seen. In ventricular pacing, the electrical spike is followed immediately by a widened QRS complex. In fact, most right ventricular pacing leads are positioned at the right ventricular apex. Because of this location, pacing would result in a QRS complex that has a QS pattern in lead V_1 and a QS pattern in the inferior limb leads (II, III, and aVF). In AV sequential pacing, there are two spikes: one before the P wave and another preceding the QRS complex.

Zipes DP, Libby P, Bonow RO, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 11th ed. Philadelphia, PA: Elsevier; 2019:780–799.

A.11. What is a biventricular PPM or CRT device? What are the indications for such a device?

It has long been recognized that individuals with interventricular conduction abnormalities have a predilection toward impaired left ventricular systolic function. In fact, one of the more common interventricular conduction delays seen in patients with congestive heart failure is LBBB. On a mechanistic level, individuals with LBBB demonstrate ventricular dyssynchrony, a phenomenon whereby the left ventricle contracts in a stepwise process. Unlike normal individuals where the left ventricular septum and the left ventricular lateral free wall are electrically activated nearly simultaneously, patients with LBBB have a delay in the activation of the left lateral free wall. As a result, there is marked impairment in left ventricular systolic function and increased myocardial work and oxygen consumption. One

approach to correct this dyssynchrony is to "resynchronize" the heart through the use of a biventricular pacemaker/ICD. These devices are capable of pacing both the left ventricular septum (through a pacemaker lead in the right ventricle) and the left ventricular lateral free wall simultaneously (through a pacemaker lead in the coronary sinus), thereby allowing for activation of the entire left ventricle at the same time. Candidates for implantation of a biventricular device include individuals on optimal heart failure medications with

- Sinus rhythm, EF ≤35%, LBBB with QRS >120 milliseconds, NYHA II to IV symptoms
- Sinus rhythm, EF ≤35%, non-LBBB with QRS >150 milliseconds, NYHA III to IV symptoms
- Patients requiring >40% of ventricular pacing with EF ≤35%

Al-Khatib SM, Stevenson WG, Ackerman MJ, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: executive summary. *Circulation*. 2018;138(13):e210–e271. Erratum in *Circulation*. 2018;138(13):e415–e418.

Jarcho JA. Biventricular pacing. *N Engl J Med*. 2006;355:288–294.

A.12. What are the usual lifespans of PPMs and implantable cardioverter-defibrillators (ICDs)?

Modern-day pacemakers are lithium-powered and can on average last 10 to 15 years. The lifespan of current ICDs relies not only on the battery but also on the high-voltage capacitor. Hence, typical lifespans are 8 to 12 years. Recently, leadless pacemakers and subcutaneous ICDs have been introduced into the market. These devices have typical lifespans of 7 and 5 years, respectively.

Ellenbogen KA, Wilkoff B, Kay GN, et al, eds. *Clinical Cardiac Pacing, Defibrillation and Resynchronization Therapy*. 5th ed. Philadelphia, PA: Elsevier; 2016:251–269.

A.13. What is an ICD? How does it work? What is a

subcutaneous ICD?

An ICD system consists of a pulse generator and leads for tachyarrhythmia detection and therapy. ICDs provide antitachycardia and antibradycardia pacing, synchronized (cardioversion) or nonsynchronized (defibrillation) shocks, telemetry, and diagnostics including stored event electrograms and history logs. Essentially, the pulse generator is a self-powered computer within a hermetically sealed titanium casing (can). A battery with high power density is used to power the pulse generator, circuitry, and aluminum electrolytic storage capacitors. Most ICD designs use two capacitors in series to achieve a maximum voltage for defibrillation. A major challenge in ICD design is the large range of voltages that must be controlled in a very small package. Modern devices can charge up to 41 joules of energy.

ICDs commonly use transvenous lead systems for sensing, pacing, and shocks. Epicardial leads are still used in infants and small children. Ventricular demand pacing for bradycardia is a standard feature of all ICDs. Modern-day ICDs have all the capabilities of modern-day pacemakers, including rate-adaptive pacing and automatic mode switching. However, the response of ICDs to magnets differs from that of a pacemaker (see section C.8).

Current ICDs have many programmable features, but essentially, they measure each cardiac R-R interval and categorize the rate as normal, too fast (short R-R interval), or too slow. When the device detects a sufficient number of short R-R intervals within a period of time (all programmable), it will declare a tachycardia episode. The internal computer will decide between antitachycardia pacing (less energy use, painless therapy) and shock based on its programmed algorithm. If shock is chosen, an internal capacitor is charged that takes approximately 5 to 13 seconds depending on the amount of

energy to be delivered and age of the device. Most devices are programmed to reconfirm ventricular tachycardia or ventricular fibrillation immediately after charging to confirm that the arrhythmia persists. Once therapy is delivered, the ICD will redetect to determine whether or not the therapy successfully terminated the arrhythmia. A tachycardia episode is considered terminated when sinus rhythm has been restored for a certain period (varies by manufacturer). Typically, ICDs deliver no more than six shocks for a given episode.

The subcutaneous ICD was approved for use in the United States on September 28, 2012. Unlike traditional ICD systems, this device does not require implantation of transvenous leads within the heart. The ICD can is implanted along the left midaxillary line, and the defibrillator lead is tunneled subcutaneously across the left costal margin to the xiphoid process. From there, the lead is then tunneled superiorly along the left sternal border toward the sternal notch so that the defibrillator coil is positioned alongside the sternum (**Figs. 8.2** and **8.3**). The vector for defibrillation is defined between the can and the defibrillator coil. These systems are unique and provide a solution to patients who have vascular issues or may not want indwelling transvenous leads. Because sensing and defibrillation occurs from the chest wall, a couple of unique considerations exist. First, the size of the surface T waves can complicate device sensing so some patients may not be eligible. Second, the amount of energy required for defibrillation is typically higher compared to traditional ICD systems because there is more energy that gets dissipated because energy is being delivered further away from the heart. As a result, the battery and capacitors are larger and result in a larger device. Lastly, these systems differ from traditional ICDs in that they do not provide pacing support or deliver antitachycardia pacing because of the pain that is associated with transcutaneous pacing delivery.

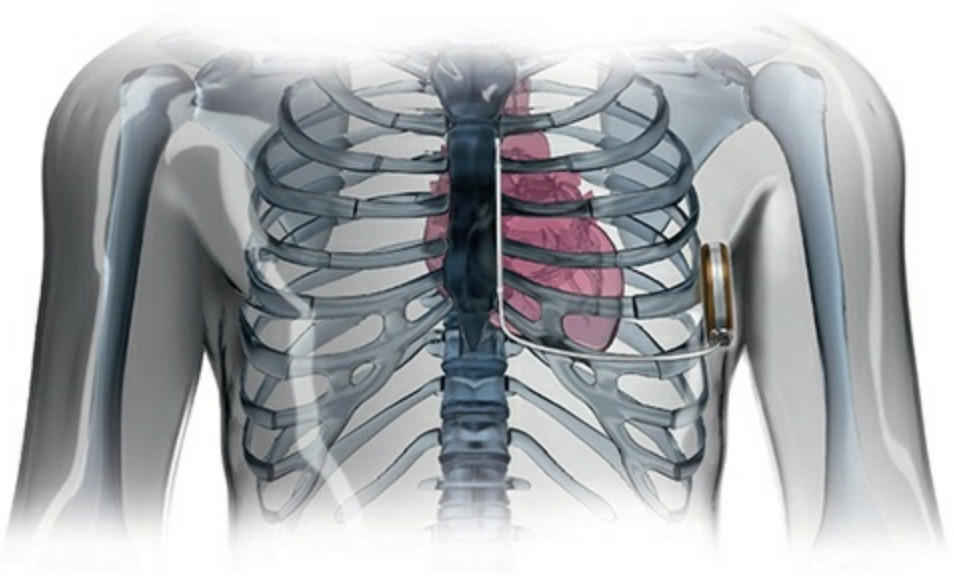


FIGURE 8.2. The subcutaneous ICD. ICD can is implanted along the left midaxillary line, and the lead is tunneled across the left lower chest to the xiphoid process. The lead is then directed superiorly along the left sternal border so that the lead's defibrillator coil is alongside the sternum. Defibrillation vector involves the can to the coil. (*Image provided courtesy of Boston Scientific. © 2019 Boston Scientific Corporation or its affiliates. All rights reserved.*)

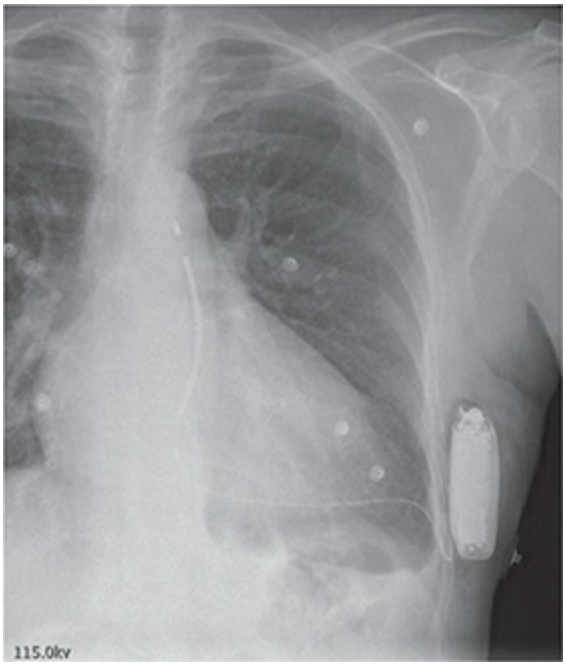


FIGURE 8.3. Chest x-ray of implanted subcutaneous ICD.

Al-Khatib SM, Stevenson WG, Ackerman MJ, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: executive summary. *Circulation*. 2018;138(13):e210–e271. Erratum in *Circulation*. 2018;138(13):e415–e418.

Bardy GH, Smith WM, Hood MA, et al. An entirely subcutaneous implantable cardioverter-defibrillator. *N Engl J Med*. 2010;363:36–44.

Burke MC, Gold MR, Knight BP, et al. Safety and efficacy of the totally subcutaneous implantable defibrillator: 2-year results from a pooled analysis of the IDE study and EFFORTLESS registry. *J Am Coll Cardiol*. 2015;65(16):1605–1615.

A.14. What are the indications for ICDs?

Initially, ICDs were indicated for hemodynamically significant ventricular tachycardia or ventricular fibrillation. Newer indications include the following and continue to evolve:

- Survivors of cardiac arrest because of ventricular tachycardia/ventricular fibrillation not resulting from a transient or reversible cause
- Spontaneous or induced at electrophysiology study sustained ventricular tachycardia in the presence of structural heart disease
- Syncope of undetermined origin with clinically relevant, hemodynamically significant sustained ventricular tachycardia or ventricular fibrillation-induced at electrophysiology study
- Ischemic cardiomyopathy (EF ≤30%) without a recent myocardial infarction (within the last 40 days) or revascularization in the past 3 months
- Ischemic or nonischemic dilated cardiomyopathy (EF ≤35%) with NYHA class II or III heart failure symptoms
- Inherited channelopathies including Brugada syndrome (RBBB and ST-segment elevation leads V_1 to V_3), catecholaminergic polymorphic ventricular tachycardia, long QT syndrome, short QT syndrome, idiopathic ventricular fibrillation
- Inherited or acquired high-risk states including arrhythmogenic right ventricular dysplasia, hypertrophic cardiomyopathy, cardiac sarcoidosis, or Chagas

cardiomyopathy.

Al-Khatib SM, Stevenson WG, Ackerman MJ, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: executive summary. *Circulation*. 2018;138(13):e210–e271. Erratum in *Circulation*. 2018;138(13):e415–e418.

Epstein AE, DiMarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to revise the ACC/AHA/NASPE 2002 guideline update for implantation of cardiac pacemakers and antiarrhythmia devices): developed in collaboration with the American Association for Thoracic Surgery and Society of Thoracic Surgeons. *Circulation*. 2008;117:e350–e408.

Tracy CM, Epstein AE, Darbar D, et al. 2012 ACCF/AHA/HRS focused update of the 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol*. 2012;60:1297–1313.

Zipes DP, Libby P, Bonow RO, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 11th ed. Philadelphia, PA: Elsevier; 2019:780–799.

A.15. What is the NASPE and BPEG generic defibrillator (NBD) code?

Like pacemakers, ICDs have a generic code to indicate lead placement and function. The NBD code is shown in **Table 8.2**. The most robust form of identification, referred to as the "label form," replaces the fourth letter of the NBD with the appropriate generic pacemaker code.

TABLE 8.2 NASPE/BPEG Generic Defibrillator Code

Letter I	Letter II	Letter III	Letter IV
Shock Chamber(s)	Antitachycardia Pacing Chamber(s)	Tachycardia Detection	Antibradycardia Pacing Chamber(s)
O = None	O = None	E = Electrogram	O = None
A = Atrium	A = Atrium	H = Hemodynamic	A = Atrium

V = Ventricle	V = Ventricle	(Not yet available)	V = Ventricle
D = Dual (A + V)	D = Dual (A + V)		D = Dual (A + V)

BPEG, British Pacing and Electrophysiology Group; NASPE, North American Society of Pacing and Electrophysiology.

American Society of Anesthesiologists. Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices. *Anesthesiology*. 2011;114:247–261.

B. Preoperative Evaluation and Preparation

B.1. How would you preoperatively evaluate the patient described earlier?

Preoperative evaluation should include the routine systemic workup, paying particular attention to cardiovascular disorders. The comprehensive evaluation includes complete blood count, urinalysis, coagulation screening with prothrombin time and partial thromboplastin time, serum electrolytes, blood urea nitrogen, blood sugar, chest radiograph, and ECG. Special attention should be paid to the history, symptoms and signs of myocardial infarction, congestive heart failure, and arrhythmias. Serum electrolytes, especially potassium level, must be in the normal range. For the patient with a CIED, recent guidelines have recommended that all CIEDs be properly interrogated within 3 to 6 months before surgery. This evaluation should include the following:

- Establish whether a patient has a CIED—this is best accomplished by a detailed history and verifying by reviewing a recent chest x-ray.
- Define the type of CIED—patients typically have a CIED information card.
- Determine dependency on the pacing function of the CIED—

review recent device interrogation report.

- Determine CIED function and programming details—review recent device interrogation report.
- Determine magnet behavior and whether CIED requires reprogramming on the day of surgery to avoid inappropriate device behavior from EMI.

American Society of Anesthesiologists. Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices. *Anesthesiology*. 2011;114:247–261.

Crossley GH, Poole JE, Rozner MA, et al. The Heart Rhythm Society (HRS)/American Society of Anesthesiologists (ASA) expert consensus statement on the perioperative management of patients with implantable defibrillators, pacemakers and arrhythmia monitors: facilities and patient management this document was developed as a joint project with the American Society of Anesthesiologists (ASA), and in collaboration with the American Heart Association (AHA), and the Society of Thoracic Surgeons (STS). *Heart Rhythm*. 2011;8:1114–1154.

B.2. How do you determine whether the patient has a cardiac implantable electronic device (CIED) and define what type of CIED?

Determining whether a patient has a CIED should be based on (1) a focused history including but not limited to the patient interview, medical records review, review of available chest radiograph, ECG, or any available monitor or rhythm strip information and (2) a focused physical examination (e.g., checking for scars, palpating for device). Of note is the recent introduction of leadless pacemakers (all three major device manufacturers are developing one, but only one is currently US Food and Drug Administration (FDA) approved [Micra, Medtronic, Mounds View, MN]), which are small capsule-sized devices delivered through a catheter inserted in the groin and fully implanted into the heart (**Fig. 8.4**). Therefore, there are no

obvious signs of a device by physical examination and one must review a recent chest radiograph to confirm its presence (**Fig. 8.5**).

FIGURE 8.4. Micra leadless pacemaker. (*Reproduced with permission of Medtronic, Inc.*)

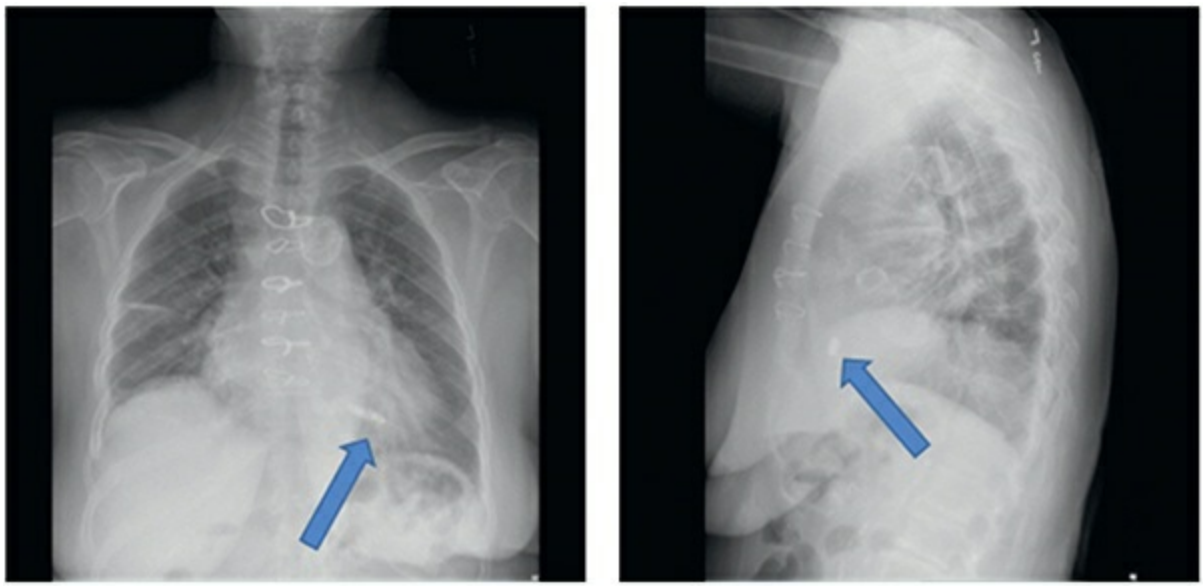


FIGURE 8.5. Chest x-ray of Micra leadless pacemaker implanted in the right ventricle (*blue arrows*) in anterior-posterior and lateral views. (*With courtesy of Hiroshi Ashikaga, MD, PhD.*)

Defining the type of device is accomplished by (1) obtaining the manufacturer's identification card from the patient or other source, (2) ordering chest radiography studies if no other data are available, or (3) referring to supplemental resources (e.g., manufacturer's databases, pacemaker clinic records,

consultation with a cardiologist).

American Society of Anesthesiologists. Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices. *Anesthesiology*. 2011;114:247–261.

Sideris S, Archontakis S, Dilaveris P, et al. Leadless cardiac pacemakers: current status of a modern approach in pacing. *Hellenic J Cardiol*. 2017;58(6):403–410.

B.3. How do you determine whether the patient is dependent on the pacing from the CIED?

Pacemaker dependency is not defined by an absolute amount of pacing seen over time. Rather, it is defined by how functionally dependent a patient is to pacing support. For instance, a patient with a dual-chamber pacemaker may not pace 100% of the time. But during periods of pacing, if pacing were to be temporarily discontinued and the patient developed light-headedness or presyncope, then he or she would be considered functionally dependent. Functional dependency on pacing support may be determined by one or more of the following: (1) a verbal history or an indication in the medical record that the patient has experienced a bradyarrhythmia that has caused syncope or other symptoms requiring CIED implantation, (2) a history of successful AV nodal ablation that resulted in CIED placement, or (3) a CIED evaluation that shows clinically evidenced hemodynamic compromise when the pacing function of the CIED is temporarily disabled or programmed to the lowest programmable rate.

For emergency surgery, an ECG or rhythm strip should be examined for pacing spikes. If pacing spikes are noted before most or all of either the P waves or QRS complexes, then the patient should be treated as if pacemaker dependent. All

pacemaker-dependent patients and patients with ICDs should have transcutaneous pacing and defibrillator pads available during surgery. A magnet should always be available, and its use is recommended in the pacemaker-dependent patient as well as the patient with an ICD. Regardless of the type of device, interrogation of the CIED under the direction of a physician knowledgeable in the function of devices should occur as soon as possible.

American Society of Anesthesiologists. Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices. *Anesthesiology*. 2011;114:247–261.

B.4. How do you know if the implanted PPM or ICD is working?

The CIED function is best assessed by interrogating the device, and this is the recommended approach. But if interrogating the device is not an option and this information is urgently needed, one can attempt to slow the intrinsic heart rate to a rate below that of the pacemaker by carotid massage or the Valsalva maneuver. Carotid massage to slow the heart rate should be used cautiously because it could result in an arteriosclerotic plaque embolizing to the cerebral circulation. If the rate does not slow down enough for the pacemaker to take over the ventricle, the device can be tested by placing a magnet over it that will temporarily program it to a fixed-rate pacing mode. In this mode, pacing spikes march through the rhythm strip with no regard for the intrinsic electrical activity of the heart. The rate at which the pacemaker will pace in the presence of a magnet varies among device manufacturers and is dependent on the battery life. Once the magnet is removed, the device returns to its normal programming. Of note, placing a magnet over an ICD

does not temporarily program the device to pace asynchronously. The magnet on an ICD will only temporarily disable the ICD therapies and will have no effect on the pacing function. Additionally, leadless pacemakers also do not respond to the magnet by pacing asynchronously.

American Society of Anesthesiologists. Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices. *Anesthesiology*. 2011;114:247–261.

Sideris S, Archontakis S, Dilaveris P, et al. Leadless cardiac pacemakers: current status of a modern approach in pacing. *Hellenic J Cardiol*. 2017;58(6):403–410.

B.5. What information would you like to obtain from interrogating this device?

Device interrogations provide information on the status and current programmed settings of a PPM or ICD. The important primary information for anesthesiologists include (1) battery life, (2) programmed pacing mode such as VVIR and DDDR, (3) pacemaker dependency, (4) intrinsic rhythm, (5) behavior to a magnet, (6) prior recorded arrhythmic events, and (7) pacemaker lead parameters (including pacing threshold, ability to sense intrinsic activity, and lead impedance).

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B.6. How do you preoperatively prepare the patient for surgery and anesthesia?

Preparation for patient safety and proper maintenance of the device during a procedure includes the following:

- Determining whether EMI is likely to occur during the planned procedure as well as the location of the EMI
- Properly positioning the electrocautery grounding pad so that device exposure to the path of conduction from the electrocautery instrument to the grounding pad is minimized to the fullest extent
- Determining whether reprogramming the CIED pacing function to an asynchronous pacing mode or disabling any special algorithms, including rate-adaptive features, is needed
- Suspending antitachyarrhythmia functions if present
- Advising the surgeon performing the procedure to minimize prolonged bursts of monopolar cautery or consider use other less EMI-generating sources of energy including bipolar electrocautery or ultrasonic (harmonic) scalpel
- Ensuring the availability of temporary pacing and defibrillation equipment
- Evaluating the possible effects of anesthetic techniques and of the procedure on CIED function and patient—CIED interactions

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American Society of Anesthesiologists. Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices. *Anesthesiology*. 2011;114:247–261.

B.7. Would you recommend reprogramming this device to asynchronously pace before surgery? What would you recommend regarding the ICD functions of the device?

Given the number of patients with CIEDs, recommending that all patients undergo reprogramming immediately before surgery is untenable and would significantly compromise perisurgical throughput. Moreover, reports have described individuals with

ICDs or PPMs who later expired because the device was not reactivated before discharge after surgery. These issues raise the need for proper triaging of patients who truly need their devices reprogrammed before surgery. The patient in this example has a CRT-D. It is likely that the patient is functionally dependent on the CIED. Furthermore, the location of the EMI delivered in this case is close to the device system and therefore would likely result in inappropriate inhibition of pacing and/or sensing of EMI that the device would inappropriately mark as ventricular fibrillation. Given functional dependency on the device and the location of the EMI delivered, reprogramming the device would be recommended to deactivate the ICD and pace asynchronously before surgery for the following reasons:

- Electrocautery during surgery may inhibit pacing function.
- A magnet cannot convert the pacemaker in an ICD system to asynchronous mode pacing. A magnet placed over an ICD only disables tachycardia detection and therapy of the ICD. This is true of all devices used in the United States. One notable exception are ICDs manufactured by LivaNova Medical (London, United Kingdom), which, in the presence of a magnet, will not only disable tachycardia detection therapy but also convert pacing to a fixed rate at 96 beats per minute.

American Society of Anesthesiologists. Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices. *Anesthesiology*. 2011;114:247–261.

B.8. The patient requires an abdominal magnetic resonance imaging (MRI) prior to the surgery. What considerations should you make regarding her CIED?

MRIs were generally contraindicated in patients with a CIED, but more recent generation generators and leads have been engineered to be labeled as "MRI conditional." These newer devices have the ability to manage the increased energy introduced to the CIED during the scan while minimizing the potential risks of myocardial ablation and induction of arrhythmias. Hence, patients with these newer device systems can undergo MRI scanning if clinically indicated and the CIED appears to be functioning normally. Although a patient may have a CIED system that is conditionally approved to undergo MRI scanning, there are other aspects of the system that need to be evaluated to confirm that it is safe. Patients with abandoned or fractured leads, for example, may not be appropriate candidates for MRI scanning despite the CIED system being labeled as MRI conditional. If MRI must be performed, consult with the ordering physician, the patient's cardiologist or electrophysiologist, the diagnostic radiologist, and the CIED manufacturer.

MRIs can cause rapid pacing, inhibition, resetting of DDD pacemakers, and transient reed switch malfunction with asynchronous pacing. Serious malfunction with no output or rapid pacing may occur because pulsed energy from MRIs can enter the lead by capacitive coupling and cause rapid ventricular pacing. All CIEDs being exposed to MRIs should be checked before and after MRI scanning.

Jung W, Jäckle S, Zvereva V. MRI and implantable cardiac electronic devices. *Curr Opin Cardiol*. 2015;30(1):65–73.

Roguin A, Schwitter J, Vahlhaus C, et al. Magnetic resonance imaging in individuals with cardiovascular implantable electronic devices. *Europace*. 2008;10:336–346.

Santini L, Forleo GB, Santini M, et al. Evaluating MRI-compatible pacemakers: patient data now paves the way to widespread clinical application? *Pacing Clin Electrophysiol*. 2013;36(3):270–278.

Zipes DP, Libby P, Bonow RO, et al, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 11th ed. Philadelphia, PA: Elsevier; 2019:780–799.

C. Intraoperative Management

C.1. How would you monitor this patient?

Intraoperative monitoring should include both continuous ECG and continuous peripheral pulse monitoring. Peripheral pulse can be monitored by palpation of the pulse, auscultation of heart sounds, pulse plethysmography or oximetry, a tracing of arterial wave form, or ultrasound peripheral pulse monitoring.

Arterial line and central venous pressure or pulmonary artery pressure monitoring may need to be used in patients with poor ventricular function. The pacing detection feature on the ECG monitor should be enabled to detect the pacing spikes. The ECG monitor should be set in diagnostic mode instead of monitoring mode.

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Crossley GH, Poole JE, Rozner MA, et al. The Heart Rhythm Society (HRS)/American Society of Anesthesiologists (ASA) expert consensus statement on the perioperative management of patients with implantable defibrillators, pacemakers and arrhythmia monitors: facilities and patient management this document was developed as a joint project with the American Society of Anesthesiologists (ASA), and in collaboration with the American Heart Association (AHA), and the Society of Thoracic Surgeons (STS). *Heart Rhythm*. 2011;8:1114–1154.

C.2. What drugs and equipment would you like to have on hand in the operating room?

A complete array of drugs and equipment must be immediately

available for cardiopulmonary resuscitation. The minimal requirements include ECG monitor, a transcutaneous external pacing and direct current (DC) defibrillator as well as the usual drugs for resuscitation.

Atlee JL, Bernstein AD. Cardiac rhythm management devices (part I): indication, device selection, and function. *Anesthesiology*. 2001;95:1265–1280.

C.3. How would you set up the transcutaneous external pacer and defibrillator?

We prefer applying defibrillating electrodes such as ZOLL® pads to paddles because the electrodes can be placed before surgery at the desired positions and connected to a defibrillator/pacemaker for pacing and defibrillation. The electrodes should be placed as far (more than 6 in. or 15 cm) from a CIED as possible. The three recommended electrode placements are as follows:

- *Anteroposterior placement*. The right arm (RA) electrode placed under the left scapula and the left leg (LL) electrode at apex of the heart (as shown in **Fig. 8.6**).
- *Apex-anterior placement*. The RA electrode placed under the right clavicle and the LL electrode at the apex of the heart (**Fig. 8.7A**).
- *Apex-posterior placement*. The RA electrode placed over the right scapula and the LL electrode at the apex of the heart (**Fig. 8.7B,C**).

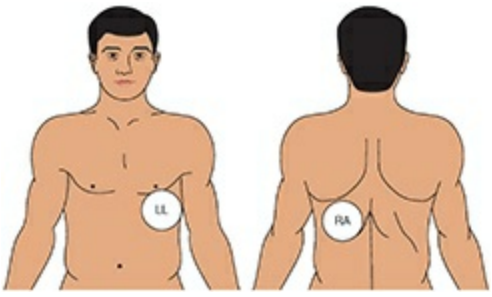

FIGURE 8.6. Anteroposterior placement of defibrillating electrodes. The right arm (RA) electrode

is placed under the left scapula, and the left leg (LL) electrode is placed at the apex of the heart.

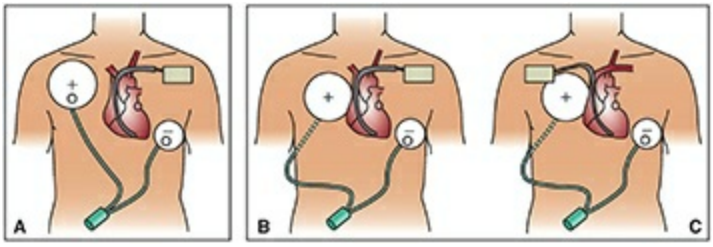

FIGURE 8.7. Placement of defibrillating electrodes. A. Apex-anterior placement with both pads placed anteriorly. **B and C.** Apex-posterior placement shown with the device in the left prepectoral region **(B)** and the right pectoral region **(C)**. (*Adapted from Ellenbogen KA, Kay GN, Wilkoff BL, eds.* Clinical Cardiac Pacing and Defibrillation. *2nd ed. Philadelphia, PA: Saunders; 2000:944. Copyright © 2000 Elsevier. With permission.*)

It is important to remember that the presence of a CIED should not deter standard resuscitation efforts.

Stone KR, McPherson CA. Assessment and management of patients with pacemakers and implantable cardioverter defibrillator. *Crit Care Med*. 2004;32(suppl 4):S155–S165.

C.4. Had this patient's ICD been implanted the day before surgery, would you consider avoiding certain inhalational gases for anesthesia?

It has been reported that nitrous oxide could cause pacemaker malfunction by increasing gas in the prepectoral pacemaker pocket. Despite air evacuation with antibiotic solution before closure of the prepectoral pocket, a small amount of air remains entrapped in the pocket. In general, this small amount of air should have no clinical significance. Nitrous oxide is 35 times more soluble in blood than nitrogen. When nitrous oxide is used for anesthesia, the amount of nitrous oxide diffused from blood to the air pocket is much more than the amount of nitrogen diffused from the air pocket to blood. Therefore, this causes an expansion of the gas in the pocket that leads to loss of anodal contact and pacing system malfunction. It is advisable not to use nitrous oxide in a patient with a newly implanted pacemaker.

Lamas GA, Rebecca GS, Braunwald NS, et al. Pacemaker malfunction after nitrous oxide anesthesia. *Am J Cardiol*. 1985;56:995.

C.5. Electromagnetic interference (EMI) from electrocautery results in significant noise on your cardiac monitor. You recall that EMI also can inhibit pacing function from the PPM. In this pacemaker-dependent patient, how can you determine whether inappropriate inhibition of the PPM is occurring?

During electrocautery, the ECG is frequently useless because of interference. The best monitor available to determine if inhibition is taking place is a hand on the pulse. The precordial or esophageal stethoscope, pulse oximeter, or blood pressure is also acceptable.

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C.6. What are the potential responses of pacemakers and ICDs to electrocautery?

The responses of pacemakers to electrocautery or other EMI include the following:

- Inhibition of pacing
- Asynchronous pacing
- Reset to backup mode
- Myocardial burns, rare
- Ventricular fibrillation, rare

The responses of ICDs include the following:

- Inhibition of pacing
- Asynchronous pacing
- Inappropriate tachy therapy

- Inhibition of tachy therapy

Salukhe TV, Dob D, Sutton R. Pacemakers and defibrillators: anaesthetic implications. *Br J Anaesth*. 2004;93:95–104.

Stone KR, McPherson CA. Assessment and management of patients with pacemakers and implantable cardioverter defibrillator. *Crit Care Med*. 2004;32(suppl 4):S155–S165.

C.7. How would you prevent the effects of EMI on the pacemaker or ICD from the electrocautery?

The safest way to prevent intraoperative EMI response is appropriate reprogramming. The following precautions should be taken to minimize the effects of electrocautery:

- Place the cautery grounding plate as close to the operative site and as far from the CIED as possible to make sure that the current pathway does not pass through or near the CIED system. For some cases, the grounding plate might need to be placed on a site different from the thigh (e.g., the superior posterior aspect of the shoulder contralateral to the CIED generator position for a head and neck case).
- Do not use cautery within 15 cm of the pacemaker because it may interfere with the battery circuitry. If in contact with a break in the insulation of the electrode, it may cauterize the myocardium at the electrode tip, rendering it insensitive to pacing impulses.
- Limit cautery use to 1-second bursts every 10 seconds to prevent repetitive asystolic periods (if possible).
- If the pacemaker is inhibited by the cautery, place a high-powered magnet over the demand nonprogrammable pacemaker to convert it to fixed-rate mode.
- Using bipolar electrocautery forceps or ultrasonic (harmonic) scalpel reduces EMI.

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pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices. *Anesthesiology*. 2011;114:247–261.

Salukhe TV, Dob D, Sutton R. Pacemakers and defibrillators: anaesthetic implications. *Br J Anaesth*. 2004;93:95–104.

Stone KR, McPherson CA. Assessment and management of patients with pacemakers and implantable cardioverter defibrillator. *Crit Care Med*. 2004;32(suppl 4):S155–S165.

C.8. What are the effects of a magnet on pacemakers and ICDs?

The effect of placing a magnet over a pacemaker or ICD can vary quite considerably depending on the device manufacturer, model, and individual programmed modes. This information may be obtained by consulting the device manufacturer's representative. Most pacemakers will switch to a fixed-rate pacing mode when a magnet is placed. The exception to this is that the Micra leadless pacemaker will not respond to the magnet by pacing asynchronously.

The response of an ICD to magnet placement is different from the response of a pacemaker. Magnets will disable tachyarrhythmia detection and therapy that, except in some Boston Scientific devices, are reenabled when the magnet is removed. Magnets generally will, with a few exceptions, not affect the pacing mode or rate of ICDs. Therefore, the pacemaker in an ICD can be inappropriately inhibited by electrocautery even when a magnet is placed.

It is important to remember that some early generation Boston Scientific ICDs are permanently disabled when a magnet is placed for more than 30 seconds. The ICD will not be reactivated when the magnet is removed. To reactivate the Boston Scientific ICDs, the magnet has to be reapplied over the ICD for more than 30 seconds and then removed. If a magnet is to be used during surgery, the magnet effects should be tested in

the operating room before surgery to ensure that the desired effects will occur during surgery.

Crossley GH, Poole JE, Rozner MA, et al. The Heart Rhythm Society (HRS)/American Society of Anesthesiologists (ASA) expert consensus statement on the perioperative management of patients with implantable defibrillators, pacemakers and arrhythmia monitors: facilities and patient management this document was developed as a joint project with the American Society of Anesthesiologists (ASA), and in collaboration with the American Heart Association (AHA), and the Society of Thoracic Surgeons (STS). *Heart Rhythm*. 2011;8:1114–1154.

Salukhe TV, Dob D, Sutton R. Pacemakers and defibrillators: anaesthetic implications. *Br J Anaesth*. 2004;93:95–104.

C.9. In the middle of surgery, the patient developed ventricular tachycardia. What would you do?

For a patient with an ICD and magnet-disabled therapies:

- Advise the surgeon performing the procedure to terminate all sources of EMI.
- Remove the magnet to reenable antitachycardia therapies.
- Observe the patient and the monitors for appropriate CIED therapy. This can be delayed for as long as 10 to 12 seconds as the ICD is charging.
- If the activities mentioned in the preceding text do not restore ICD function, proceed with emergency external defibrillation.

For a patient with an ICD and programming-disabled therapies:

- Advise individual performing the procedure to terminate all sources of EMI while magnet is removed.
- Reenable therapies through programming if the programmer is immediately available and ready to be used.
- Observe the patient and the monitors for appropriate CIED therapy.
- If the activities mentioned in the preceding text do not restore ICD function, proceed with emergency external

defibrillation.

For external defibrillation (see also section C.3):

- Position defibrillation/cardioversion pads or paddles as far as possible from the CIED generator.
- If it is technically impossible to place the pads or paddles in locations that help to protect the CIED, defibrillate/cardiovert the patient in the quickest possible way and be prepared to provide pacing through other routes.
- Use a clinically appropriate energy output.

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C.10. What precautions should be taken when a patient with a CIED is undergoing extracorporeal shock wave lithotripsy (ESWL)?

ESWL is no longer contraindicated for patients with pacemakers. The only exception to this general statement is the abdominally placed pacemaker generators. Because these generators are in the blast path of the shock wave, such patients should not be treated with ESWL. Nevertheless, most transvenous pacemaker generators are placed in a pectoral location that is at a safe distance from the blast path. Consider preoperative disabling of atrial pacing if the lithotripsy system triggers on the R wave. Avoid focusing the lithotripsy beam near the pulse generator.

Although most pacemakers are not affected by ESWL, sometimes it may cause pacemaker malfunctions that include the following:

- Switching to magnet mode
- Reaching upper rate limit

- Pacing irregularity
- Oversensing of asynchronous shocks
- Damage to rate-sensing piezoelectric crystal
- Intermittent inhibition of ventricular output in dual-chamber pacemaker
- EMI

There may be a rate increase in a rate-response (adaptive) pacemaker after ESWL shocks. Therefore, special precautions should be taken preoperatively. The type of pacemaker, indications for its placement, degree of patient dependence, and pacemaker programmability must be determined before lithotripsy. A dedicated pacemaker programmer should be available in the lithotripsy suite should pacemaker malfunction be caused by the shock waves. In addition, an alternative means of pacing, such as transcutaneous pacing, should also be available in case the pacemaker becomes permanently damaged. Low-energy shock waves (less than 16 kV) should be used initially; then the energy level is gradually increased while pacemaker function is monitored carefully. It is best to disable tachycardia detection of an ICD during ESWL and to thoroughly test the ICD following the procedure.

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C.11. Is electroconvulsive therapy (ECT) contraindicated in patients with pacemakers or ICDs?

It is advisable to consult with the ordering physician, the patient's cardiologist, a cardiac rhythm management device service, or the device manufacturer. ECT appears safe for patients with pacemakers or ICDs because little current flows

within the heart due to the high impedance of body tissues. Nevertheless, the seizure and succinylcholine fasciculations may generate sufficient myopotentials for pacemaker inhibition (unipolar devices) or ventricular tracking (adaptive-rate devices). Therefore, it is advisable to program the pacemaker to a nonsensing (asynchronous) mode for pacemaker-dependent patients either by reprogramming prior to the procedure or using a magnet during the case. It is also important to keep in mind that a magnet placed over an ICD will only disable tachytherapies and will not cause the ICD to pace asynchronously. An external pacemaker should also be available. Current guidelines also suggest that all ICDs should be programmed so that tachycardia detection is disabled before ECT and reprogrammed to its original programmed parameters prior to discharge.

American Society of Anesthesiologists. Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices. *Anesthesiology*. 2011;114:247–261.

C.12. What precautions should be taken during radiofrequency ablation for a patient with a CIED?

- Avoid contact of radiofrequency catheter with the CIED generator and leads.
- Radiofrequency current path as far away from the CIED generator and leads as possible.
- Discuss these concerns with the operator.

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C.13. During surgery, the patient developed frequent premature ventricular complexes and some of these resulted in rapid ventricular pacing (see Fig. 8.8). What is accounting for the pacemaker's behavior?

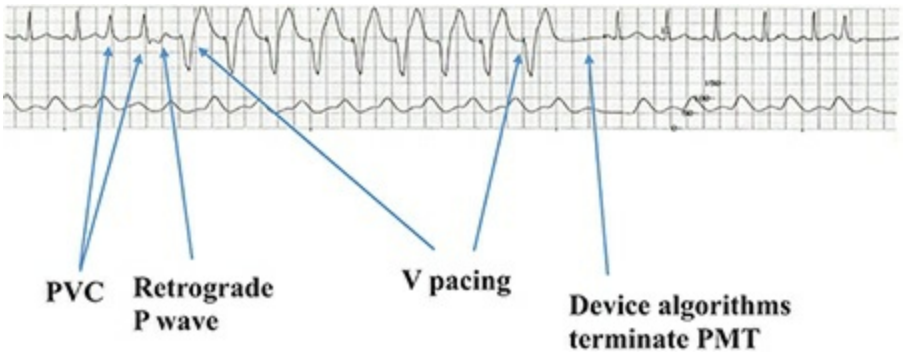

FIGURE 8.8. Rhythm strip of pacemaker-mediated tachycardia (PMT). Premature ventricular complexes (PVCs) are seen initially followed by a run of wide complex tachycardia with each QRS complex preceded by a pacing spike suggesting ventricular (V) pacing. This phenomenon occurs because the PVCs conducted through the atrioventricular node in a retrograde fashion and resulted in an atrial sensed event that the DDD device detects. Because of the DDD programming, ventricular pacing is triggered and the paced ventricular beat perpetuates the cycle by conducting through the atrioventricular node again in a retrograde fashion and resulting in another atrial sensed event. The tachycardia eventually terminates because the device has an anti-PMT algorithm.

Ventricular ectopy can often interfere with proper functionality of a dual-chamber pacemaker or defibrillator. In many instances, premature ventricular complexes can conduct retrograde up the AV node and result in atrial sensed events that are detected by the atrial lead. Depending on when this occurs, a dual-chamber pacemaker programmed to DDD may track this and trigger ventricular pacing, thus resulting in what is often termed *pacemaker-mediated tachycardia* (**Fig. 8.8**).

Current devices are equipped with algorithms that can limit the duration of these episodes. During surgery, it is important to be aware of this phenomenon and not mistake these runs of pacing induced wide complex tachycardia as ventricular tachycardia. Look for pacing spikes in front of the wide complex beats as a quick way to determine if they are being caused by

pacing.

Ellenbogen KA, Kaszala K, eds. *Cardiac Pacing and ICDs*. 6th ed. Hoboken, NJ: Wiley Blackwell; 2014:211–271.

D. Postoperative Management

D.1. How would you monitor this patient in the postanesthesia care unit?

Cardiac rate and rhythm should be continuously monitored throughout the immediate postoperative period. Backup pacing capability and cardioversion-defibrillation equipment should be immediately available at all times.

American Society of Anesthesiologists. Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices. *Anesthesiology*. 2011;114:247–261.

Crossley GH, Poole JE, Rozner MA, et al. The Heart Rhythm Society (HRS)/American Society of Anesthesiologists (ASA) expert consensus statement on the perioperative management of patients with implantable defibrillators, pacemakers and arrhythmia monitors: facilities and patient management this document was developed as a joint project with the American Society of Anesthesiologists (ASA), and in collaboration with the American Heart Association (AHA), and the Society of Thoracic Surgeons (STS). *Heart Rhythm*. 2011;8:1114–1154.

D.2. How would you confirm that the CIED is functioning properly after surgery?

Postoperative interrogation and restoration of CIED function are basic elements of postoperative management. But given the robustness of modern devices, not all CIEDs require postoperative interrogation before discharge, especially in cases in which the EMI is remote from the device system. CIEDs that should be interrogated postoperatively before discharge include

the following:

- CIEDs that were reprogrammed or deactivated before surgery so that baseline settings can be restored
- Patients who underwent hemodynamically embarrassing surgeries such as cardiac surgery or significant vascular surgery
- Patients who experienced significant intraoperative events, including cardiac arrest, requiring temporary pacing or cardiopulmonary resuscitation, and/or tachyarrhythmias requiring external electrical cardioversion during surgery

All other individuals should have their devices evaluated as an outpatient within the next 3 months.

American Society of Anesthesiologists. Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices. *Anesthesiology*. 2011;114:247–261.

9 Thoracic and Thoracoabdominal Aortic Aneurysms

Yong Zhan, Frederick C. Cobey, Sharon L. McCartney, Madhav Swaminathan, and Jamel Ortoleva

A 68-year-old man presents for surgical repair of a thoracoabdominal aortic aneurysm (TAAA). He has a significant past medical history that includes a type A aortic dissection (TAAD) 12 years ago, for which he underwent a Bentall repair; poorly controlled hypertension; chronic obstructive pulmonary disease (COPD); tobacco use (45 pack-years); and stage III chronic kidney disease (CKD). His type A dissection event was complicated by end-organ ischemia, including ischemic colitis and renal failure. He has been undergoing routine surveillance of his aorta, and computed tomography (CT) reveals his aortic aneurysm has recently enlarged to 5.5 cm starting at the innominate artery and extending into the abdominal aorta, proximal to the renal arteries. Chest radiograph demonstrates thoracic aortic aneurysmal dilation, without compression of surrounding structures. Transthoracic echocardiogram demonstrates normal left and right ventricular function, trivial aortic insufficiency (AI), and trivial mitral insufficiency. Laboratory studies indicate a hemoglobin of 14.5 g per dL, hematocrit 44%, blood urea nitrogen (BUN) 22 mg per dL, and

creatinine 1.8 mg per dL.

A. Pathophysiology and Differential Diagnosis

1. What is a thoracic aortic aneurysm (TAA) and TAAA, and how do they typically present?
2. How are TAAs and TAAAs classified?
3. What is the pathogenesis of aortic aneurysms and what genetic conditions predispose to their formation?
4. What are the risk factors for TAA rupture?
5. What is the natural history and medical management of thoracic aneurysms?
6. What is a thoracic aortic dissection, and how does it typically present?
7. How are thoracic aortic dissections classified?

B. Preoperative Evaluation and Preparation

1. What are the indications and timing of surgical intervention for TAAs?
2. Which patients are candidates for endovascular aortic repair, and what are the advantages to this approach?
3. What are the preoperative considerations for the anesthesiologist before TAA repair?
4. What is the preoperative management of a patient presenting with an acute aortic dissection (AAD)?
5. What is the spinal cord blood supply?

C. Intraoperative Management

1. What are the surgical approaches to thoracic aneurysm repair?
2. How is the open repair performed?
3. How are endovascular repairs of TAAAs performed?
4. What are the surgical approaches to aortic dissections?
5. What are the specific considerations for anesthetic management of the patient presenting for open TAAA repair?

6. What are the specific considerations for anesthetic management of the patient presenting for endovascular TAAA repair?
7. What hemodynamic monitors should be used for the patient undergoing thoracic aneurysm repair?
8. What strategies are used for spinal cord protection during a TAAA repair?
9. What strategies are used for mesenteric and renal preservation?
10. What is the pathophysiology of aortic clamping and unclamping?
11. Why does a coagulopathy ensue and how is it prevented/treated?

D. Postoperative Anesthetic Management

1. What are the postoperative complications after open TAAA repair?
2. What are the postoperative complications after endovascular TAAA repair?

A. Pathophysiology and Differential Diagnosis

A.1. What is a thoracic aortic aneurysm (TAA) and TAAA, and how do they typically present?

TAAs and TAAAs are abnormal dilations of the thoracic and/or abdominal aorta to greater than 150% of its expected diameter. They can occur at any point along the aorta, including the root, ascending, arch, and descending portions with occasional extension into branching vessels. The dimensions that define normal aortic size are determined by patient age, gender, and body surface area.

One of the greatest challenges in the care of patients with thoracic aortic disease is identifying them prior to the onset of a catastrophic aortic event. Despite their propensity for life-

threatening complications, TAAs are often clinically silent and are often diagnosed during imaging for an unrelated disorder. When symptoms do occur, they are often nonspecific, and diagnosis requires a high index of clinical suspicion. Symptoms of TAAs frequently result from compression of adjacent structures. Patients may exhibit hoarseness from recurrent laryngeal nerve compression, stridor from bronchial or tracheal compression, dyspnea from lung compression, dysphagia from esophageal compression, and/or facial edema from superior vena cava (SVC) compression. Pain in the neck, jaw, back, shoulders, or abdomen may also be present. Additionally, new-onset heart failure symptoms may occur as aortic enlargement results in progressive AI (**Fig. 9.1**).

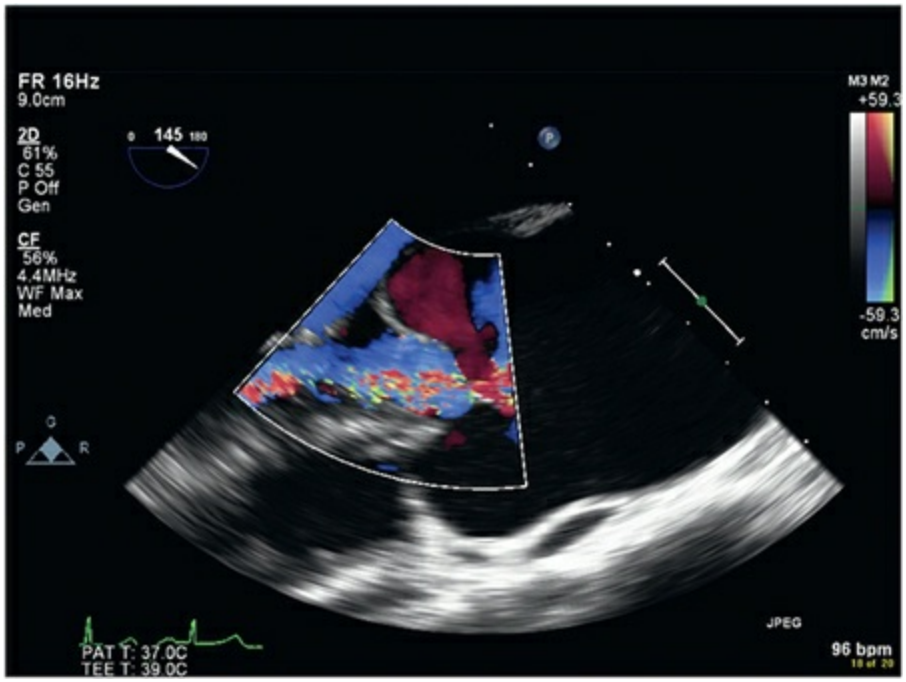

FIGURE 9.1. Midesophageal AV long-axis view on TEE demonstrating moderate central AI secondary to aortic root and ascending aortic dilatation in a young woman with Turner syndrome.

Once identified, dedicated imaging with either CT (**Fig. 9.2**) or magnetic resonance imaging (MRI) should be undertaken to delineate the extent of the aneurysm, its maximum dimension,

branch vessel involvement, and the presence or absence of a coexisting intramural hematoma or penetrating aortic ulcer. Transesophageal echocardiography (TEE) is also performed to assess for valvular disease, evaluate cardiac function, and more carefully assess the anatomy of the aortic root (**Fig. 9.3**).

FIGURE 9.2. Three-dimensional (3D) CT reconstruction demonstrating a thoracoabdominal aneurysm that begins in the descending thoracic aorta and extends to the infrarenal aorta, above the bifurcation into the iliac arteries. Also seen is a chronic type B aortic dissection.

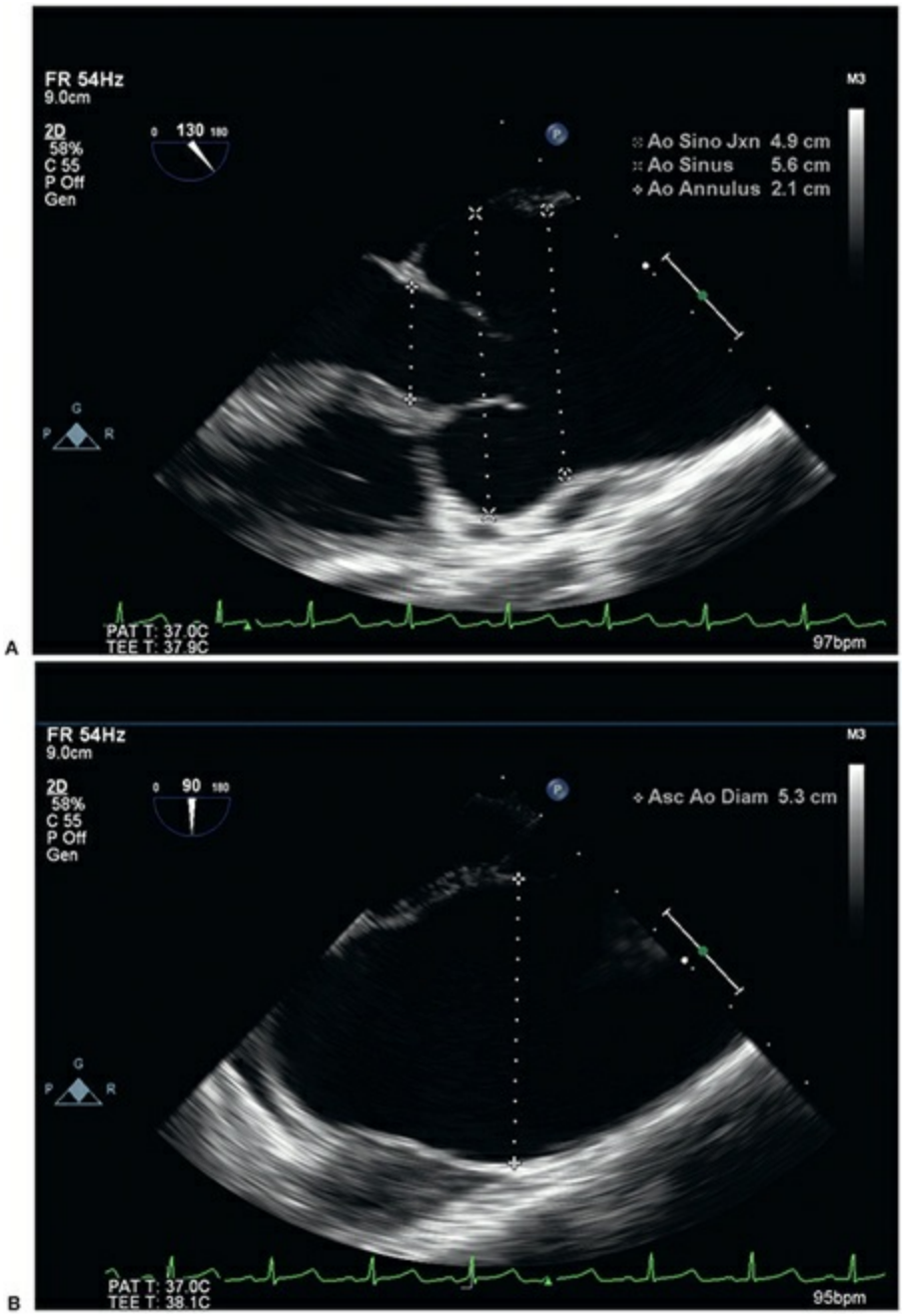

FIGURE 9.3. **A.** Midesophageal AV long-axis view on TEE demonstrating AV annulus, sinus, and sinotubular junction dimensions at mid-systole. **B.** Ascending aorta in short axis demonstrating aneurysmal enlargement with a diameter of 5.3 cm in a young woman with Turner syndrome.

Booher AM, Eagle KA. Diagnosis and management issues in thoracic aortic aneurysm. *Am Heart J*. 2011;162:38.e1–46.e1.

Hiratzka LF, Bakris GL, Beckman JA, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease. A report of the American College of Cardiology Foundation/American Heart Association

Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. *J Am Coll Cardiol*. 2010;55(14):e27–e129.

A.2. How are TAAs and TAAAs classified?

TAAs do not follow a specific classification system but are described by the extent of the aorta that is involved, including the aortic root, ascending aorta, aortic arch, and descending thoracic aorta. TAAAs are described using the modified Crawford classification, which subdivides TAAAs into five types according to the extent of the surgical repair required (**Fig. 9.4**).

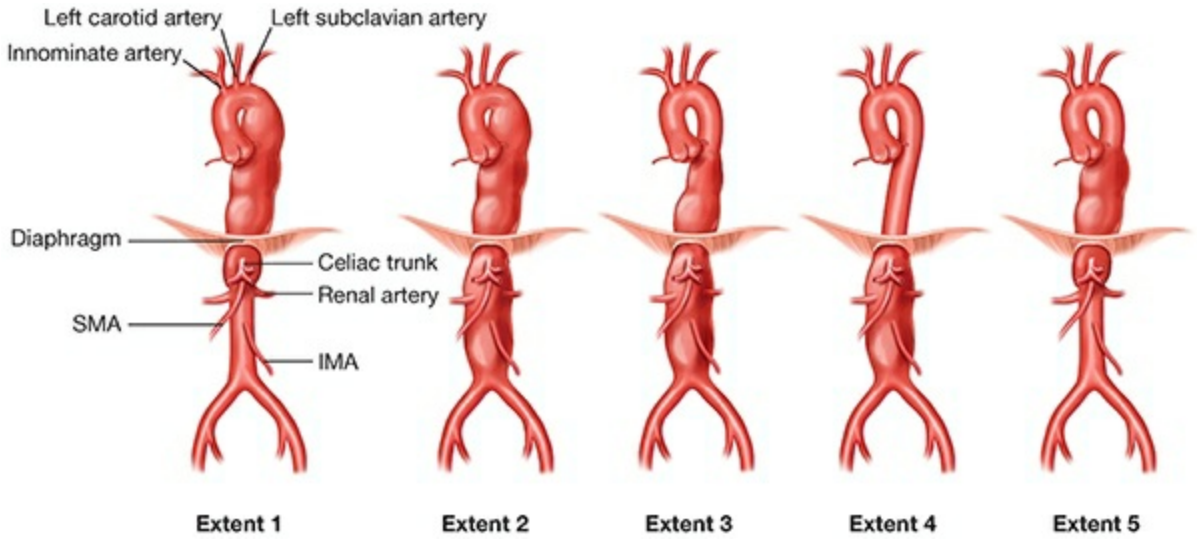

FIGURE 9.4. The modified Crawford classification of TAAAs. (*Reprinted with permission from Bolman R, Kaneko T. Open thoracoabdominal aneurysm repair. In: Darling RC, Ozaki CK, eds.* Vascular Surgery: Arterial Procedures. *Philadelphia, PA: Wolters Kluwer; 2016:74.*)

- *Type I* begins distal to the left subclavian artery and extends down below the diaphragm to above the renal arteries.
- *Type II* begins distal to the left subclavian above the sixth intercostal space. It extends through the diaphragm and ends below the renal arteries.
- *Type III* begins below the sixth intercostal space but above

the diaphragm. It extends below the renal arteries.

- *Type IV* begins below the diaphragm but above the renal arteries, with extension to below the renal arteries.
- *Type V* begins above the diaphragm and ends above the renal arteries.

Crawford ES, Crawford JL, Safi HJ, et al. Thoracoabdominal aortic aneurysms: preoperative and intraoperative factors determining immediate and long-term results of operations in 605 patients. *J Vasc Surg*. 1986;3:389–404.

Frederick JR, Woo YJ. Thoracoabdominal aortic aneurysm. *Ann Cardiothorac Surg*. 2012;1(3):277–285.

Hoel AW. Aneurysmal disease: thoracic aorta. *Surg Clin North Am*. 2013;93:893–910.

A.3. What is the pathogenesis of aortic aneurysms and what genetic conditions predispose to their formation?

TAAs primarily arise from focal degeneration of the elastic and muscular tissue of the aortic wall. The resulting tissue weakness predisposes the wall to dilate under the stress of high pressures within the aorta. The dilation of the aorta is associated with decreased vessel wall compliance, increased wall stress, and a propensity for subsequent rupture of the aneurysm. Although the majority of TAAs follow a degenerative pattern, there are a number of congenital disease processes that are associated with aneurysm formation.

Marfan syndrome (MFS) is an autosomal dominant disorder caused by a mutation in the fibrillin-1 gene. Patients with MFS have characteristic overgrowth of the long bones of the arms and legs, increased finger length (arachnodactyly), and joint laxity. They can also demonstrate ocular abnormalities, most commonly lens dislocation. In addition to the musculoskeletal and ocular manifestations of MFS, patients are also at increased risk of aortic root dilation, ascending and descending aortic

aneurysms, and aortic dissection. Valvular disease can also be present, with mitral regurgitation and associated pulmonary hypertension being the most common cause of MFS-related infant mortality. On a molecular level, mutations in the fibrillin-1 gene result in disordered formation of the microfibril matrix, leading to disruption of the elasticity of the aorta. More recent evidence suggests that excessive transforming growth factor β (TGF-β) signaling also plays a role in the clinical phenotype of MFS.

Vascular Ehlers-Danlos syndrome (vEDS) is the result of mutation in the COL3A1 gene coding for type III procollagen. Mutations in type III procollagen can result in a number of complications, including spontaneous intestinal or uterine rupture, fragile skin, and vascular dissection. Children may also present with inguinal hernias, pneumothoraces, or recurrent joint dislocations. Although diagnosis is often made clinically, many patients are only diagnosed after a major arterial or gastrointestinal event.

Loeys-Dietz syndrome (LDS) is a heterogeneous disease stemming from mutations in either the TGFBR1 or TGFBR2 gene, resulting in a relative increase in TGF-β signaling. LDS presents with characteristic craniofacial, skeletal, and cardiovascular anomalies with a broad range of phenotype. Because patients with milder disease exhibit limited skeletal features and no typical ophthalmologic manifestations of the disease, the diagnosis is often made within a family after a significant aortic event. These patients are also at risk for complicated cerebral aneurysms, and imaging of all major arterial structures is recommended after diagnosis.

Turner syndrome is a genetic disorder characterized by the lack of an X-chromosome in a female patient (45, X). Women with Turner syndrome are often short in stature, have dysfunctional ovaries, and are at increased risk of cardiovascular

disease. Bicuspid aortic valve (AV) disease is present in between 10% and 25% of women with Turner syndrome, and approximately 8% have coarctation of the aorta. The risk of AAD is also increased in women with Turner syndrome and tends to occur at a younger age and smaller aortic diameter than the general population.

Less common genetic etiologies of thoracic and thoracoabdominal aortic disease include mutations in the MYH11, ACTA2, MYLK, SLC2A10, or SMAD3 gene. Despite progress in discerning the genetic mechanisms of familial TAAs, up to 80% are without a clear molecular etiology.

There are a number of rheumatologic diseases that may affect the thoracic aorta. Takayasu arteritis, giant cell arteritis, Behçet disease, and ankylosing spondylitis have all been demonstrated to contribute to the development of aneurysmal dilation of the aorta with varying degrees of frequency.

Patients may also develop aneurysms with an infectious etiology, although this is rare. There are several mechanisms by which this can occur, including direct spread from adjacent structures, septic embolic events from bacterial endocarditis, and hematogenous seeding of the aorta from bacteremia. Although most infections are caused by bacteria, immunosuppressed patients are also susceptible to fungal and mycobacterial infection. Interestingly, HIV infection also appears to be associated with an increased risk of TAA formation.

Finally, patients with a *bicuspid AV* have a markedly increased risk of TAA formation. Aortic dilation in bicuspid AV disease most commonly involves enlargement of the ascending aorta in addition to dilation of the aortic root (**Fig. 9.5**). Risk factors for aneurysm development include older age, male sex, systolic hypertension, valve stenosis or regurgitation, and the specific morphology of the valve itself. Although a specific unifying gene remains elusive, bicuspid aortic disease

demonstrates familial inheritance.

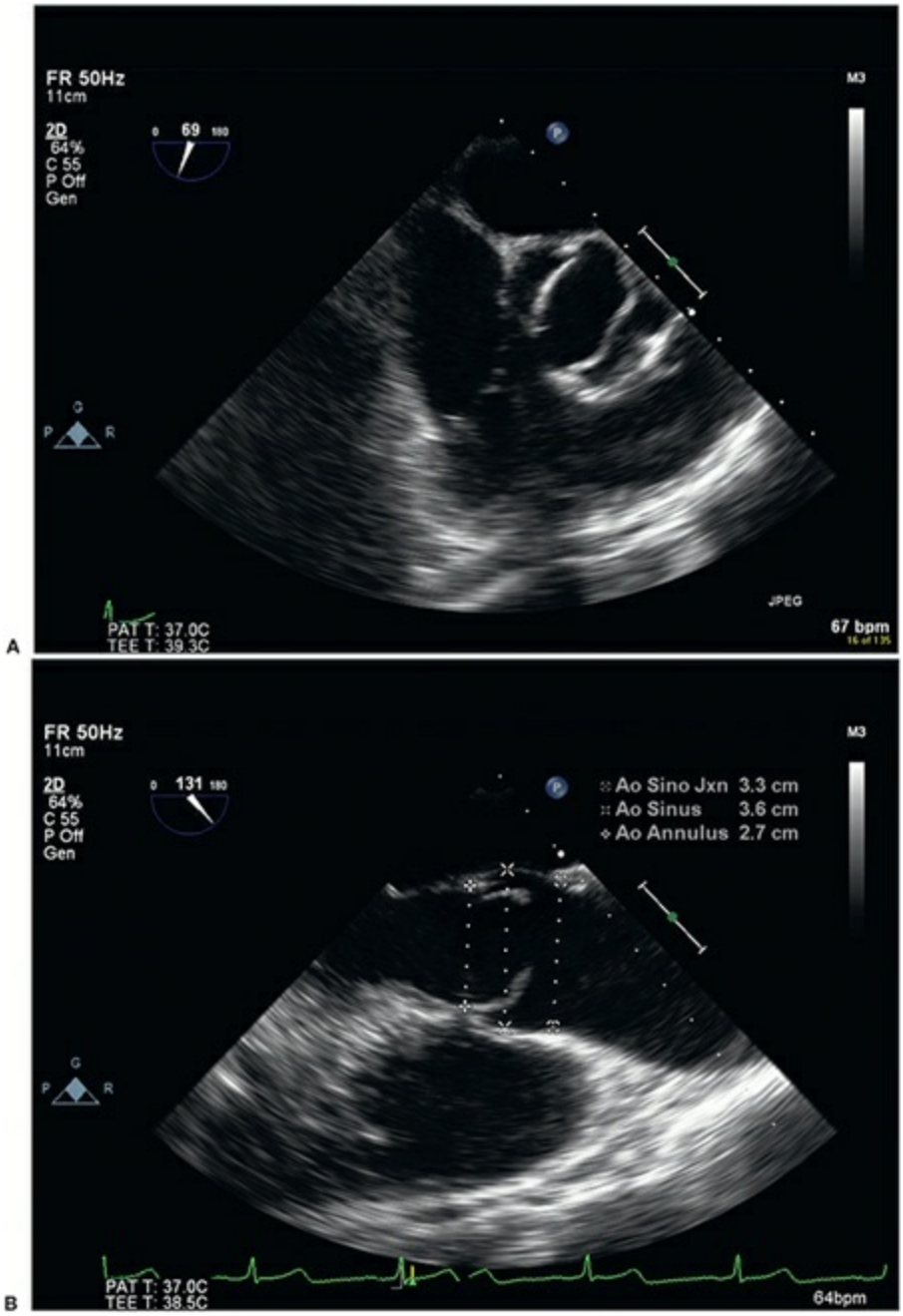

FIGURE 9.5. **A.** Midesophageal AV short-axis view on TEE showing a bicuspid valve, with fusion of the left and right coronary cusps. **B.** Midesophageal AV long-axis view on TEE demonstrating the characteristic doming of a stenotic bicuspid AV and blunting of the sinotubular junction due to aortic root (ascending aortic) dilatation.

Boodhwani M, Andelfinger G, Leipsic J, et al. Canadian Cardiovascular Society position statement on the management of thoracic aortic disease. *Can J Cardiol*. 2014;30:577–589.

Hoel AW. Aneurysmal disease: thoracic aorta. *Surg Clin North Am*. 2013;93:893–910.

Jondeau G, Boileau C. Genetics of thoracic aortic aneurysms. *Curr Atheroscler Rep*. 2012;14:219–226.

Jones JA, Ikonomidis JS. The pathogenesis of aortopathy in Marfan syndrome and related diseases. *Curr Cardiol Rep*. 2010;12:99–107.

Pomianowski P, Elefteriades JA. The genetics and genomics of thoracic aortic disease. *Ann Cardiothorac Surg*. 2013;2(3):271–279.

Ramanath VS, Oh JK, Sundt TM III, et al. Acute aortic syndromes and thoracic aortic aneurysm. *Mayo Clin Proc*. 2009;84(5):465–481.

Verma S, Siu SC. Aortic dilatation in patients with bicuspid aortic valve. *N Engl J Med*. 2014;370:1920–1929.

A.4. What are the risk factors for TAA rupture?

The size of a TAA is the most important predictor of rupture (**Table 9.1**). For every 1 cm increase in aneurysm diameter, the risk of rupture roughly doubles. The "hinge point" at which the risk of rupture increases dramatically is approximately 6 cm in diameter for ascending aneurysms and 7 cm for descending aneurysms, although 31% and 43%, respectively, of patients will have experienced rupture or dissection by the time they reach this point. Patients with COPD, advanced age, and symptomatic aneurysms appear to have an increased risk of rupture. Although women tend to develop TAAs later in life, they appear to also have an increased risk of aneurysm rupture relative to their male counterparts.

TABLE 9.1 Annual Rate of Rupture for Thoracic Aortic Aneurysms

Size of Aneurysm	Annual Rate of Rupture
<5 cm	2%
5–5.9 cm	3%
>6 cm	7%

Chau KH, Elefteriades JA. Natural history of thoracic aortic aneurysms: size matters, plus moving beyond size. *Prog Cardiovasc Dis*. 2013;56:74–80.

Davies RR, Goldstein LJ, Coady MA, et al. Yearly rupture or dissection rates

for thoracic aortic aneurysms: simple prediction based on size. *Ann Thorac Surg*. 2002;73:17–27.

Elefteriades JA. Natural history of thoracic aortic aneurysms: indications for surgery, and surgical versus nonsurgical risks. *Ann Thorac Surg*. 2002;74:S1877–S1880.

Frederick JR, Woo YJ. Thoracoabdominal aortic aneurysm. *Ann Cardiothorac Surg*. 2012;1(3):277–285.

A.5. What is the natural history and medical management of thoracic aneurysms?

The location and etiology of thoracic and thoracoabdominal aneurysms determines their rate of growth and subsequent propensity for rupture. Ascending TAAs typically grow at a rate of 0.1 cm per year, whereas descending aneurysms grow slightly faster at 0.3 cm per year. The rate of growth is greater in patients with larger aneurysms, dissected aortas, and certain familial causes of TAA. The aortic size is a strong predictor of the risk of complications, with a marked increase in risk profile as the aneurysm increases to greater than 6 cm.

Medical therapy to slow aneurysm growth or to reduce the risk of dissection or rupture has only been modestly successful thus far. Initial therapy consists of lifestyle modifications including smoking cessation and minimization of heavy lifting to avoid significant spikes in systolic blood pressure, which may precipitate rupture or aortic dissection.

Despite a relative paucity of clinical evidence, β-blocker therapy is often prescribed with the goal of reducing the rate of aortic dilatation by decreasing left ventricular contractility and subsequently decreasing shear stress. Although this has been demonstrated to be beneficial in patients with MFS, evidence for its use in the broader population of patients with TAAs is still lacking.

Statins have also recently been shown to be beneficial in the medical management of TAAs, with patients receiving statin

therapy showing a slower rate of aneurysmal growth, a smaller percentage requiring surgery, and a decrease in the overall number of adverse events.

Angiotensin receptor blockade has shown promise in the murine model of MFS, with a small human study showing a decrease in the rate of aneurysmal growth. This data formed the basis for the ongoing MARFANSARTAN trial (study of the efficacy of losartan on aortic dilatation in patients with MFS). Current recommendations suggest aggressive blood pressure reduction with β-blockers and angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers to the lowest level that patients can tolerate without adverse effects.

Brooke BS, Habashi JP, Judge DP, et al. Angiotensin II blockade and aortic-root dilation in Marfan's syndrome. *N Engl J Med*. 2008;358:2787–2795.

Chau KH, Elefteriades JA. Natural history of thoracic aortic aneurysms: size matters, plus moving beyond size. *Prog Cardiovasc Dis*. 2013;56:74–80.

Danyi P, Elefteriades JA, Jovin IS. Medical therapy of thoracic aortic aneurysms. *Trends Cardiovasc Med*. 2012;22(7):180–184.

Devereux RB, Roman MJ. Aortic disease in Marfan's syndrome. *N Engl J Med*. 1999;340:1358–1359.

Stein LH, Berger J, Tranquilli M, et al. Effect of statin drugs on thoracic aortic aneurysms. *Am J Cardiol*. 2013;112(8):1240–1245.

A.6. What is a thoracic aortic dissection, and how does it typically present?

An AAD typically develops when a tear in the intimal layer of the aorta permits blood to enter into the medial layer, creating a false lumen that may rapidly expand both proximally and distally (**Fig. 9.6**). This can cause ischemia of the brain and viscera when the vasculature supplying these organs is occluded. Proximal dissections may cause AI, cardiac ischemia from coronary artery occlusion, or accumulation of blood in the pericardium resulting in tamponade (**Fig. 9.7**). Finally, the false lumen can rupture, resulting in rapid exsanguination.

FIGURE 9.6. Midesophageal AV short-axis view on TEE demonstrating an AAD *(arrow)* that extends proximally to the AV in a young patient with MFS.

FIGURE 9.7. Transgastric midpapillary view on TEE demonstrating accumulation of blood in the posterior pericardial space *(arrow)* after AAD.

Hypertension is the most common comorbid disease in patients experiencing aortic dissection, although hyperlipidemia,

tobacco use, and cocaine use are other risk factors. Pregnancy can also increase the risk of AAD, with most women typically presenting during their third trimester or in the early postpartum period. There are several genetic conditions that increase the risk of AAD, including MFS, Ehlers-Danlos syndrome, familial aortic dissection, LDS, and annuloaortic ectasia. AAD can also occur iatrogenically during cardiac surgery, cardiac catheterization, and insertion of an intra-aortic balloon pump.

Patients typically present with the acute onset of severe chest and back pain, although this is not a universal finding. Less commonly, patients can present with abdominal pain, syncope, or symptoms of limb or visceral malperfusion. In roughly 6% of cases, the aortic dissection is painless and presents as new-onset heart failure, stroke, or syncope. These patients tend to be diabetic, have a history of aortic aneurysm, or have a history of prior cardiac surgery. Hypertension is common on initial presentation, and the diastolic murmur of AI is present in 44% of patients with a type A dissection. Hypotension is an ominous sign and portends a poor clinical prognosis.

It is important to differentiate AAD from acute coronary syndrome (ACS) because they may have similar presentations. Symptomatically, patients with AAD typically present with acute, severe chest pain, whereas patients with ACS typically have pain that is more gradual in onset. This differentiation is important because the treatment of ACS (antiplatelet agents, anticoagulation, and occasionally thrombolytics) is potentially catastrophic in patients with an aortic dissection. AAD should be in the differential diagnosis for any patient presenting with syncope; new-onset chest, abdominal, or back pain; acute heart failure; or clinical evidence of malperfusion. The diagnosis is most commonly made via spiral CT scan or TEE, although aortography and MRI may also be used.

Ramanath VS, Oh JK, Sundt TM III, et al. Acute aortic syndromes and thoracic aortic aneurysm. *Mayo Clin Proc*. 2009;84(5):465–481.

Tsai TT, Trimarchi S, Nienaber CA. Acute aortic dissection: perspectives from the International Registry of Acute Aortic Dissection (IRAD). *Eur J Vasc Endovasc Surg*. 2009;37:149–159.

A.7. How are thoracic aortic dissections classified?

There are several systems used to classify aortic dissections that focus on anatomic or clinical factors noted on presentation (**Fig. 9.8**).

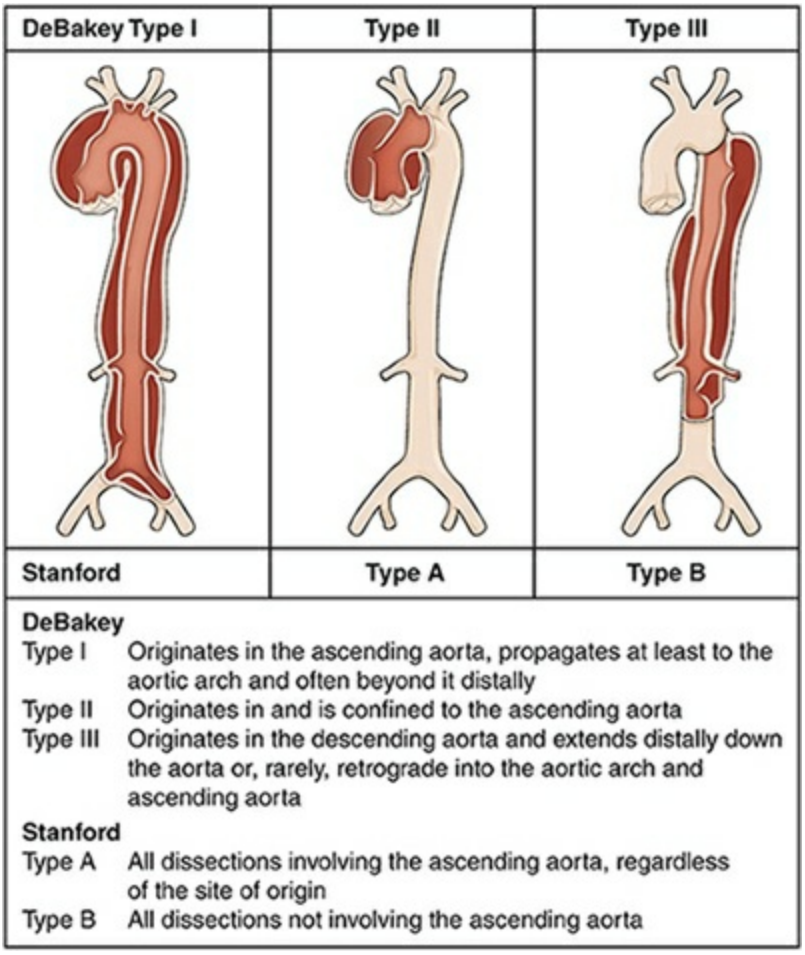

FIGURE 9.8. The Stanford and DeBakey classifications of aortic dissections. (*Reprinted with permission from Nienaber CA, Eagle KA. Aortic dissection: new frontiers in diagnosis and management: part I: from etiology to diagnostic strategies.* Circulation. *2003;108:628–635.*)

DeBakey Classification

The DeBakey classification system categorizes aortic dissections

based on their site of origin and degree of distal extension.

Type I dissection originates in the ascending aorta and propagates to at least the level of the aortic arch and often beyond, sometimes extending as distal as the iliac arteries.

Type II dissection begins in, and is limited to, the ascending aorta. Although these occur on occasion in patients with MFS, they are the rarest form of aortic dissection. Type I and type II dissections are almost always treated surgically.

Type IIIa dissection begins beyond the origin of the left subclavian artery and is limited to the descending thoracic aorta.

Type IIIb dissection begins beyond the left subclavian origin and extends more distally beyond the diaphragm. Type III dissections are often managed medically.

Stanford Classification

The Stanford classification system is similar to the DeBakey system in that it describes aortic dissections based on their anatomic site of origin.

Stanford type A aortic dissections originate in the ascending aorta and include DeBakey type I and type II dissections.

Stanford type B aortic dissections originate in the descending aorta and include DeBakey type IIIa and IIIb dissections. These may occasionally also propagate proximally into the ascending aorta or aortic arch.

A notable limitation to both the Stanford and DeBakey classification systems is their inability to classify dissections originating in the aortic arch.

Penn Classification

More recently, patients with acute Stanford TAAD have been subcategorized according to ischemic symptoms noted on presentation in what has been termed the Penn classification. This has been successfully validated as a predictor of perioperative mortality.

Penn Class Aa patients have no ischemic symptoms on presentation. This is the most common clinical finding in TAAD, encompassing approximately 60% of all patients. It is also associated with the best clinical outcome with a 30-day mortality of 3% and a 5-year cumulative survival approaching 85% in one cohort.

Penn Class Ab patients present with branch vessel malocclusion producing clinically significant organ ischemia. This includes patients presenting with stroke, paraplegia, renal dysfunction, mesenteric malperfusion, and occlusion of vascular supply to the extremities.

Penn Class Ac patients present with circulatory collapse with or without cardiac involvement. Class Ab and Ac patients have similar perioperative and long-term survival profiles.

Penn Class Abc patients present with symptoms of both local and generalized ischemia. These patients have the worst prognosis with a 30-day perioperative mortality of 40%. Most deaths are secondary to multisystem organ failure, hemorrhage, cardiac failure, or central nervous system (CNS) dysfunction.

Augoustides JG, Geirsson A, Szeto WY, et al. Observational study of mortality risk stratification by ischemic presentation in patients with acute type A aortic dissection: the Penn classification. *Nat Clin Pract Cardiovasc Med*. 2009;6:140–146.

Daily PO, Trueblood HW, Stinson EB, et al. Management of acute aortic dissections. *Ann Thorac Surg*. 1970;10:237–247.

DeBakey ME, Cooley DA, Crawford ES, et al. Aneurysms of the thoracic aorta; analysis of 179 patients by resection. *J Thorac Surg*. 1958;36:393–420.

Hiratzka LF, Bakris GL, Beckman JA, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. *J Am Coll Cardiol*.

2010;55(14):e27–e129.

Kimura N, Ohnuma T, Itoh S, et al. Utility of the Penn classification in predicting outcomes of surgery for acute type A aortic dissection. *Am J Cardiol*. 2014;113(4):724–730.

Nienaber CA, Eagle KA. Aortic dissection: new frontiers in diagnosis and management: part I: from etiology to diagnostic strategies. *Circulation*. 2003;108:628–635.

B. Preoperative Evaluation and Preparation

B.1. What are the indications and timing of surgical intervention for TAAs?

Patients diagnosed with aneurysms of the thoracic aorta require frequent surveillance to assess for aneurysmal expansion. The goal is to facilitate surgical intervention prior to the onset of aortic dissection or aneurysm rupture. Important considerations include the appropriate interval for surveillance imaging and the diameter at which surgical intervention should be recommended.

Patients diagnosed with TAAs and TAAAs should undergo initial CT or MRI to define the size and extent of the aneurysm. Follow-up surveillance imaging is typically performed 6 months after diagnosis, with continued follow-up imaging at an interval determined by the rate of growth. These aneurysms tend to grow slowly, with arch and ascending aneurysms growing 0.1 cm per year and descending aneurysms growing 0.3 cm per year.

Determining when to intervene depends on the underlying pathology, size, rate of expansion, and presence or absence of symptoms (**Table 9.2**). In patients without known connective tissue disease, surgical repair is recommended at 5.5 cm in ascending aortic aneurysms and 6.5 cm in descending aneurysms. In patients with concomitant AV disease who are scheduled to undergo AV replacement, an aneurysm should be repaired if it is greater than 4.5 cm in diameter. Patients with symptomatic aneurysms of any size should be considered for

surgical intervention. Very large and very small patients may be better managed by indexing aortic diameter to body size to determine the appropriate timing of repair.

TABLE 9.2 Guidelines for Elective Intervention in Patients with Ascending or Descending Thoracic Aortic Aneurysms

Normal aorta	5.5 cm for ascending aneurysms 6.5 cm for descending aneurysms
Normal aorta + valvular indication	4.5 cm
Marfan syndrome	5.0 cm for ascending aneurysms 6.0 cm for descending aneurysms
Marfan syndrome + pregnancy	4.0 cm
Loeys-Dietz syndrome	4.2 cm as measured by TEE 4.4–4.6 cm as measured by CT scan

CT, computed tomography; TEE, transesophageal echocardiography.

Special recommendations exist for patients with underlying connective tissue disorders because these patients tend to suffer significant aortic events at smaller aortic diameters. Patients with MFS require frequent surveillance, with CT imaging 6 months after initial diagnosis and then annually if aortic diameter is stable. More frequent imaging may be recommended with larger aneurysms (>4.5 cm) or if significant growth is noted. Earlier repair is recommended in MFS, and patients with ascending aneurysms of greater than 5 cm in diameter or descending aneurysms of greater than 6 cm in diameter should be considered for surgical intervention. MFS patients with a family history of early aortic dissection at less than 5 cm are often referred for early correction. Finally, women with MFS considering pregnancy should be counseled for elective aortic aneurysm surgery if the aorta is greater than 4 cm in diameter. After surgery on an ascending aortic aneurysm, continued surveillance with CT imaging is necessary to evaluate for the development of aneurysms of the arch and descending aorta.

Patients with LDS also represent a population requiring early

repair. Surveillance imaging is similar to patients with MFS, but operative repair is recommended earlier in the disease process. Patients with aneurysms that demonstrate an internal diameter of 4.2 cm on TEE or an external diameter of 4.4 to 4.6 cm on CT are referred for surgical intervention. Similarly, patients with a bicuspid AV with an accompanying TAA are typically repaired at 5 cm, although patients with a valvular indication for surgery are typically repaired if the aortic diameter exceeds 4.5 cm. First-degree relatives of patients with a suspected familial TAA syndrome should be screened with CT imaging at 5-year intervals.

Once the decision is made to proceed with surgery, there are several decision points that dictate the course of the operation. These include the decision to employ hypothermic circulatory arrest (HCA) or cardiopulmonary bypass (CPB) and whether to utilize an open or endovascular approach. If an endovascular approach is utilized, some patients may require additional aortic debranching procedures prior to endograft placement, depending on the extent of the aneurysm.

Overall, surgical decision making in patients with TAAs, thoracoabdominal aneurysms, and combined aneurysmal and AV disease require a careful comparison of a patient's operative risk with his or her risk of a significant aortic event. Consideration of medical comorbidities and the underlying pathology adds additional nuance to the decision of whether to undertake a surgical repair, and when that repair is recommended, what surgical technique should be utilized.

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B.2. Which patients are candidates for endovascular aortic repair, and what are the advantages to this approach?

Thoracic endovascular aortic repair (TEVAR) is a commonly used alternative to open repair. It is less invasive, and evidence suggests it is associated with lower rates of perioperative respiratory, renal, and neurologic complications, which facilitates shorter intensive care unit (ICU) and hospital stays with similar long-term outcomes. In recent years, aortic stent grafting has undergone a significant liberalization in its use for many aortic pathologies. In addition to repair of TAAs, many centers are now treating complicated type B aortic dissections (TBADs), traumatic aortic injuries, intramural hematomas, and penetrating aortic ulcers via the endovascular approach.

Determination of whether to undertake open or endovascular approach is dependent on multiple factors, including patient age, comorbidities, life expectancy, aneurysm morphology and diameter, the presence of "landing zones" of normal aorta on either side of the aneurysm, and the experience of the operating surgeon. Relative contraindications to TEVAR include mycotic aneurysms, aneurysms secondary to connective tissue disease (MFS, Ehlers-Danlos, etc.), and aneurysms extending proximal to the left subclavian artery. Connective tissue disease presents a relative contraindication due to concern for the longevity of the

endovascular repair in this patient population.

Many patients with extensive visceral involvement or multiple comorbidities now undergo "hybrid" procedures, which consist of debranching of the visceral arterial supply followed by endovascular repair of the aneurysm. Advantages of this approach include decreased visceral ischemic time, avoidance of aortic cross-clamping, and avoidance of the need for thoracotomy that accompanies an open repair.

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Svensson LG, Kouchoukos NT, Miller DC, et al. Expert consensus document on the treatment of descending thoracic aortic disease using endovascular stent-grafts. *Ann Thorac Surg*. 2008;85:S1–S41.

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B.3. What are the preoperative considerations for the anesthesiologist before TAA repair?

Surgery for TAA repair involves the potential for significant morbidity and mortality. A thorough preoperative workup is important to define the patient's risk of postoperative complications and to facilitate a coordinated anesthetic and surgical plan that provides the greatest likelihood of a good clinical outcome. Particular attention should be given to the patient's cardiac, respiratory, renal, and neurologic function because threats to these systems present the greatest risk to increase morbidity and mortality. Although thoracic and thoracoabdominal aneurysm repairs represent high-risk surgical procedures at baseline, patients presenting for urgent or

emergent intervention are at the greatest risk of postoperative complications. Unfortunately, these patients may also be clinically unstable and thorough preoperative workup may not be feasible.

Cardiovascular

Detailed evaluation of the patient's cardiovascular system is essential prior to undertaking complex aortic repair. Major fluid shifts, aortic cross-clamping, and the physiologic stress of intraoperative and postoperative blood loss represent a significant threat to the cardiovascular system. Major thoracic aortic surgery falls into the highest risk group for perioperative cardiac morbidity. Up to two-thirds of patients demonstrate diastolic dysfunction with aortic cross-clamping, and 30% of patients manifest some degree of cardiac dysfunction postoperatively. Hypertension is a common comorbidity, and elderly patients may also have coexisting coronary artery disease (CAD). Evidence of congestive heart failure may also be present as a result of progressive AI due to aneurysm enlargement.

Cardiac workup should at least include an electrocardiogram (ECG) and a TTE, although stress testing and/or coronary angiography are routinely performed at many centers. Patients who are found to have unstable CAD, left main stenosis, or three-vessel disease are typically revascularized prior to or during the repair of the aneurysm. There is debate whether or not to perform percutaneous coronary intervention (PCI) on less complex lesions because the antiplatelet therapy that accompanies PCI may complicate surgical hemostasis. Occasionally, aneurysmal expansion can result in ischemia from compression of the coronary arteries. Patients taking antihypertensive and antianginal drugs should continue these until the time of surgery, and titrated preoperative anxiolysis medication is important to prevent stress-induced hypertension

and tachycardia, which could precipitate aneurysm rupture. Therapeutic anticoagulation or antiplatelet agents should be discontinued or bridged with short-acting alternatives prior to surgical intervention.

Respiratory

The respiratory system also deserves special attention in the preoperative evaluation of patients undergoing thoracic aneurysm repair. Perioperative respiratory failure is the most common serious complication of thoracic and thoracoabdominal aneurysm repair, and patients with a history of smoking or COPD are at especially high risk. Pulmonary function should be evaluated preoperatively because one-lung ventilation (OLV) is important for open surgical repair of Crawford type I, II, III, and V aneurysms. Patients with very poor pulmonary reserve may require CPB because of an inability to tolerate OLV. Preoperative smoking cessation should be encouraged.

In addition to the evaluation of pulmonary mechanics, history should include consideration of positional dyspnea or stridor, which may indicate aneurysmal compression of the trachea or, more commonly, the left mainstem bronchus. Review of the CT or MRI is important to determine whether significant bronchial compression is present because this may complicate airway management and double-lumen endotracheal tube placement. Finally, patients with significant preoperative respiratory dysfunction should be counseled about the possible need for prolonged postoperative mechanical ventilation, including tracheostomy placement.

Renal

Many patients also have baseline renal insufficiency, which places them at risk for subsequent postoperative renal failure. Up to 25% of patients undergoing TAAA repair develop some degree of postoperative renal insufficiency, with 8% of patients

requiring hemodialysis. Although evidence for preoperative hydration is minimal, at many centers, it is common practice to admit patient the night before surgery for intravenous (IV) hydration.

Neurologic

Finally, the neurologic system deserves special consideration given the risk to both the brain and spinal cord during aneurysm repair. In an effort to minimize stroke risk, carotid and brachiocephalic angiography are often performed preoperatively, especially in patients with a prior history of stroke or transient ischemic attack. Patients should also be counseled about the risk of possible postoperative paralysis from spinal cord ischemia. Although the risk was historically much higher, the current incidence of postoperative spinal cord injury is between 2% and 6%, depending on the anatomy of the aneurysm. Onset can either be immediate or delayed. Risk factors for postoperative paralysis include preoperative renal dysfunction, Crawford type II aneurysm repair, and AAD. Preoperative identification and preservation of the artery of Adamkiewicz decreases the risk of paraplegia from 50% to roughly 5%.

In summary, preoperative assessment prior to thoracic aneurysm repair is important for both anesthetic and surgical planning. Although aortic surgery represents a high-risk procedure, evaluation of clinical risk factors, multisystem assessment, thoughtful preoperative testing, and, when appropriate, referral to subspecialists for medical optimization can improve perioperative outcome.

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predictors of delayed neurologic deficit following repair of thoracoabdominal aortic aneurysm. *J Thorac Cardiovasc Surg*. 2003;126(5):1288–1294.

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B.4. What is the preoperative management of a patient presenting with an acute aortic dissection (AAD)?

Patients presenting with an AAD will either be admitted to the ICU or progress immediately from the emergency department to the operating room. Invasive monitoring of blood pressure in both arms, large-bore IV access, and aggressive control of blood pressure and heart rate are priorities.

Blood pressure reduction is typically accomplished with β-blockers and vasodilators aiming to reduce myocardial contractility and minimize further extension of the dissection. The goal systolic blood pressure and heart rate are 100 to 120 mmHg and less than 60 beats per minute, respectively. If heart rate and blood pressure control remain inadequate after initializing β-blocker and vasodilator therapy, calcium channel blockers may be an additional adjunct. Hydralazine is typically not used because it may precipitate a reflex tachycardia, which can worsen the dissection. Conversely, patients who are hypotensive on presentation should be treated aggressively with vasopressors and fluid resuscitation in an effort to maintain end-organ perfusion until the patient can undergo definitive operative repair.

A Stanford TAAD is typically treated as a surgical emergency because it is a highly lethal condition with a mortality of 1% to

2% per hour after onset. After 24 hours, 20% of patients will die without surgical intervention. Conversely, patients with a Stanford TBAD that is not complicated by limb ischemia, malperfusion, or rupture may be managed medically with aggressive blood pressure and heart rate reduction.

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Ramanath VS, Oh JK, Sundt TM III, et al. Acute aortic syndromes and thoracic aortic aneurysm. *Mayo Clin Proc*. 2009;84(5):465–481.

B.5. What is the spinal cord blood supply?

The spinal cord blood supply consists of both longitudinal and segmental components (**Fig. 9.9**). The longitudinal arteries include the anterior and paired posterior spinal arteries. The anterior spinal artery (ASA) arises from paired feeding vessels that originate in the vertebral arteries near the foramen magnum. It extends the length of the spinal cord and is situated in the anterior spinal sulcus. The ASA is fed by a series of radicular arteries, and the areas between these radicular contributions are watershed areas that are at the greatest risk of ischemia. The most significant of these radicular arteries is the artery of Adamkiewicz. It is a large radicular contribution that most commonly arises between T8 and L2, although it can originate as high as T5 and as low as L4. The artery of Adamkiewicz is critical to the maintenance of adequate collateral blood supply to the lower two-thirds of the spinal cord. The ASA supplies the anterior two-thirds of the spinal cord, including the corticospinal and spinothalamic tracts and is dependent on a robust collateral circulation, making it particularly susceptible to ischemic injury.

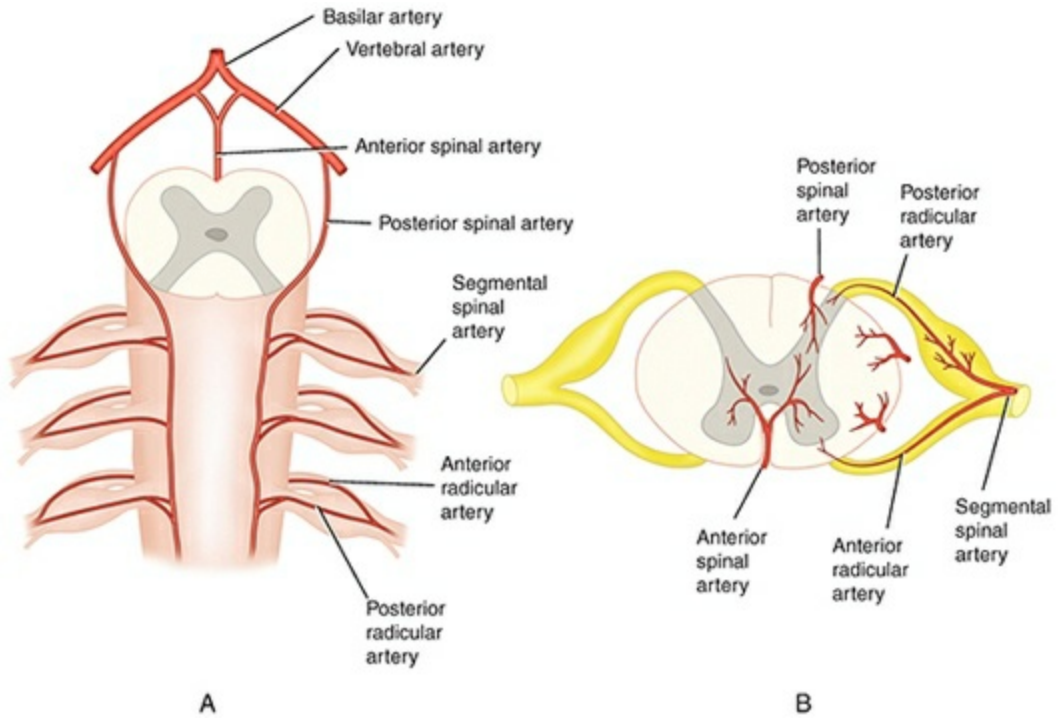

FIGURE 9.9. Spinal cord blood supply. (*Reprinted with permission from Splittgerber R. Blood supply of the brain and spinal cord. In:* Snell's Clinical Neuroanatomy. *8th ed. Philadelphia, PA: Wolters Kluwer; 2018:471.*)

There are two paired posterior spinal arteries that originate as branches of either the vertebral or posterior inferior cerebellar arteries and descend along the posterolateral portion of the spinal cord. The posterior spinal arteries are also fed by numerous radicular arteries. The anterior and posterior spinal arteries are connected to each other via a circular anastomosis known as the vasocorona medullaris.

In addition to the longitudinal arteries, there are multiple segmental branches that arise from the posterior portion of the aorta. These include the intercostal, subcostal, and lumbar segmental arteries. These arteries travel posteriorly and branch to supply the vertebral bodies, muscle and cutaneous structures, and spinal cord. The spinal division enters through the intervertebral foramen and subdivides to supply either the vertebral and ligamentous structures or the nerve roots and dura. At some levels, the arteries supplying the nerve roots and dura

also supply the spinal cord. These vessels are termed radiculomedullary arteries and play an important role in supplying accessory flow to both the anterior and posterior spinal arteries.

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C. Intraoperative Management

C.1. What are the surgical approaches to thoracic aneurysm repair?

Ascending and Arch Aortic Aneurysms

Proximal ascending aneurysms not only cause aortic rupture and dissection but also alter the three-dimensional conformation of the aortic root and AV complex, leading to AI (**Fig. 9.1**). The extent of involvement of the aortic root determines the surgical procedure necessary for repair (**Table 9.3**). When the AV and aortic root are not diseased, a graft can be implanted above the sinuses of Valsalva, called a supracoronary tube graft. The Wheat procedure is performed when the AV and proximal aorta are diseased, without dilation of the aortic root. It involves a supracoronary graft and an AV replacement but spares the sinuses of Valsalva, making coronary artery reimplantation unnecessary.

TABLE 9.3 Types of Thoracic Ascending Aorta Aneurysm Repairs

Aortic Valve	Root	Ascending Aorta	Surgical Approach	Name of Procedure
Normal	Normal	Aneurysmal	Supracoronary tube graft	
Diseased	Normal	Aneurysmal	AVR + supracoronary tube	Wheat procedure

			graft	
Diseased	Aneurysmal	Aneurysmal	AVR + replacement of aortic root and reimplantation or coronary arteries	Bentall
Normal	Aneurysmal	Aneurysmal	Valve-sparing root replacement	David procedure

AVR, aortic valve replacement.

The Bentall procedure is performed when the aortic root and AV are involved in the aneurysm. The Bentall procedure involves replacement of the AV, replacement of the aortic root, and reimplantation of the coronary buttons onto the neoaorta. Modifications of the Bentall procedure have focused on resuspending the AV to the neoaorta in patients with normal AV leaflets but poor coaptation due to the dilated aortic root. Resuspension of the AV to the neoaorta can decrease AI without requiring AV replacement. This is referred to as the David procedure.

Sixty percent of aortic arch aneurysms are located in the proximal arch and involve the distal ascending aorta. Surgical options for aortic arch aneurysms include hemiarch replacement or total arch replacement with or without a distal elephant trunk. A hemiarch replacement is performed in patients whose aneurysm does not extend to the proximal descending aorta. In patients whose aneurysm extends to the proximal descending aorta, either a total arch replacement with reimplantation of the great vessels separately or as a button can be performed (**Fig. 9.10**), or the elephant trunk procedure can be performed. The elephant trunk procedure includes an aortic arch graft and reimplantation of the great vessels to the prosthetic graft, in addition to a distal 5- to 7-cm “trunk” that dangles in the proximal descending aorta and is available for grafting for current or future descending aortic aneurysms (**Fig. 9.11**).

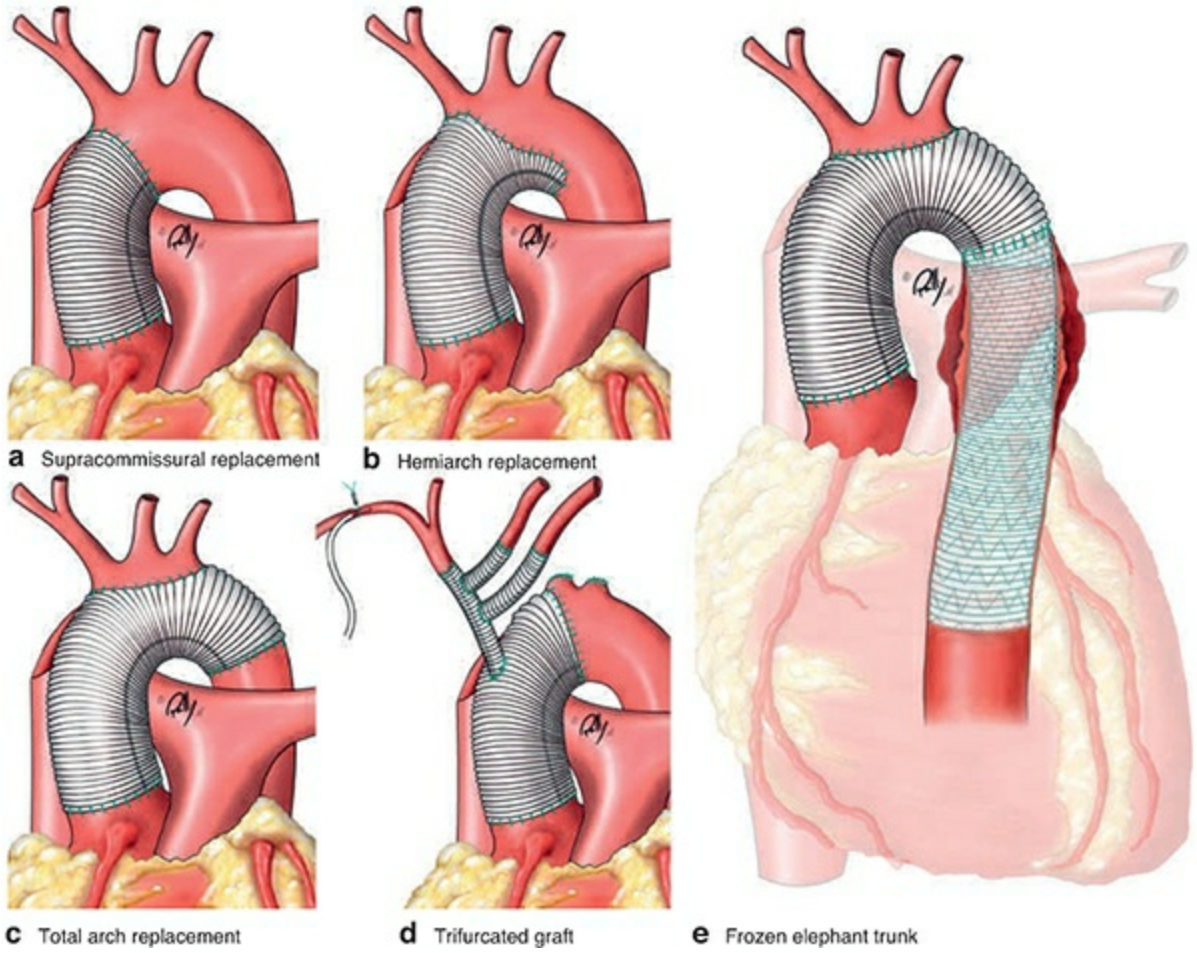

FIGURE 9.10. Surgical options for TAAs and thoracic aortic dissections. A. Supracommissural replacement of the ascending aorta. **B.** Hemiarch replacement, aortic resection is extended to the lesser curvature (inferior portion) of the aortic arch. Reimplantation of the arch branches is not necessary. **C.** Total arch replacement, the aortic arch is resected and the arch branches are reimplanted either as a button or with a composite graft. **D.** Trifurcated graft. **E.** FET procedure. (*From Krüger T, Conzelmann IO, Bonser RS, et al. Acute aortic dissection type A.* B J Surg. *2012;99[10]:1331–1344. Copyright © 2012 British Journal of Surgery Society Ltd. Reprinted by permission of John Wiley & Sons, Inc.*)

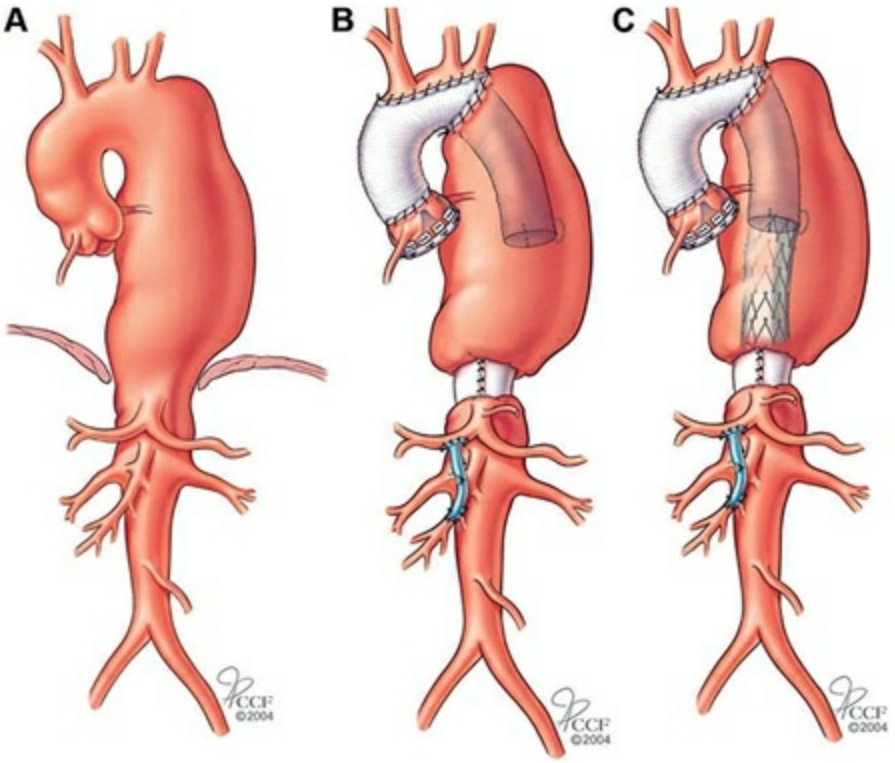

FIGURE 9.11. Elephant trunk procedure. A. Preoperative disease. **B.** Stage I with replacement of the ascending aorta and arch with a Dacron graft, with the distal graft sutured circumferentially to the aorta distal to the left subclavian artery and the free end of the graft ("elephant trunk") within the descending aneurysm. **C.** Completion of the procedure using an endovascular stent graft attached proximally to the "elephant trunk" and the distal end secured to a Dacron graft cuff. (*Reprinted from Hiratzka LF, Bakris GL, Beckman JA, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease.* J Am Coll Cardiol*. 2010;55[14]:e27–e129.*)

Surgery for the proximal ascending aorta, including Bentall, Wheat, David, and hemiarch procedures, is performed through a median sternotomy with CPB, with or without HCA. If the procedure involves the aortic arch, HCA is necessary.

Thoracoabdominal Aneurysms

Open repair of TAAAs is the treatment of choice for appropriate surgical candidates. Open repair includes a large thoracoabdominal incision and reimplantation of branch arteries on the surrounding aorta, after resection of the diseased aorta and graft placement. Additionally, total arch replacement and elephant trunk procedures are performed by utilizing a left

thoracotomy approach with the patient in the right lateral decubitus position.

Endovascular treatment of TAAAs has become common, particularly in patients with comorbid diseases precluding them from open repair. Endovascular treatment includes deployment of a stent graft into the diseased segment of the aorta via the femoral artery (**Fig. 9.12**). For TAAAs, endovascular treatment usually incorporates visceral arteries in the repair. This is accomplished via application of branched or fenestrated aortic grafts, which allow perfusion of the major visceral arteries. The branched or fenestrated aortic grafts can be custom-made or commercially available.

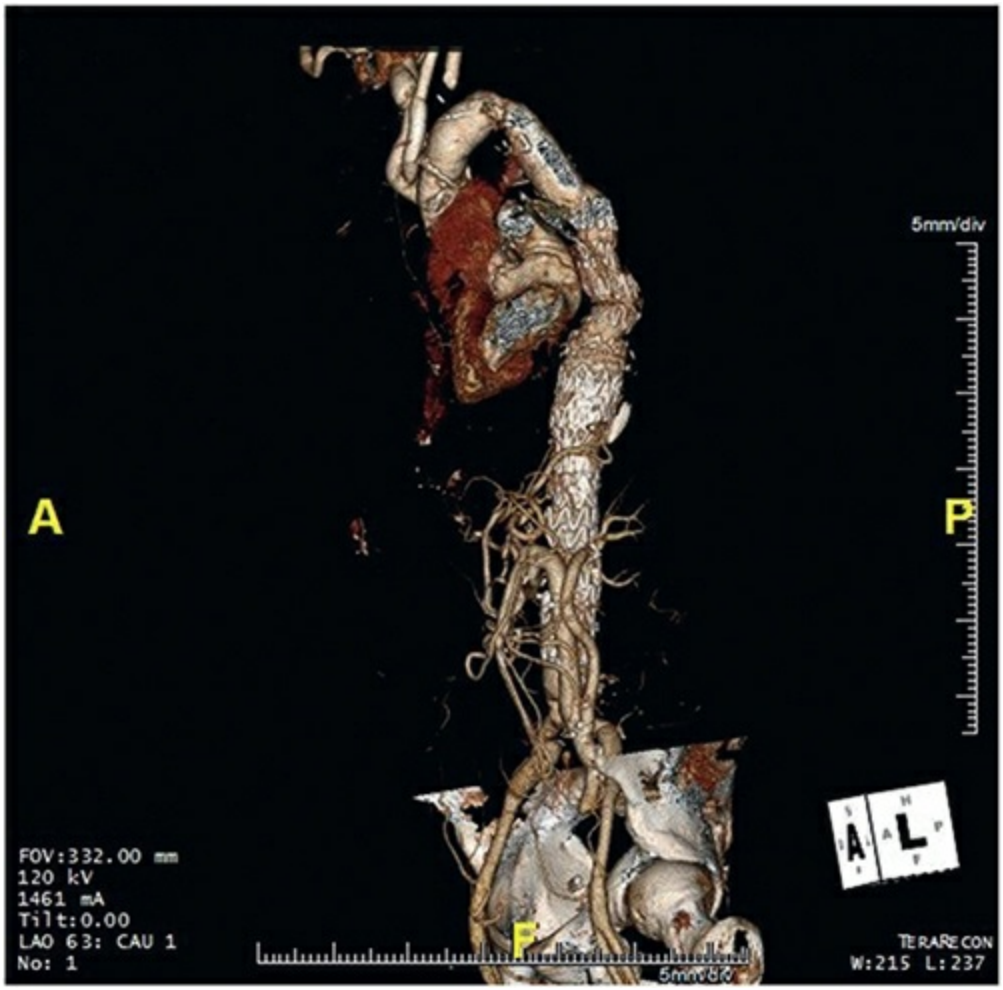

FIGURE 9.12. Three-dimensional (3D) CT reconstruction demonstrating endovascular exclusion of the descending thoracic aorta aneurysm after abdominal and arch debranching.

A hybrid procedure combines an open surgical approach with an endovascular stenting procedure to expand the anatomic suitability for deployment of stent grafts into the aorta. Hybrid procedures can either be staged or performed concurrently. In patients who have transverse aortic arch aneurysms without an adequate proximal landing zone for the stent graft, a first-stage total arch replacement is performed to create a proximal landing zone using CPB and HCA. This procedure is followed by a concomitant or second-stage endovascular repair of the distal portion of the aortic aneurysm.

Aortic visceral debranching procedures allow for endovascular stenting of TAAAs that involve the visceral arteries. Open debranching procedures can revascularize the visceral and renal arteries from the iliac arteries in a retrograde fashion or from the descending thoracic aorta above the aneurysm being treated (**Fig. 9.13**). After open debranching, the patient undergoes endovascular stent placement in the diseased segment of the aorta to exclude the aneurysm. The hybrid procedure exploits the benefit of both techniques and provides a favorable treatment option for high-risk patients. The hybrid technique avoids the need for custom-designed fenestrated or branched grafts and avoids the dangers of occluding vital visceral vessels.

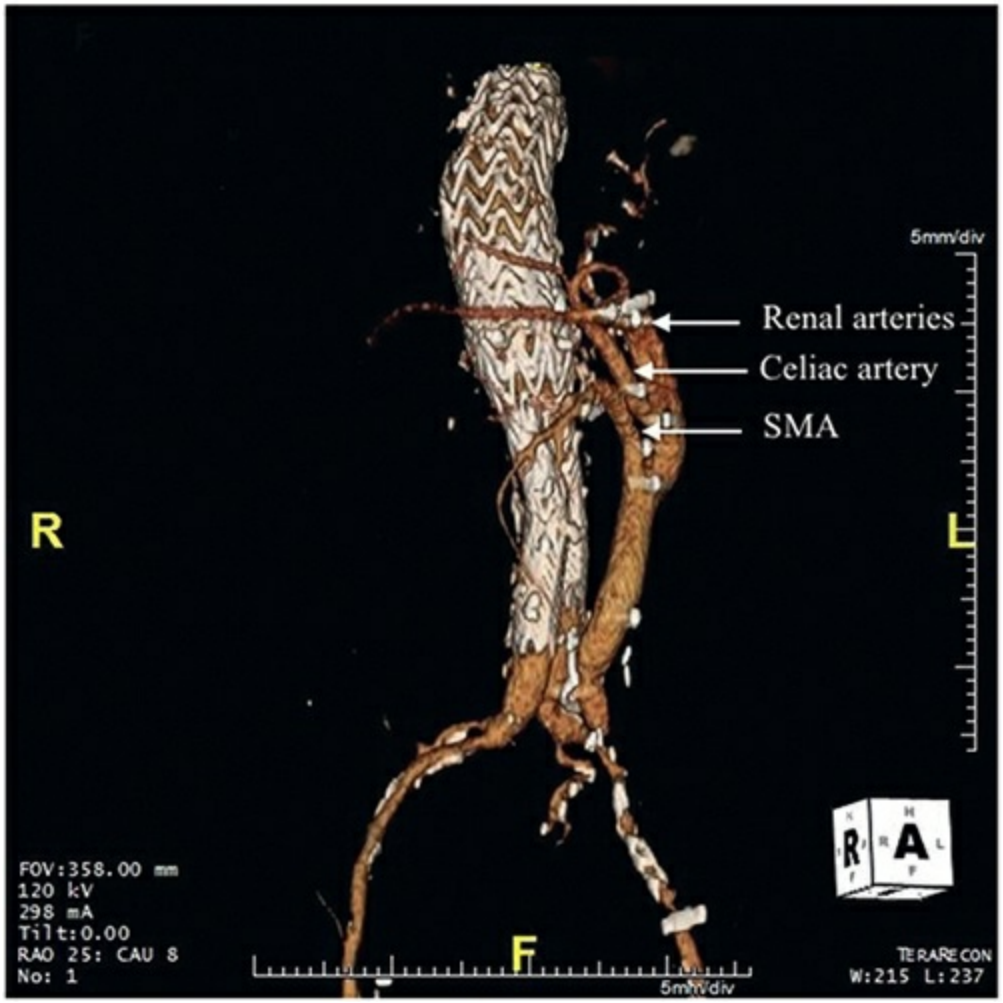

FIGURE 9.13. Three-dimensional (3D) CT reconstruction after abdominal debranching. The superior mesenteric artery (SMA), celiac artery, and renal arteries arise from a left iliac artery graft.

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Ziganshin BA, Elefteriades JA. Surgical management of thoracoabdominal aneurysms. *Heart*. 2014;100:1577–1582.

C.2. How is the open repair performed?

Ascending and Arch Aortic Aneurysms

Position: The surgical approach is through a median sternotomy with the patient positioned supine.

Cannulation for CPB: The CPB circuit requires a venous cannula that provides blood to the CPB pump and an arterial cannula that provides blood from the CPB pump to the patient. For aortic surgery, the arterial cannula can reside in any large artery, including the femoral, axillary, innominate, or carotid artery. Direct aortic cannulation can also be performed away from the site of the aneurysm if the anatomy allows. Arterial cannulation can be accomplished either directly or with the use of a graft anastomosis to the target artery. Direct aortic and femoral cannulations are used less frequently because they carry a risk of embolization or malperfusion in patients with aortic dissection or atherosclerosis. Commonly, the axillary or innominate arteries are used for cannulation sites because they can provide adequate arterial flow from the CPB pump during CPB and can also provide antegrade cerebral perfusion (ACP) during HCA. Cannulation of these smaller arteries is achieved with end-to-side anastomosis with a synthetic graft. The venous cannula for CPB is commonly inserted into the right atrium or femoral vein.

Hypothermic circulatory arrest: Neurologic injury remains a major cause of morbidity and mortality after open aortic arch repair. Cerebral protection depends on decreasing metabolic demand and providing metabolic supply with adequate cerebral perfusion while excluding blood flow through the great vessels. The safe limit of deep hypothermic circulatory arrest (DHCA) at 18°C is 30 minutes. Moderate HCA provides 10 to 20 minutes of safe circulatory arrest time. Regional cerebral perfusion both assists with metabolic supply and increase the safe duration of

circulatory arrest. Regional cerebral perfusion can be achieved in either an antegrade or retrograde fashion. ACP is accomplished by cannulating the axillary artery and clamping the proximal portion of the brachiocephalic artery, which provides perfusion to the right common carotid artery without disrupting the surgical site. A retrospective study of nearly 400 patients shows ACP can be either unilateral or bilateral. Commonly, a unilateral approach is performed via the right axillary artery, and DHCA with unilateral ACP of less than 50 minutes is tolerated. With bilateral ACP, DHCA can be tolerated for a longer period of time, up to 160 minutes. Retrograde cerebral perfusion (RCP) can be achieved by SVC cannulation, delivering oxygenated blood via the venous system. The SVC is clamped above the right atrium to separate this system from the venous return to the CPB pump. The proposed advantages of RCP include de-airing of arch vessels and decreased cerebral embolic events, whereas the disadvantage is a possible increase in transient postoperative neurologic dysfunction. Traditionally, the use of DHCA, with temperatures less than 20°C had been most commonly used. More recently, use of moderate (20°C to 28°C) or even mild HCA (28°C to 34°C) with antegrade or RCP has been advocated due to possible beneficial effects on transfusion rates and shortened bypass time. There is no apparent difference in the rate of renal dysfunction with DHCA and RCP compared to moderate HCA with ACP. The decision to use mild, moderate, or deep HCA with retrograde or ACP is still debated, and formal recommendations do not yet exist with respect to the superiority of techniques. Regardless of the technique, it is important that rewarming not be undertaken at too rapid a rate; sources recommend a temperature differential of no more than 10°C between perfusate and nasopharyngeal or oropharyngeal temperature to avoid cerebral hyperactivity and subsequent ischemia due to elevated oxygen consumption.

Other neuroprotective strategies are used at variable rates including topical head cooling, barbiturates, corticosteroids, mannitol, lidocaine, and nimodipine. Most providers endorse the use of some neuroprotective strategies in addition to hypothermia, but high-quality evidence supporting their use is lacking. Topical head cooling is used to assist in maintaining low temperatures during HCA as well as the prevention of rapid rewarming during emersion from DHCA. Strong human evidence to support this practice is lacking, although there are some animal studies. Concerns about this method include pressure on the eyes from the application of ice as well as interference with monitors such as electroencephalogram (EEG) and cerebral saturation probes. Barbiturates, specifically thiopental, have been used to minimize cerebral oxygen consumption by achieving electrical silence. Barbiturates also result in cerebral vasoconstriction, which may be beneficial during the rewarming period to reduce the risk of embolic phenomena. Barbiturates are also significant myocardial depressants and result in significant venous and arterial dilation, which can contribute to hypotension after the HCA period. Strong human evidence to support the use of barbiturates is lacking. Corticosteroids are frequently given (typically high doses of methylprednisolone: 500 to 1,000 mg) in hopes of attenuating the inflammatory response in the CNS. Concerns include hyperglycemia, which is known to be detrimental to patients with potential or known neurologic injury. As before, strong evidence for the use of corticosteroids is lacking. Mannitol is used by some to reduce cerebral edema and has free radical scavenging capabilities. The use of a continuous lidocaine infusion, through the induction of EEG silence has theoretical benefits but has not been definitively shown to improve neurologic outcomes in studies. Finally, nimodipine, recognized for the treatment of vasospasm, is no longer

commonly used after a study was stopped early due to worsening outcomes in the intervention group.

Thoracoabdominal Aneurysms

Position: The surgical approach is typically through the left chest, with the patient positioned in a partial right lateral decubitus position, with the shoulders at 60 degrees and the hips at 30 degrees. The patient is supported with the use of a bean bag.

Incision: A thoracoabdominal incision is the preferred approach for the majority of aneurysms. The proximal extent of the incision is dictated by the patient's body habitus and the aortic pathology. Typically, if the distal aortic arch and proximal descending aorta are to be exposed (Crawford types I and II), an incision to the 5th intercostal space is necessary. If the proximal extent of the aneurysm involves the distal thoracic aorta (Crawford types III and V), an incision to the 7th or 8th intercostal space is required. If the aneurysm is localized to the abdominal aorta (Crawford type IV), the proximal incision is made at the 9th or 10th intercostal space. The abdominal portion of the incision is typically limited to the retroperitoneum. Diaphragm preservation, defined as division only of the muscular portion of the diaphragm with preservation of the central tendinous portion, is performed to help improve postoperative respiratory mechanics.

Cannulation for left-heart bypass (LHB): Open surgical procedures on the thoracoabdominal aorta require a period of ischemia to the lower portion of the body during the period of time that the aorta is cross-clamped. This poses the risk of ischemia to the spinal cord, viscera, and kidneys during complex procedures requiring long cross-clamp times. LHB is utilized to reduce the risk of ischemia to the abdominal organs and spinal cord. LHB delivers oxygen-rich blood to the lower body and

viscera while permitting longer cross-clamp times for the surgeon to perform the repair. In LHB, the left atrium or pulmonary vein is cannulated and blood is directed to the femoral artery via a centrifugal pump (**Fig. 9.14**). Alternatively, passive axillary artery to femoral artery bypass can be used, which is dependent on the mean arterial blood pressure (MAP) proximal to the cross-clamp. In addition to the benefit of distal aortic perfusion, atrial-femoral bypass reduces preload to the left ventricle, reducing myocardial stress during cross-clamping. The use of LHB requires less systemic heparinization (100 units per kg given 5 minutes prior to cannulation) than CPB. It also minimizes ischemia to the lower extremities, thereby decreasing the acidosis that can develop after cross-clamp release. During the period of aortic cross-clamp, flow through the LHB is maintained to provide a proximal aortic pressure of 90 mmHg or distal aortic pressure of 70 mmHg.

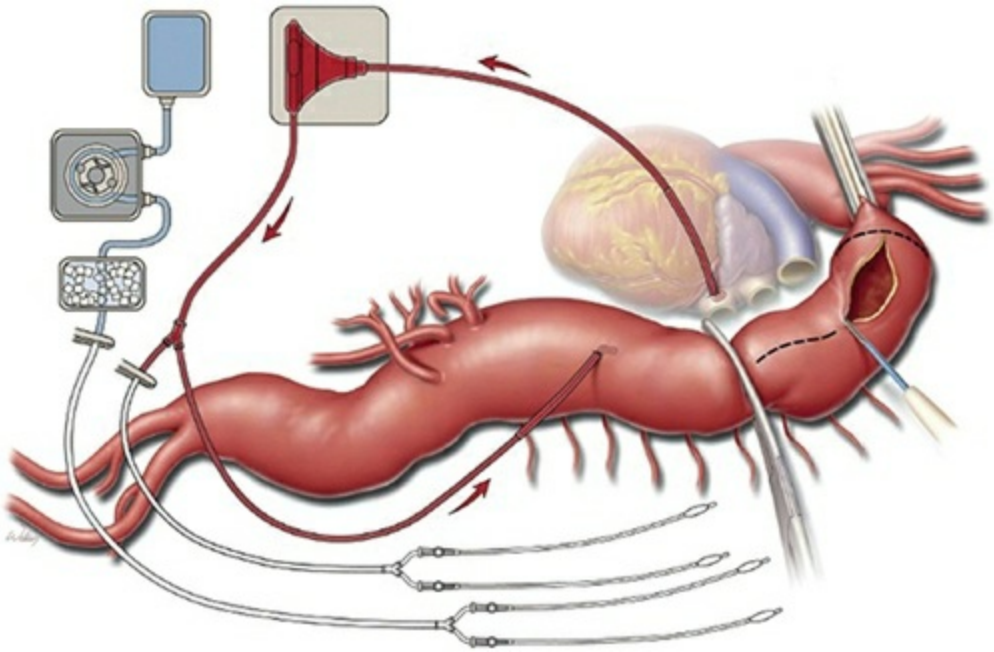

FIGURE 9.14. LHB is utilized for distal perfusion during TAAA repair. The drainage cannula is placed in the left atrium, and the outflow cannula is placed in the thoracic aorta distal to the site of aortic cross-clamping. Additional catheters are available for selective perfusion of visceral arteries with blood during operative repair. A separate line may be set up to provide cold lactated Ringer's solution through the renal arteries for renal protection. (*Used with permission from de la Cruz KI, LeMaire SA,*

Weldon SA, et al. Thoracoabdominal aortic aneurysm repair with a branched graft. Ann Cardiothorac Surg. *2012;1[3]:381–393.*)

Cannulation for CPB with or without hypothermic circulatory arrest: Similar to ascending aorta repairs, the use of CPB with HCA obviates the need for proximal aortic cross-clamping and therefore reduces the potential for spinal cord injury. Preserved end-organ function and decreased incidence of paraplegia are some of the benefits of using CPB with HCA. Typically, a venous cannula is placed via the femoral vein prior to or after right lateral positioning of the patient. Arterial cannulation can reside in the distal aortic arch, proximal descending aorta, axillary artery, or femoral artery. During circulatory arrest, antegrade or RCP may be used for neuroprotection and direct cannulation of the visceral segments with antegrade perfusion may be used for gastrointestinal protection.

Cross-clamp: The surgeon must develop an operative plan for safe aortic cross-clamping such that an adequate aortic cuff is available for proximal anastomosis and is not compromised by aortic cross-clamp placement.

Anastomoses: In type I and II repairs, the aorta is first dissected away from the esophagus to help prevent the formation of an esophageal-aortic fistula. The proximal aorta is cross-clamped, and the proximal anastomosis of the graft is sewn on to the aorta in an end-to-end fashion. Intercostal arteries in the T4–T8 region are often ligated if they exhibit excessive retrograde bleeding indicative of good collateral flow. When feasible, patent intercostal arteries from T8 to L1 are reattached to the graft. The clamp is then moved distally and reapplied above the visceral vessels. The superior mesenteric artery, renal arteries, and celiac artery are then anastomosed to the graft. Finally, the clamp is moved distally past the visceral vessels, allowing for the distal anastomosis of the graft to the descending aorta.

Clamp and sew technique: The "clamp and sew" technique involves cross-clamping the proximal aorta and replacing the aneurysmal aorta with a graft. In this technique, distal aortic perfusion with the use of LHB or HCA are not utilized. The technique poses a time limit to the surgeon as the patient's organs are not being supported during cross-clamp. This technique is typically inadequate for difficult repairs and has been largely abandoned.

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C.3. How are endovascular repairs of TAAAs performed?

Position: Endovascular repair of TAAAs are performed with the patient supine for adequate access to the femoral artery.

Incision: During endovascular repair, the endograft is typically introduced via the femoral artery, although the iliac artery or infrarenal aorta may be used if the femoral artery is inadequate in size or is heavily calcified.

Deployment: Branched and fenestrated grafts are handmade for each individual case and require over a month before they can be delivered and implanted. Due to the emergent need for surgery in some patients with aortic aneurysms or dissections, commercially available endovascular grafts are often modified by the surgeon with fenestrations to accommodate the patient's anatomy.

The left subclavian artery may need to be covered by the endograft in order to achieve an adequate proximal landing zone. The proximal left subclavian artery is covered, with the distal subclavian artery gaining perfusion from collateral vessels, including the left internal mammary artery (LIMA) and vertebral artery. In some instances, occlusion is not tolerated, necessitating left carotid to subclavian bypass.

In patients with aneurysms involving the mid transverse arch, aortic arch debranching with reimplantation to the ascending aorta may be performed (**Fig. 9.15**), without the use of CPB via a median sternotomy with extension of the incision along the anterior border of the sternocleidomastoid muscle.

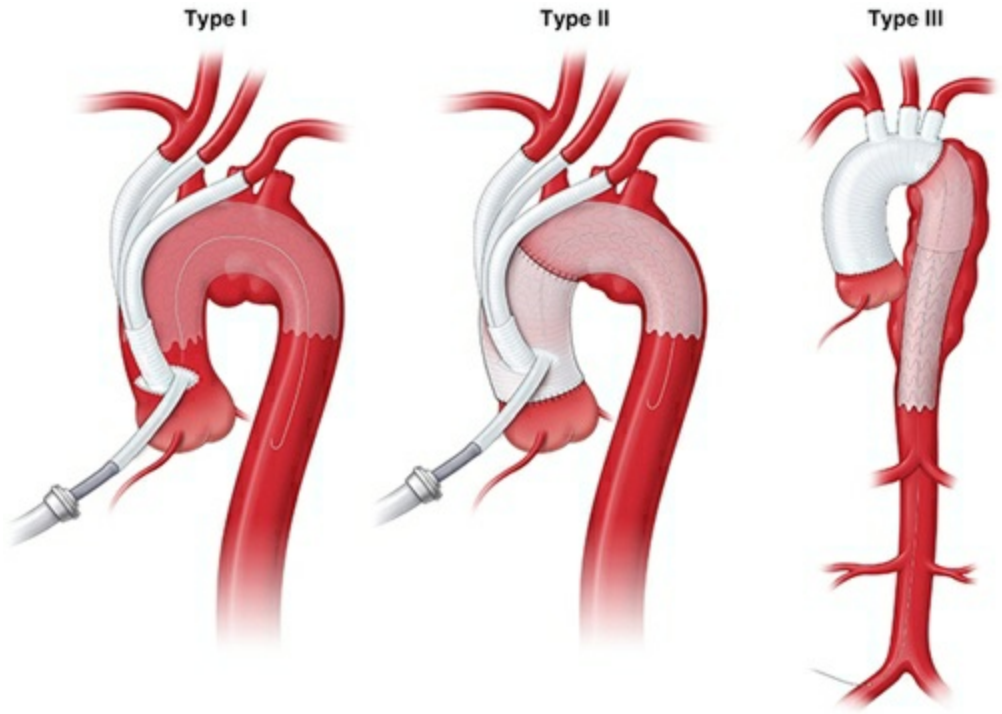

FIGURE 9.15. Surgical strategies for aortic arch debranching and TEVAR for aortic arch aneurysms. A. Reimplantation of great vessels to the proximal ascending aorta to create a landing zone for TEVAR. **B.** Replacement of the ascending aorta with reimplantion of great vessels to the proximal ascending aortic graft. **C.** Total arch replacement, reimplantation of great vessels, and elephant trunk procedure. (*Reprinted with permission from Vallabhajosyula P, Szeto WY, Desai N, et al. Type II arch debranching procedure.* Ann Cardiothorac Surg. *2013;2[3]:378–386.*)

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C.4. What are the surgical approaches to aortic dissections?

Type A Aortic Dissection

Unlike elective surgery for TAAs, TAAD repair is generally an emergency surgery, and the real-time operative approach can deviate from the original plan. As the extent of surgical repair is dictated primarily by the location(s) of the intimal entry tear(s), intraoperative decision making is critical.

A median sternotomy is generally performed for exposure,

preceded or followed by arterial and venous cannulation, initiation of CBP, and cooling to the desired temperature for circulatory arrest. Placement of a left ventricular vent and retrograde cardioplegia cannula is usually necessary in the setting of aortic regurgitation. Basic principles of surgery for TAAD include excision of the primary intimal tear, obliteration of the false lumen, resumption of forward blood flow through the true lumen, and correction of associated pathologic conditions such as aortic regurgitation and malperfusion. After aortic resection is performed, the aorta is repaired by reapproximating the intimal and the adventitial layers using either sutures or endovascular stent grafts. Resecting to the level of the lesser curve of the aortic arch allows for maximal removal of the diseased aorta, known as a hemiarch repair.

Selection of cannulation site is important and can be challenging. Right axillary artery cannulation is preferred because it also facilitates selective ACP during HCA. Despite a meta-analysis failing to confirm improved neurologic results, there is evidence that right axillary artery cannulation is associated with superior outcomes compared to femoral artery cannulation. These results may be explained by inadequate cerebral perfusion and retrograde atherosclerotic embolization in patients undergoing femoral artery cannulation. However, femoral cannulation is still commonly performed especially when prompt initiation of CPB is desired. In recent years, central cannulation, which aims to supply blood flow to the true lumen in a timely fashion, is increasingly being used. This approach involves access of the true lumen of the ascending aorta using the Seldinger technique to direct the insertion of the aortic cannula into the true lumen via an undissected area or through the false lumen. TEE or epiaortic ultrasound is used for guiding the insertion. Placement of the guidewire into the true lumen needs to be confirmed.

Other vascular access points for aortic cannulation, including the innominate artery, the apex of the left ventricle, and insertion of the cannula into the true lumen by dividing the ascending aorta, are usually used in the event of hemodynamic instability or aortic rupture, when emergent institution of CPB is necessary.

The minimal surgery for TAAD is a “standard” supracoronary ascending aortic replacement with distal anastomosis performed under HCA to allow inspection of the aortic arch and ensure that excision and repair of the entire aorta within the pericardium is adequate to minimize the risk of aortic rupture. When an intimal tear extends into the aortic root, an aortic root procedure such as a Bentall procedure or valve-sparing aortic root repair may become necessary especially when the left and right coronary sinuses are involved. Limited repair of the aortic root, for instance, an isolated repair of the noncoronary sinus can be done without the need for reimplantation of the coronary arteries. Other circumstances that necessitate aortic root operations include connective tissue disorders known at the time of aortic dissection, such as MFS, or aortic root aneurysms. In selected patients, valve-sparing root repair can be performed. However, patients’ characteristics, hemodynamical stability, institutional preference, and individual surgeon’s experience should be taken into consideration.

Distal extent of the TAAD repair is more controversial. The surgical approaches to the distal dissected aorta vary from an ascending aorta replacement to hemi- or total-aortic arch repair with or without a frozen elephant trunk (FET) procedure (**Fig. 9.10**). Traditionally, hemiarch repair where the inferior portion of the aortic arch is resected and repaired in conjunction with the ascending aorta is recommended to avoid reimplantation of the aortic arch branches, thereby reducing the complexity of the operation and associated procedural risks. Some aortic surgery experts advocate a standard total arch repair approach to reduce

the risk of future reinterventions. However, there appears to be no one-size-fits-all operation for TAAD. The likelihood of future reintervention should always be weighed against the operative risk. The generally accepted criteria for aortic arch replacement is an aortic arch aneurysm greater than 4.5 cm at the time of TAAD and the presence of intimal tear in the greater curvature of the aortic arch such that the preservation of arch vessels would preclude adequate repair.

On average, 20% to 30% of patients who survive the initial surgery for aortic dissections extending into the abdominal aorta (DeBakey type I) require reinterventions on the distal aorta at later stage. Although the utmost goal of TAAD surgery is operative survival and the surgical outcomes have been improving over time, identifying patients at risk for future intervention and preparing accordingly has become an area of interest to aortic surgeons. The FET procedure has shown promises as an adjunct to the standard surgical repair. In the FET procedure, an endovascular stent graft is deployed under direct vision during the period of circulatory arrest into the true lumen of the distal aorta. It has been shown to facilitate false-lumen thrombosis and aortic remodeling and to expedite the second-stage surgery for the downstream aorta. Questions have been raised about a potential increase in spinal cord ischemia associated with the procedure, and for this reason, short endografts (10 to 15 cm in length) are used. The endograft can also serve as the extended landing zone for future endovascular repair. Some user-friendly devices designed for utilization with the FET have been developed for this purpose, and some are on the horizon for commercial use. In the current era, the conventional elephant trunk (CET) procedure is rarely performed in the setting of TAAD. Instead, the FET procedure is gaining popularity because it offers the advantage of improved effectiveness in the remodeling of the downstream aorta,

although endoleak can sometimes be an issue. Several modified approaches to hybrid aortic arch repair have been reported. These simplified techniques for arch repair do not require extensive arch resection, thereby reducing the impact on operative morbidity and mortality (**Fig. 9.16**). The long-term outcomes of these procedures are being investigated.

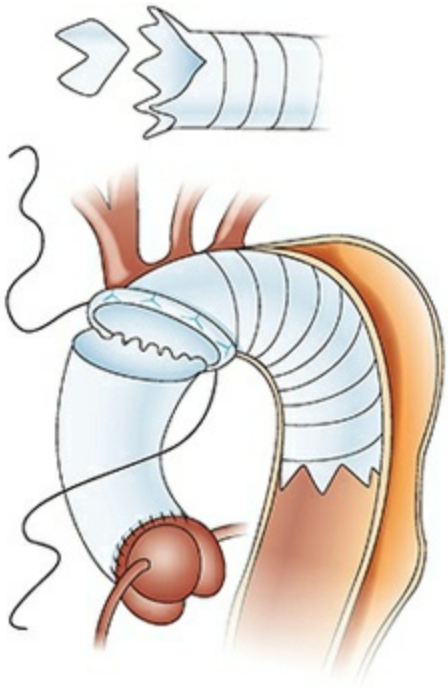

FIGURE 9.16. Illustration demonstrating a hybrid aortic arch repair, where an endograft is placed in the aortic arch and the proximal descending aorta to facilitate aortic remodeling and create the landing zone for future reinterventions. (*Adapted from Roselli EE. We should replace the aortic arch and more in DeBakey type I dissection—a perspective from the Cleveland Clinic.* Ann Cardiothorac Surg. *2013;2[2]:216–221.*)

Type B Aortic Dissection

TBAD is managed medically unless complications have developed or are impending. The notion that surgical repair of an uncomplicated TBAD does not improve survival is evolving with recent studies revealing the benefits of early endovascular repair. Surgical intervention is currently reserved for treatment of TBAD with concerns for complications, such as rupture, rapid expansion, and malperfusion. It is clear that traditional

open surgical treatment of TBAD is associated with an exceedingly high mortality and considerable morbidity. In the current era, open surgical repair is rarely considered for TBAD. Instead, endovascular repair has been accepted as the procedure of choice when intervention is indicated.

Although the role of TEVAR in treatment of complicated TBAD is well acknowledged, as recommended per the American College of Cardiology Foundation (ACC)/American Heart Association (AHA) guidelines (2010) and the European Society of Cardiology (ESC) guidelines (2014), its use in the treatment of uncomplicated TBAD remains to be elucidated. The INvestigation of STEnt Grafts in Patients With Type B Aortic Dissection (INSTEAD) trial, which is a prospective, multicenter, randomized trial investigating the outcomes for TEVAR in patients with uncomplicated TBAD in comparison to optimal medical treatment, failed to show a survival benefit in patients who underwent TEVAR. Nevertheless, it showed a much higher rate of aortic remodeling (91.3% in 2 years vs. 19.4% for optimal medical treatment). After 5 years follow-up (INSTEAD-XL trial), the TEVAR group has exhibited improved all-cause and aorta-specific mortality, suggesting that TEVAR may be beneficial in a subset of patients who have favorable anatomy but carry high risks of aortic events.

The goal of TEVAR for TBAD is to obliterate the blood flow into the false lumen by covering the intimal entry tear, therein promote thrombosis and expansion of the true lumen. Due to the anatomic restraints of TBADs that are typically located in proximity to the left subclavian artery, partial or complete coverage of the left subclavian artery is frequently necessary. Intravascular ultrasound can be used during the procedure to identify the intimal tear in conjunction with aortic angiography. Left subclavian revascularization via carotid-subclavian bypass or transposition is recommended for patients at relatively young

age, with left dominant vertebral arteries, in non-emergent situations, or with a patent LIMA after coronary artery bypass graft.

It is a common practice to cover only the segment of the aorta at risk for expansion or rupture and follow with serial imaging studies to rule out aortic growth because extensive coverage increases the risk of paraplegia. The presence of multiple intimal tears is attributable to the persistence or even continuous growth of the false lumen after TEVAR for TBAD, potentially requiring reinterventions.

TEVAR can be associated with retrograde dissection that results in new-onset TAAD requiring emergent surgical repair. TEE is proven to be a useful tool in the intraoperative setting to identify retrograde dissection expansion in a timely fashion preventing fatal complications. In addition, TEE also helps identify intimal tears and guides operative planning.

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Waterford SD, Gardner RL, Moon MR. Extent of aortic replacement in type A dissection: current answers for an endless debate. *Ann Thorac Surg*. 2018;106(4):1246–1250.

C.5. What are the specific considerations for anesthetic management of the patient presenting for open TAAA repair?

Patients presenting for TAAA repair typically have multiple preexisting comorbid conditions, and open repair of the TAAA poses a direct and immediate threat to the cardiac, pulmonary, renal, gastrointestinal, and neurologic systems.

Induction of anesthesia should include a slow and hemodynamically stable induction, avoiding hypertension and tachycardia. Short-acting antihypertensive agents such as nitroglycerin, nicardipine, esmolol, and labetalol are useful to assist in hemodynamic stability.

Anesthetic management must seek to avoid hemodynamic changes that will increase the risk of aneurysm rupture while maintaining adequate end-organ perfusion. As surgical dissection exposes the aorta, the counterforce to the systemic blood pressure on the aneurysm wall is decreased, increasing the risk of aneurysm rupture. Prior to cross-clamp removal and reperfusion of the visceral organs and lower extremities, systemic blood pressure should be increased because removal of the cross-clamp and reperfusion can lead to profound hypotension.

Lung isolation is necessary for repair of type I, II, and some type III TAAAs. A double-lumen endotracheal tube is superior to a bronchial blocker because it provides access to the

nonventilated lung for suctioning and addition of continuous positive airway pressure (CPAP) when oxygenation is inadequate. Either right- or left-sided double-lumen endotracheal tubes may be used; however, a type I or II aneurysm may distort the anatomy of the left mainstem bronchus, making a left-sided double-lumen tube difficult and possibly unsafe to place. An alternative to double-lumen tube placement involves the use of the EZ-Blocker, a bronchial blocker with a Y configuration and two balloons that can isolate either lung and allows for lung isolation via a single-lumen tube. Tube exchange at the end of surgery in a potentially edematous airway is avoided with this technique, and it is generally easier to place a larger single-lumen tube with this blocker than with a double-lumen tube.

If motor-evoked potentials (MEPs) are being monitored, either succinylcholine or a short-acting nondepolarizing neuromuscular blocker should be used to facilitate tracheal intubation and then discontinued. Anesthetic maintenance may be achieved using a low concentration of volatile anesthetic, combined with an infusion of propofol and/or narcotics. If MEPs are not being monitored, neuromuscular blockers can be used with inhalation agents and narcotics.

Some institutions will institute a wake-up test prior to transportation to the ICU. If this is performed, anesthetic management must take this into consideration. During the wake-up test, the patient is asked to move his lower extremities. After completion of the wake-up test, the patient is resedated and the double-lumen endotracheal tube is changed to a single-lumen endotracheal tube.

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C.6. What are the specific considerations for anesthetic management of the patient presenting for endovascular TAAA repair?

Endovascular treatment of thoracic aneurysms is typically less invasive than open surgical repair, but preparation for possible open repair must be undertaken. General and regional anesthetic techniques have been described, but general anesthesia remains the primary choice because TEE and neuromonitoring can occur when the patient is under general anesthesia. Hemodynamic stability must be sought, avoiding hypertension and tachycardia. During deployment of the stent, transient balloon occlusion of the aorta may result in significant transient hemodynamic instability, particularly if the patient has poor cardiac function. Vasopressors and inotropes must be available to treat hemodynamic instability.

Although the risk of spinal cord ischemia is lower in endovascular procedures, it does occur. Cerebrospinal fluid (CSF) drains may be placed selectively in patients considered high risk for spinal cord ischemia for neuroprotection. Neuromonitoring of somatosensory evoked potentials (SSEPs) and MEPs may be used. If MEPs are used for neuromonitoring, this may necessitate the use of a total IV anesthetic.

Blood loss during the endovascular surgery may be difficult to quantify, necessitating frequent hemoglobin checks.

Escobar GA, Upchurch GR Jr. Management of thoracoabdominal aortic aneurysms. *Curr Probl Surg*. 2011;48(2):70–133.

Hughes GC, Sulzer CF, McCann RL, et al. Endovascular approaches to complex thoracic aortic disease. *Semin Cardiothorac Vasc Anesth*. 2008;12(4):298–319.

C.7. What hemodynamic monitors should be used for the patient undergoing thoracic aneurysm repair?

In addition to the standard monitoring recommended by the American Society of Anesthesiologists, there are additional monitors that should be applied to the patient undergoing open repair of a TAA. Electrocardiographic monitoring with ST-segment analysis is essential because the incidence of intraoperative myocardial ischemia and arrhythmias is significant. During open repair of TAAs, systemic blood pressure should be measured with the use of an arterial line, which may be placed awake to allow strict blood pressure control during induction. Patients presenting for TAA repair frequently have peripheral vascular disease and as such, reviewing imaging studies for subclavian or other arterial stenosis may affect the placement of arterial catheters. During repair of Crawford type I and II aneurysms, the arterial catheter should be placed in the right radial artery because flow to the left subclavian artery may be disrupted from the proximal aortic cross-clamp. Left radial monitoring may be useful to determine the patency of the left subclavian artery but should not be used independently because left subclavian flow can be altered. If distal aortic perfusion through bypass or a shunt is performed, a femoral arterial line is inserted to monitor distal perfusion pressure. A femoral arterial line is also useful in determining the pressure gradient across the surgical repair by comparing the femoral blood pressure to the radial blood pressure. Depending on the extent of ascending aortic repair, bilateral upper extremity arterial catheters may need to be used. The left radial arterial line is used to monitor the systemic pressure reliably prior to and during CPB, whereas the right radial arterial catheter will measure the blood pressure during HCA with ACP. The right radial arterial catheter is not used during other intraoperative periods because the presence of an axillary aortic cannula can

make the readings unreliable.

The potential for rapid blood loss during the repair is significant; therefore, large-bore IV access should be obtained. The ability to transfuse blood products rapidly with a rapid infusion device should be available. Left upper extremity IV access should be avoided during aortic arch repairs because the left innominate vein may be injured or ligated during the procedure. Pulmonary artery (PA) catheters are often used to allow hemodynamic monitoring and assess cardiac output, but the routine use of PA catheters during these procedures varies among different institutions.

TEE should be used in all open thoracic aorta repairs, unless contraindications exist. TEE can assess the extent and severity of aortic disease, evaluate valvular and functional abnormalities, and assist with cannula placement. TEE should also be used in endovascular thoracic aorta procedures for cardiac monitoring, procedural guidance, and endovascular graft leak detection. During balloon occlusion of the aorta, TEE can monitor the cardiac performance and guide vasoactive therapies.

Hughes GC, Sulzer CF, McCann RL, et al. Endovascular approaches to complex thoracic aortic disease. *Semin Cardiothorac Vasc Anesth*. 2008;12(4):298–319.

Levine WC, Lee JJ, Black JH, et al. Thoracoabdominal aneurysm repair: anesthetic management. *Int Anesthesiol Clin*. 2005;43(1):39–60.

C.8. What strategies are used for spinal cord protection during a TAAA repair?

Spinal cord injury with resultant paraplegia remains one of the most serious complications of surgical procedures on the descending and thoracoabdominal aorta despite major advances in surgical technique. Several components of TAAA surgery impart risk to the spinal cord. Temporary occlusion of the aorta with a cross-clamp, permanent deletion of intercostal arteries,

and embolization of air or particulate matter to the aorta may contribute to the development of spinal cord injury. Several techniques have been instituted to minimize the risk of postoperative paraplegia.

Left-Heart Bypass

LHB is commonly used to provide distal aortic perfusion during aortic cross-clamp and repair (**Fig. 9.14**). During LHB, the arterial inflow cannula typically resides in the femoral artery and provides antegrade flow to the lower extremities with retrograde flow to the visceral organs and spinal cord. The venous cannula resides in the left atrium or pulmonary veins and drains oxygenated blood. LHB circuits can be equipped with or without an oxygenator.

Intraoperative Neuromonitoring

Neuromonitoring of SSEPs and MEPs has been instituted at various centers as a means of timely diagnosis of ischemia and modification of the surgical technique when ischemia occurs. SSEPs monitor the dorsal column of the spinal cord by stimulating the posterior tibial nerve and recording the responses from the somatosensory cortex. MEPs monitor the function of the corticospinal tract and anterior horn motor neurons by stimulating the motor cortex or cervical spinal cord and recording the response from the anterior tibial muscle. Unfortunately, monitoring of SSEPs produces a significant amount of false-positive results, and relying on SSEPs alone for determining the need for revascularization does not affect the incidence of postoperative neurologic injury. Current guidelines state that the use of neurophysiologic monitoring with SSEPs and MEPs may be considered.

Cerebrospinal Drainage

During aortic cross-clamp and surgical retraction, CSF pressure

may acutely increase. Additionally, the spinal cord may suffer from spinal cord reperfusion injury, whereby spinal canal edema forms following reperfusion. Spinal cord perfusion pressure is the difference between MAP and CSF pressure. The rationale for CSF drainage is based on this premise because decreasing the compartment pressure of the spinal cord should improve spinal cord perfusion pressure. Studies have shown that reducing the CSF pressure to less than 15 mmHg is beneficial, and meta-analysis supports the use of CSF drainage as an adjunct to prevent paraplegia. The current guidelines recommend the use of CSF drainage in open and endovascular thoracic aortic repair in patients at high risk for spinal cord ischemia.

Hypothermia

Mild hypothermia to 32°C may provide neuronal protection by reducing excitatory neurotransmitter release, decreasing free oxygen radical production, decreasing post-ischemic edema, and stabilizing CNS blood flow.

Moderate systemic hypothermia has been associated with improved neurologic outcomes after TAAA surgery. Hypothermia is achieved via passive heat loss during surgery or active cooling by heat exchangers on bypass circuits. Current guidelines state that the use of moderate hypothermia is reasonable for protection of the spinal cord.

Some institutions implement regional hypothermia to avoid the detrimental effects of systemic hypothermia on the coagulation system. Epidural cooling can be instituted with the insertion of a T12–L1 epidural catheter and an L3–L4 intrathecal thermistor catheter, selectively cooling the spinal cord after aortic cross-clamp. The spinal cord is cooled at the T8–L1 region, a watershed area with variation in collateral blood supply most susceptible to ischemic injury. The thermistor catheter allows measurement of temperature and CSF pressure.

After full TAAA reconstruction is completed, epidural cooling is stopped.

Similar to ascending aortic aneurysms, HCA may be used during repair of TAAAs. The use of HCA obviates the need for an aortic cross-clamp and the use of LHB to protect the spinal cord and viscera.

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C.9. What strategies are used for mesenteric and renal preservation?

Over the past few decades, strategies have been developed to minimize ischemic damage to downstream organs while the aorta is clamped. One strategy is the use of a passive shunt to provide distal aortic perfusion. Passive shunting is uncommonly utilized due to the popularity of mechanical circulatory support and the inability to adjust flow rates through the shunt.

LHB, as previously described, is now a common approach to

maintain distal aortic perfusion. The advantage of LHB is that flow rates can be adjusted to help provide stable hemodynamics. The disadvantage of LHB is that it is associated with increased incidence of postoperative renal dysfunction. Selective visceral perfusion may be used in combination with LHB, perfusing the four branching arteries with cold blood or crystalloid.

Femoro-femoral CPB with a range of protective hypothermia strategies, from mild (34°C) to profound (18°C), have been described to provide end-organ protection. Separate roller pumps may be used to selectively perfuse the celiac artery, superior mesenteric artery, and renal arteries during CPB. Lastly, HCA may be combined with CPB to avoid aortic cross-clamping and preserve end-organ function.

Selective renal artery perfusion can be performed by infusing a cold (4°C) crystalloid or blood solution into the renal artery ostia during aortic cross-clamp occlusion to achieve renal hypothermia. Mannitol and methylprednisolone may also be added to the perfusate. Mannitol decreases renal oxygen demand, and steroids stabilize cell membranes during ischemia. Mannitol also assists in maintaining urine output during the cross-clamp period. Additives such as histidine-tryptophan-ketoglutarate have recently shown promise in decreasing renal dysfunction. Current guidelines support the use of either cold crystalloid or blood perfusion to the kidneys but do not recommend the use of furosemide, mannitol, or dopamine solely for renal protection.

As concomitant atherosclerotic disease is commonly present in this patient population, the renal and visceral arteries often contain occlusive disease. Endarterectomy and balloon-expandable stent placement may be beneficial in decreasing postoperative renal dysfunction.

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C.10. What is the pathophysiology of aortic clamping and unclamping?

Aortic Clamping

Hemodynamics: As for any major vascular surgery, it is imperative to be familiar with the pathophysiology of aortic cross-clamping to understand and treat the hemodynamic disturbances appropriately. The most reliable response to aortic cross-clamping is systemic arterial hypertension. This is due to both an increase in afterload and redistribution of the blood volume. Blood volume redistributes after aortic cross-clamping, with a decrease in venous capacitance below the clamp, expelling blood from the splanchnic and nonsplanchnic vascular beds, and an increase in venous capacitance above the clamp. The increase in upper body blood volume results in increased filling pressures. Central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP), and left ventricular end-diastolic pressure (LVEDP) all increase with aortic cross-clamp placement. Differences in hemodynamic responses are observed with occlusion of different levels of the aorta and may be the result of different degrees and patterns of blood volume

distribution. Supraceliac cross-clamp application results in the most consistent redistribution of blood flow, whereas infraceliac aortic cross-clamp has inconsistent effects on blood flow redistribution and preload.

Oxygen consumption: Oxygen consumption in the part of the body distal to the aortic occlusion decreases. Paradoxically, oxygen uptake above the aortic occlusion also decreases. The reason for the decrease in oxygen consumption above the cross-clamp is unclear but may be related to sympathetic discharge from the adrenal glands, arteriovenous shunting, or blood volume redistribution and proximal hypervolemia. Mixed venous oxygen saturation increases during aortic cross-clamp, indicating decreased extraction. Plasma levels of epinephrine and norepinephrine significantly increase after thoracic aorta cross-clamping.

Coronary blood flow and contractility: Aortic cross-clamping is associated with increases in preload and afterload, leading to an increase in myocardial oxygen demand. In an intact coronary blood supply, an increase in demand would lead to coronary artery vasodilation and a concomitant increase in oxygen supply. When coronary blood flow increases, the subendocardium is perfused and contractility will increase in response to aortic cross-clamping. In the presence of inadequate coronary blood flow, the LVEDP increases, the subendocardium is not perfused, and the cardiac output decreases.

Level and duration of aortic cross-clamp: The level of the aortic cross-clamp affects the hemodynamic response observed. Changes in MAP, filling pressures, ejection fraction, and wall motion are minimal during infrarenal aortic cross-clamping but exaggerated during supraceliac aortic cross-clamping. With increased duration of aortic cross-clamping, systemic vascular resistance (SVR) increases and cardiac output decreases.

Renal effects: Cross-clamping of both the suprarenal and

infrarenal aorta results in an increase in renin and angiotensin. The increase in angiotensin is thought to contribute to the hypertension observed during cross-clamping. Cross-clamping of the thoracic aorta is associated with severe decreases in renal blood flow, glomerular filtration rate, and urine output. Ischemia-reperfusion injury to the kidneys plays a central role in renal dysfunction after aortic surgery and is also present after infrarenal cross-clamping.

Effects on spinal cord: Cross-clamping of the aorta is associated with a decrease in distal aortic pressure (decreasing ASA pressure, depending on the anatomy and presence of collateral supply), increase in CSF pressure, and a decrease in the compliance of the spinal fluid space. Vasodilators used to decrease proximal aortic pressure should possess minimal cerebral vasodilating properties because these will decrease spinal cord perfusion pressure by decreasing distal aortic pressure and increasing CSF pressure. In this regard, sodium nitroprusside, which decreases distal aortic pressure and increases CSF pressure, and nitroglycerin, which predominantly decreases distal aortic pressure, both decrease spinal cord perfusion pressure, which can lead to worse neurologic outcome.

Aortic Unclamping

Hemodynamics: Unclamping of the thoracic aorta leads to a decrease in SVR with a resultant decrease in arterial blood pressure. Cardiac output may increase, decrease, or remain the same. Myocardial blood flow increases and LVEDP decreases. Central hypovolemia develops due to pooling of blood into reperfused tissues distal to the aortic occlusion. Hypoxia-mediated vasodilation, in addition to accumulation of myocardial-depressant metabolites contributes to the hypotension that is seen after cross-clamp removal.

Acidosis: Metabolic acidosis and an increase in lactate

concentration are seen after release of the aortic cross-clamp. The degree of acidosis present depends on the underlying pathology and is greatest in patients undergoing abdominal aortic aneurysm repair. Aortic cross-clamp removal is also associated with a transient increase in carbon dioxide release and oxygen consumption.

Renal effects: Unclamping of the aorta results in a significant increase in renin and angiotensin that lasts for 6 hours but is unrelated to hypertension. A maldistribution of renal blood flow is seen, with a decrease in renal cortical blood flow. Glomerular filtration rate and renal plasma flow are decreased after unclamping and can remain at decreased values for 6 months following surgery.

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C.11. Why does a coagulopathy ensue and how is it prevented/treated?

TAA or TAAA repair is associated with significant hemorrhage from multiple causes, including surgical dissection, hypothermia, CPB, fibrinolysis, dilution or consumption of coagulation factors, anticoagulant therapy, preoperative antithrombotic therapy, and congenital or acquired coagulopathies. Communication with the blood bank should occur early to ensure an adequate supply of blood products for the patient. Five to 10 units of packed red blood cells (pRBCs) should be immediately available in the operating room, with a similar number of units available in the blood bank. Five to 10 units of fresh frozen plasma, typically given in a ratio of 1 per 1 to 2 pRBCs transfused should be readily available.

Thrombocytopenia and platelet dysfunction develop secondary to hypothermia and use of extracorporeal mechanical support, and the need for platelet transfusion is common.

In cases with refractory international normalized ratio (INR) elevation as the cause of coagulopathy or in patients with depressed cardiac or renal function, consideration of the use of prothrombin complex concentrates (PCCs) may be prudent. PCCs offer the advantage of rapid correction of INR with a minimal volume load and crossmatching is not required. Caution must be exercised given the possibility of thrombosis. Additionally, in the rare patient with heparin-induced thrombocytopenia (HIT), PCCs should not be administered because they contain heparin.

Fibrinolysis develops from the use of CPB, but supraceliac aortic cross-clamping and peripheral ischemia have also been shown to cause fibrinolysis that can be attenuated by the use of selective superior mesenteric artery perfusion. Supraceliac cross-clamping and peripheral ischemia promote activation of tissue-type plasminogen activator and decrease plasminogen activator inhibitor. The use of lysine analogs epsilon-aminocaproic acid and tranexamic acid is common in TAA repairs, but its use has been derived from studies in other cardiac surgeries and is not currently supported by the literature in TAA repair.

The use of a blood-salvaging device ("cell saver") is essential to decrease allogenic red blood cell transfusions. Unfortunately, the use of a cell saver is associated with the loss of platelets, plasma proteins, and coagulation factors. In heparinized patients, the use of cardiotomy suction permits the autotransfusion of filtered unwashed whole blood, which preserves platelets and coagulation factors.

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D. Postoperative Anesthetic Management

D.1. What are the postoperative complications after open TAAA repair?

Respiratory Failure

Respiratory failure after TAAA repair remains one of the most commonly reported complications. The large thoracoabdominal incision, diaphragmatic incision, and need for lung isolation all predispose the patient to pulmonary dysfunction. The diaphragmatic incision may lead to hemidiaphragm dysfunction or paralysis. Preoperative pulmonary dysfunction, tobacco use, postoperative cardiac complications, and postoperative renal complications are independent risk factors for postoperative respiratory failure.

Renal Failure

Postoperative renal dysfunction is a common postoperative complication, occurring in as many as 28% of patients and necessitating dialysis in 8% of patients. Risk factors associated with postoperative renal failure include age >50 years, preexisting renal dysfunction, administration of greater than 5 units of either pRBCs or salvaged washed autologous blood, and aortic cross-clamp time of more than 100 minutes. Postoperative renal dysfunction of any degree is associated with an increased perioperative mortality.

Spinal Cord Injury

Spinal cord injury remains one of the greatest fears after TAAA repair. Spinal cord injury can be immediate or delayed. Spinal cord injury occurs more often with type I and II TAAAs, emergent operations, intercostal sacrifice, and intraoperative hypotension. Spinal cord injury of any severity occurs in 11% of patients undergoing open TAAA repair, with 2% to 6% having total paraplegia. The majority of the deficits are immediate; however, delayed deficits can occur hours to weeks postoperatively. Immediate-onset deficits are irreversible and portend a poor prognosis, whereas delayed-onset deficits typically have a better prognosis with partial and reversible deficits and acceptable functional outcomes. Management of delayed-onset deficits focuses on CSF drainage (to a CSF pressure of 10 mmHg) and increasing systemic blood pressure (to an MAP of 100 mmHg) for improved spinal cord perfusion.

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D.2. What are the postoperative complications after endovascular TAAA repair?

Left Upper Extremity Ischemia

Aneurysms involving the aortic arch can pose a significant risk to cerebral and upper extremity blood flow with endovascular repair. Intentional coverage of the left subclavian artery with the endovascular graft can occur in approximately 50% of thoracic endograft implants. Most patients can tolerate left subclavian artery coverage without left upper extremity ischemia. However, if the right subclavian and vertebral arteries are not patent, ischemia can ensue. Additionally, the patient may experience

decreased blood flow to the LIMA, leading to significant ischemia to a prior coronary artery bypass graft. If left upper extremity ischemia occurs, a left subclavian artery bypass should be performed postoperatively.

Stroke

Intravascular wires and endografts that are introduced into the atherosclerotic aorta can come in contact with mobile thrombi in the arch and brachiocephalic vessels, leading to cerebral ischemia. Iatrogenic dissection of the carotid or vertebral arteries and retrograde dissection of the aorta have been described as devastating complications. If the left subclavian artery is covered during endograft deployment, cerebral ischemia may develop due to decreased flow from the left vertebral artery. A left carotid to left subclavian bypass graft should first be placed if the left subclavian will be covered by the graft. The incidence of stroke after TEVAR ranges from 2% to 8%. Risk factors for perioperative stroke include severe atheromatous aortic disease (grade IV or V aortic disease on TEE), endovascular coverage of aortic arch vessels, history of prior stroke, long extent of aortic coverage, preexisting CAD, longer procedure duration, and female gender.

Spinal Cord Ischemia

Spinal cord ischemia is also a possible complication of endovascular treatment of TAAAs, although with less incidence than after open repair. Intercostal arteries are intentionally covered during endovascular stent placement of a TAAA, possibly compromising spinal cord perfusion by obliterating the collateral circulation. Endovascular coverage of the left subclavian artery may compromise spinal cord perfusion in patients with a left dominant vertebral artery, solitary vertebral artery, carotid artery disease, or an incomplete circle of Willis. Spinal cord injury after TAAA repair is a heterogeneous

syndrome manifesting as a spectrum of impairments that varies depending on the severity and extent of ischemia. Additionally, delayed-onset neurologic deficits, similar to that seen after open repair, can also be seen after endovascular treatment. Delayed-onset deficits are thought to be due to postoperative events such as hypotension, thrombosis, hematoma, embolization, and elevated CSF pressure. Injury to the spinal cord is directly related to the extent of the aorta that is involved and is highest with Crawford type II repairs. Risk factors for spinal cord injury after TEVAR include left subclavian artery coverage without revascularization, concomitant open abdominal aortic surgery, and the use of three or more stent grafts.

Renal Failure

Similar to open repair of TAAAs, renal insufficiency can develop after endovascular repair with an incidence rate of 14%. Deployment of the endograft in a diseased, atherosclerotic aorta can lead to embolic showers, infarcting mesenteric, splenic, and renal arteries. This phenomenon contributes to the development of renal insufficiency. Risk factors for postoperative renal dysfunction after TEVAR include preoperative chronic renal insufficiency, perioperative blood transfusions, and the thoracoabdominal extent of the aneurysm.

Postimplantation Syndrome

This commonly observed phenomenon consisting of fever, leukocytosis, and an elevation in inflammatory markers normally occurs in the early postoperative period, although it may occasionally have a delayed presentation. It is usually mild and self-limiting, responding to conservative management with nonsteroidal anti-inflammatory drugs.

Endograft Collapse

Endograft collapse is a rare but serious complication after

TEVAR, typically presenting in the first 3 months after endovascular repair. Endograft collapse can present asymptomatically or can present with diminished or absent femoral pulses, abdominal pain, or multiorgan failure. Excessive oversizing of the endograft and poor apposition of the proximal endograft to the aortic wall are the primary causes of endograft collapse. Maldeployment of the endograft and progression of the aortic disease are rare causes of endograft collapse.

Endoleaks

An endoleak is a leakage of blood into an aneurysm sac previously excluded during TEVAR. Endoleaks after TEVAR occur in about 5% to 30% of patients. Endoleak is a complication unique to the endovascular approach to aortic repair, and there are four types.

Type I endoleak is caused by incomplete seal at the end of the graft, leading to blood flow into the aneurysm sac.

Type II endoleak is caused by leaking of blood into the aneurysm from collateral vessels excluded during repair.

Type III endoleak is caused by inadequate sealing of overlapping graft joints or rupture of graft fabric, leading to blood flow into the aneurysm sac.

Type IV endoleak is caused by the direct leakage of blood through a porous graft.

Management includes aggressive endovascular repair of type I and III endoleaks, with observation of type II endoleaks. Type IV endoleaks are of historical interest because new graft material has virtually eliminated the incidence of this complication. Risk factors for development of endoleaks include larger preoperative aneurysm sac diameter, greater length of stent coverage, and the use of multiple stent grafts.

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10 Abdominal Aortic Aneurysm Repair

Fun-Sun F. Yao and Anup Pamnani

The patient is a 76-year-old man with a 6-cm infrarenal aortic aneurysm discovered on routine physical examination and confirmed by abdominal computed tomography (CT) scan. He is a former smoker and complains of dyspnea on exertion and claudication. His electrocardiogram (ECG) shows Q waves in leads II, III, and aV_F; chest x-ray film displays mild hyperinflation of the lung fields; and his hematocrit is 46%. His baseline serum creatinine is 1.9.

A. Medical Disease and Differential Diagnosis

1. What risk factors are associated with an abdominal aortic aneurysm (AAA)?
2. What other diseases are commonly found in patients with aortic aneurysms?
3. What is the incidence of morbidity and mortality in these patients if they undergo elective open surgical repair? What is the natural history of the disease without surgical repair?
4. What should be done for smaller aortic aneurysms that are found in patients?
5. What is the risk of perioperative myocardial infarction (MI) in

patients with ischemic heart disease? What can be done to reduce the risk of ischemic events in these patients?

6. Does the morbidity and mortality of elective repair of an aortic aneurysm differ significantly from that of an emergency repair?

B. Preoperative Evaluation and Preparation

1. Which preoperative laboratory tests would you require for this patient?
2. What is the significance of the preoperative ECG? Would you wish to pursue a preoperative cardiac workup? What tests would you request, and what would they tell you?
3. Is it necessary to evaluate this patient's pulmonary status?
4. Preoperative arterial blood gas (ABG) measurement shows pH, 7.35; $Paco_2$, 47 mmHg; and Pao_2, 68 mmHg on room air. What is the significance of this result?
5. How would you measure creatinine clearance in this patient, and what is its value in this case?
6. Describe the blood flow to the spinal cord. What is its relevance to surgery involving the abdominal aorta?
7. How do you detect spinal cord ischemia?
8. What are the various surgical approaches to repair an AAA?
9. How does the choice of surgical technique affect the anesthetic management?
10. How would you premedicate this patient?

C. Intraoperative Management

1. Would you use an arterial line? What are the complications of arterial line placement?
2. What various monitors are available for myocardial ischemia? Is a pulmonary artery catheter (PAC) helpful in determining the occurrence of ischemia?
3. What additional monitors would you employ?
4. Is there a role for somatosensory evoked potential (SSEP)

monitoring during aortic clamping?

5. How would you anesthetize this patient for an open repair of the aorta? What techniques could be used for an endovascular aortic aneurysm repair? Discuss the various anesthetic techniques that can be employed for this surgery.
6. This patient is to be heparinized intraoperatively, and anticoagulation may be continued postoperatively. Is this a contraindication to the preoperative placement of either an epidural or intraspinal catheter? What if the patient is receiving anticoagulants in the preoperative period?
7. What are your plans for fluid and blood replacement during surgery?
8. What are the hemodynamic changes of aortic cross-clamp placement? What efforts can be made to minimize these changes both before and during cross-clamping? If the patient develops ST-segment depressions with a rising pulmonary capillary wedge pressure (PCWP) during cross-clamp, what maneuvers should be taken?
9. Because this case involves an infrarenal aneurysm, is renal blood flow affected with the placement of the cross-clamp? If an endovascular repair is chosen, what are the risks to the kidneys? Are there any treatment maneuvers that can be taken to minimize these risks in either repair?
10. What are the hemodynamic consequences of aortic cross-clamp removal? What can be done to minimize the effects of removing the aortic cross-clamp? If the systemic blood pressure remains depressed after removal of the cross-clamp, what is the differential diagnosis? How would you diagnose and correct the problem?

D. Postoperative Management

1. What are the parameters used to extubate this patient?
2. What are the anticipated changes in postoperative pulmonary

function in these patients? How does the surgical technique affect postoperative pulmonary function? Are there any postoperative maneuvers that can improve respiratory parameters?

3. How would you control postoperative pain? What are the alternatives in the management of this patient's postoperative pain?

A. Medical Disease and Differential Diagnosis

A.1. What risk factors are associated with an abdominal aortic aneurysm (AAA)?

AAA is a full-thickness dilatation of a segment of the abdominal aorta located between the diaphragm and the bifurcation of the aorta to the common iliac arteries. Approximately 200,000 AAAs are annually diagnosed, resulting in about 13,000 deaths per year in the United States. Risk factors for AAA include older age, male sex, family history of AAA, smoking, hypertension, hyperlipidemia, atherosclerotic occlusive disease, and obesity. Lifestyle factors reducing risk for AAA include regular exercise, smoking cessation, and favorable diet (includes fruit, vegetables, and nuts). Interestingly, diabetes mellitus is associated with *decreased* risk of AAA. The prevalence of AAA is lower in African Americans, Hispanics, and Asians in comparison to Whites and Native Americans.

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A.2. What other diseases are commonly found in patients

with aortic aneurysms?

The major pathologic cause of aneurysmal disease is atherosclerosis. In addition, hypertension (55%), heart disease (73.5%), peripheral vascular disease (21%), stroke and transient ischemic attacks (22%), diabetes mellitus (7%), and renal insufficiency (10%) are the most common comorbid illnesses. Smoking history has been reported in as many as 80% of patients presenting for AAA repair.

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A.3. What is the incidence of morbidity and mortality in these patients if they undergo elective open surgical repair? What is the natural history of the disease without surgical repair?

Morbidity in this patient group is most commonly due to cardiovascular, pulmonary, and renal complications. Perioperative mortality for elective open AAA repair is 2% to 5%. Increased postoperative mortality was associated with older age, elevated serum creatinine, lower forced expiratory volume in 1 second (FEV_1), and gender. One retrospective study demonstrated higher mortality in women in comparison to men: 7% versus 5% for open repair and 2% versus 1% for endovascular repair. Despite the increasing fraction of patients undergoing endovascular repair, numerous large studies have not shown significant long-term differences in mortality between open and endovascular repair. The major cause of death

in the nonsurgically treated patient is rupture, which carries a mortality of up to 80%. Ruptured AAAs account for approximately 9,000 deaths per year in the United States. One study demonstrated a doubling of expectancy after resection of AAA. The incidence of rupture within 5 years of diagnosis of AAA is 80%. The incidence of rupture increases with aneurysmal size: 25% for lesions of 4 to 7 cm in diameter, 45% for lesions 7 to 10 cm, and 60% for lesions larger than 10 cm. Repairing aneurysms smaller than 5.5 cm has not been shown to improve survival. Thus, only patients with aneurysms 5.5 cm or larger should be considered for surgical intervention.

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A.4. What should be done for smaller aortic aneurysms that are found in patients?

The U.S. Preventive Services Task Force (USPSTF) 2015 update on screening recommendations for AAA reinforces that early surgical intervention of smaller AAAs <5.5 cm (open or endovascular) does not reduce mortality. USPSTF recommends

repeat ultrasonography every 3 to 12 months for AAAs 3 to 5.4 cm with surgical referral for rapid growth (>1 cm per year) or when the aneurysm reaches 5.5 cm or larger. Therefore, watchful waiting is suggested for aneurysms that are smaller than 5.5 cm.

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A.5. What is the risk of perioperative myocardial infarction (MI) in patients with ischemic heart disease? What can be done to reduce the risk of ischemic events in these patients?

A retrospective analysis confirmed that cardiac mortality is high for patients who undergo vascular surgery and experience postoperative myocardial ischemia. Key factors that determine perioperative morbidity and mortality rates include the stress of surgery (aortic, peripheral vascular, emergency surgery), increased blood loss, poor preoperative cardiac functional status, history of congestive heart failure (CHF), a low ejection fraction, known coronary artery disease (CAD), and preoperative history of coronary artery bypass grafting.

The occurrence of a recent MI is an important independent predictor of perioperative morbidity and mortality. In a prospective cohort examining perioperative reinfarction by Rao et al., the statistical rate of reinfarction was related to the length of time since the initial MI, decreasing to less than 2% if the infarction occurred more than 6 months earlier. Acute screening and care of the MI patient has improved; risk stratification and noninvasive testing allows for a more tailored approach to the

timing of surgery in these patients.

Special consideration needs to be given to patients who have recently undergone percutaneous coronary intervention procedures for coronary revascularization, maintained on antiplatelet therapy. This is due to the significant risk of acute stent restenosis or thrombosis if antiplatelet therapy is prematurely terminated. The management of the dual antiplatelet therapy regimen should be customized to each patient depending on the type and urgency of surgery, type of coronary stent, time since the coronary intervention, and complexity of the coronary intervention. The current recommendations for perioperative management of patients with drug-eluting stent (DES) are shown in **Figure 10.1**. For patients identified at high risk for stent thrombosis, surgery should be planned in a hospital with cardiac catheterization facilities. Postoperatively, these patients require a monitored setting and immediate resumption of antiplatelet therapy. Signs and symptoms of stent thrombosis should be promptly recognized and aggressively treated with percutaneous coronary intervention.

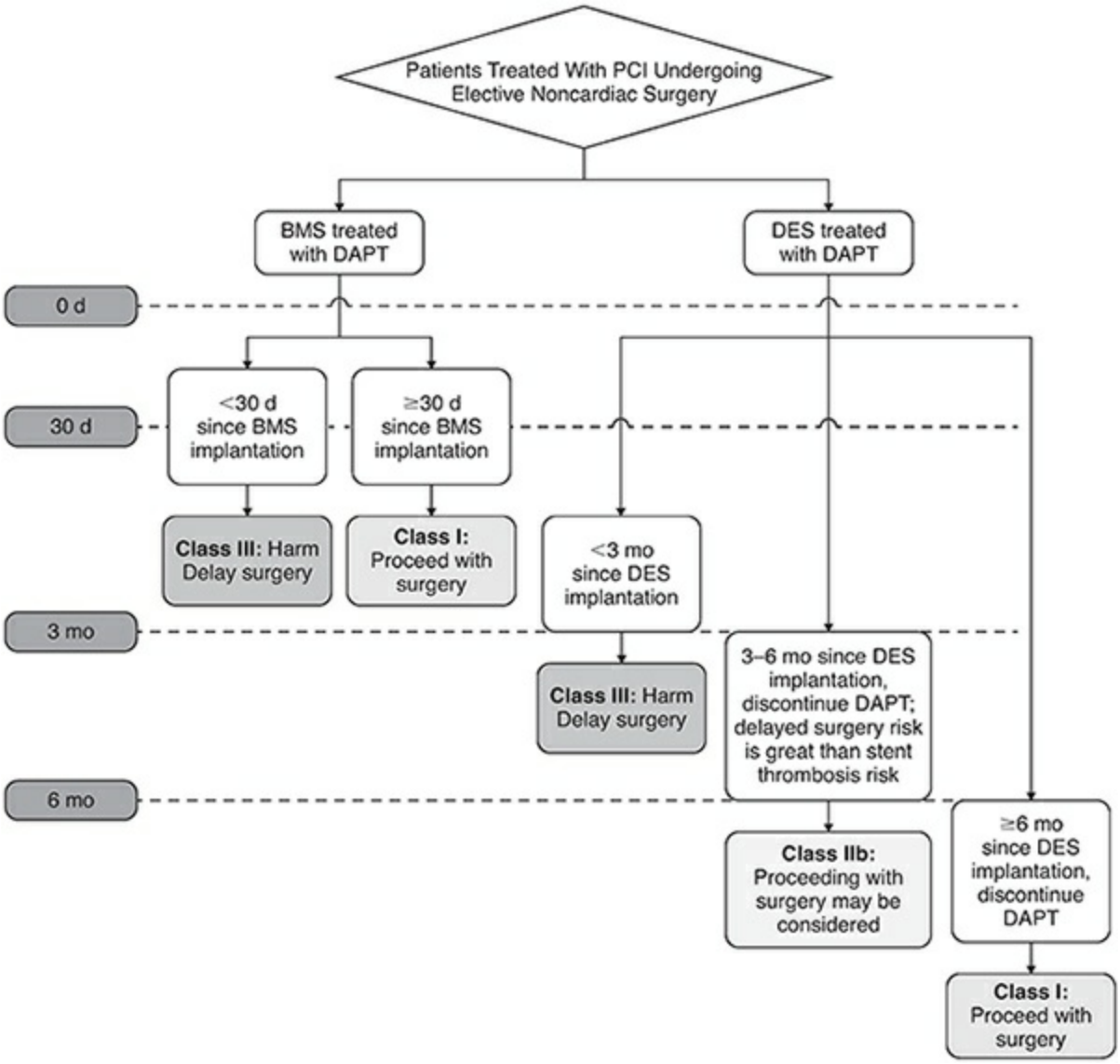

FIGURE 10.1. Treatment algorithm for timing of elective noncardiac surgery in patients with coronary stents. BMS, bare metal stent; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; PCI, percutaneous coronary intervention. (*Reprinted with permission from Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines.* Circulation*. 2016;134[10]:e123–e155.*)

The 2016 American College of Cardiology (ACC)/American Heart Association (AHA) guideline focused update on duration of dual antiplatelet therapy in patients with CAD recommended the following:

- Elective noncardiac surgery should be delayed 30 days after bare metal stent (BMS) implantation and optimally 6 months

after DES implantation.

- In patients who must undergo surgical procedures that mandate the discontinuation of $P2Y_{12}$ inhibitor therapy, aspirin be continued if possible and the $P2Y_{12}$ platelet receptor inhibitor be restarted as soon as possible after surgery.
- When noncardiac surgery is required in patients currently taking a $P2Y_{12}$ inhibitor, a consensus decision among treating clinicians as to the relative risks of surgery and discontinuation or continuation of antiplatelet therapy can be useful.
- Elective noncardiac surgery after DES implantation in patients for whom $P2Y_{12}$ inhibitor therapy will need to be discontinued may be considered after 3 months if the risk of further delay of surgery is greater than the expected risks of stent thrombosis.

In most studies, the morbidity following a perioperative MI approaches 50%. The risk after an MI may be best linked to the ongoing risk of ischemia. Patients who have survived a non–Q-wave infarction are potentially at great risk for further ischemia. Badner et al. reported a 17% post-MI mortality rate after noncardiac surgery. The mortality rate was higher in the presence of intraoperative ST-segment and T-wave changes. These patients should be evaluated by symptom-limited exercise testing and/or cardiac catheterization. The prevention of perioperative myocardial ischemia is the goal of the anesthesiologist regardless of the technique chosen. This entails reduction of myocardial oxygen demand (avoid tachycardia and hypertension), while increasing oxygen supply (prevent hypotension and anemia). Oxygen demand on the left ventricle is dependent on heart rate, contractility, and the ventricular loading conditions. Of the three, the increase in heart rate

imposes the greatest demand and should be readily controlled by the anesthesiologist. Left ventricular preload and afterload also affect oxygen demand by end-diastolic and systolic wall tension. Other factors, such as coronary collateral blood flow, hematocrit, and blood rheology may also influence myocardial ischemia.

β-Adrenergic antagonists are a well-established class of drugs effective in reducing myocardial oxygen consumption. Some studies suggest that *β*-blockers reduce perioperative ischemia and may reduce the risk of MI and cardiovascular death in patients undergoing high-risk procedures such as vascular surgery. The mechanism of reduction of myocardial oxygen consumption with *β*-antagonism is related to decreases in heart rate and myocardial contractility, counteracting the deleterious effects of sympathetic stimulation. In addition, this class of drugs has antiarrhythmic qualities. Currently, the only class I recommendation for perioperative *β*-blockers use by the AHA is to continue their use in the patients who are already on *β*-blockers. Patients undergoing vascular surgery who have multiple risk factors or have reversible ischemia on preoperative testing may benefit from perioperative *β*-blockers (class IIa). Although there are some differences between the European Society of Cardiology and the AHA guidelines, both agree that if *β*-blockers are used for prophylactic purposes, they should be slowly titrated (at least a week prior to elective surgery) and acute administration of high-dose *β*-blockers in high-risk population is not recommended.

Nitrates also can reduce myocardial oxygen demand by decreasing preload and by dilating large epicardial coronary arteries and collateral conduit vessels. However, the benefit of perioperative nitroglycerin prophylaxis has not been proven.

The use of statins in patients with cardiovascular disease is increasingly supported by multiple studies that display a

reduction in the risk of MI, stroke, and mortality. Furthermore, accumulating data suggests that continuation of statin therapy in the preoperative period reduces the risk of postoperative death and acute coronary syndromes. The mechanisms by which statin medications attenuate cardiovascular disease extend beyond their lipid-lowering properties. In addition to anti-inflammatory and antioxidant actions, they also improve endothelial function and stabilize plaques. Thus, current ACC/AHA guidelines recommend continuation of statin therapy in the perioperative period.

Abualsaud AO, Eisenberg MJ. Perioperative management of patients with drug-eluting stents. *JACC Cardiovasc Interv*. 2010;3:131–142.

Badner NH, Knill RL, Brown JE, et al. Myocardial infarction after noncardiac surgery. *Anesthesiology*. 1998;88:572–578.

Brooke BS. Perioperative beta-blockers for vascular surgery patients. *J Vasc Surg*. 2010;51:515–519.

Devereaux PJ, Yang H, Yusuf S, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. *Lancet*. 2008;371:1839–1847.

Eldrup N, Budtz-Lilly J, Laustsen J, et al. Long-term incidence of myocardial infarct, stroke, and mortality in patients operated on for abdominal aortic aneurysms. *J Vasc Surg*. 2012;55(2):311–317.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guidelines on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130:2215–2245.

Le Manach YL, Coriat P, Collard CD, et al. Statin therapy within the perioperative period. *Anesthesiology*. 2008;108:1141–1146.

Levin GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: an update of the 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention, 2011 ACCF/AHA guideline for coronary artery bypass graft surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease, 2013 ACCF/AHA

guideline for the management of ST-elevation myocardial infarction, 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes, and 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery. *Circulation*. 2016;134:e123–e155.

Lindenauer PK, Pekow P, Wang K, et al. Perioperative beta-blockade therapy and mortality after major noncardiac surgery. *N Engl J Med*. 2005;353(4):349–361.

McFalls EO, Ward HB, Moritz TE, et al. Coronary-artery revascularization before elective major vascular surgery. *N Engl J Med*. 2004;351:2795–2804.

Poldermans D, Bax JJ, Boersma E, et al. Guidelines for pre-operative cardiac risk assessment and perioperative cardiac management in non-cardiac surgery. *Eur Heart J*. 2009;30:2769–2812.

Popescu WM. Perioperative management of the patient with a coronary stent. *Curr Opin Anaesthesiol*. 2010;23:109–115.

Rao TL, Jacobs KH, El-Etr AA. Reinfarction following anesthesia in patients with myocardial infarction. *Anesthesiology*. 1983;59:499–505.

A.6. Does the morbidity and mortality of elective repair of an aortic aneurysm differ significantly from that of an emergency repair?

The overall mortality for a ruptured aortic aneurysm is greater than 50%. One study showed an overall survival rate of 19.8% as compared with an elective surgical survival rate of 95%. The worst prognosis occurred in patients older than 80 years; a systolic blood pressure of less than 80 mmHg on admission; a prior history of hypertension, angina, or previous MI; and an operating time of greater than 4 hours. Other risk factors include a systolic blood pressure less than 100 mmHg at the end of surgery and blood loss greater than 11,000 mL. Retroperitoneal rupture was more likely to be associated with a higher rate of survival. Elective surgical intervention should be considered if the size of the aneurysm changes rapidly or if its diameter is greater than 5.5 cm.

Eefting D, Ultee KH, Von Meijenfeldt GC, et al. Ruptured AAA: state of the art management. *J Cardiovasc Surg (Torino)*. 2013;54(1 suppl 1):47–53.

Lederle FA, Kane RL, MacDonald R, et al. Systematic review: repair of unruptured abdominal aortic aneurysm. *Ann Intern Med*. 2007;146(10):735–741.

B. Preoperative Evaluation and Preparation

B.1. Which preoperative laboratory tests would you require for this patient?

The patient should have the following laboratory tests as part of the preoperative evaluation: complete blood count and platelet count, serum electrolytes, blood urea nitrogen (BUN), creatinine, and coagulation profile. Chronic hypercarbia may be gleaned from the serum bicarbonate value. A chest radiograph will help ascertain whether signs of heart failure, pulmonary disease, or acute pneumonia are present. Spirometry should be considered in the patient with severe disease and those in whom an adequate medical history is not available. In addition, spirometric data may be useful in assessing the effects of inhaler therapy.

An ECG should be obtained because this patient displays multiple risk factors for ischemic disease. The ECG is a sensitive and simple screening test for active cardiac conditions, such as unstable coronary syndromes and significant arrhythmias, which necessitate further management prior to proceeding to surgery. Additionally, preoperative laboratory tests should be defined by positive findings on history and physical exam.

Edwards AF, Forest DJ. Preoperative laboratory testing. *Anesthesiol Clin*. 2018;36(4):493–507.

B.2. What is the significance of the preoperative ECG? Would you wish to pursue a preoperative cardiac workup? What tests would you request, and what

would they tell you?

The patient's preoperative ECG is consistent with a prior inferior wall MI. Patients with a history of a prior MI or angina in conjunction with an abnormal ECG have a fivefold increase in postoperative mortality when compared with those with no clinical indication of CAD. This patient's history of claudication suggests peripheral vascular disease. Peripheral artery disease is associated with a fourfold increase in risk for MI and a twofold to threefold increase in risk of stroke. In selected patients with severe or unstable cardiac ischemia, evaluation may be needed to assess if prior myocardial revascularization is indicated.

When coronary angiography was performed on 1,000 patients undergoing elective peripheral vascular surgery, it was revealed that more than half of the patients had significant CAD (greater than 50% stenosis), and 33% had severe stenosis (greater than 70%). Of the asymptomatic patients with no history or electrocardiographic evidence of ischemic heart disease, 15% had severe CAD and 22% of these seemingly normal patients had impaired left ventricular function. Hertzer et al. found that only 8% of patients undergoing elective vascular surgery had normal coronary arteries.

A comparison of this patient's current ECG with a prior ECG may aid in assessing the timing of the previous infarction if the history alone is not helpful. The 2014 update to the joint AHA/ACC guidelines concerning perioperative cardiovascular assessment suggest incorporating clinical risk factors, exercise tolerance, and surgical risk when determining whether further testing is necessary. Vascular surgeries, such as AAA repair, are categorized as high-risk procedures. In addition, clinical risk factors include a history of ischemic disease, compensated or prior heart failure, cerebrovascular disease, diabetes mellitus, and renal insufficiency. The algorithm for the cardiac assessment of patients undergoing surgical procedures

associated with a high perioperative cardiac risk is shown in **Figure 10.2**.

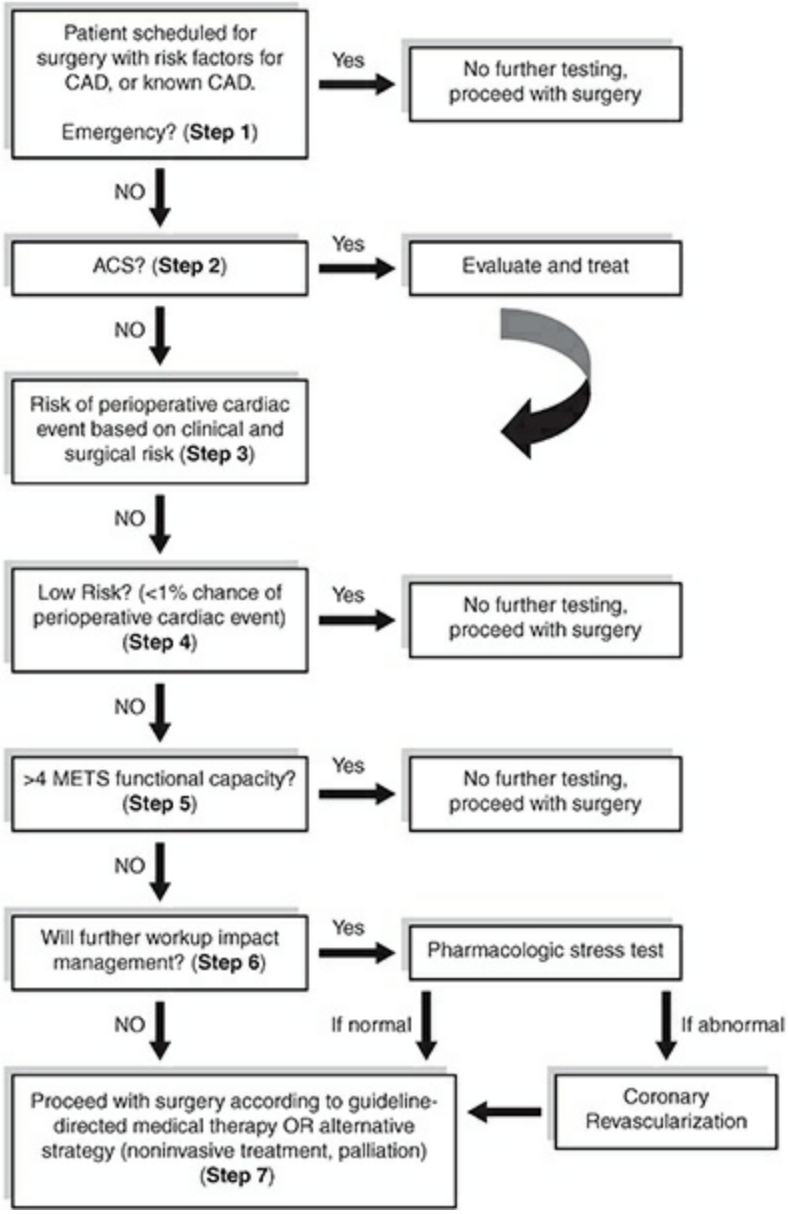

FIGURE 10.2. Stepwise algorithm for preoperative assessment for patients with coronary artery disease (CAD) undergoing noncardiac surgery. ACS, acute coronary syndrome; METS, metabolic equivalents. (*Reprinted with permission from Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guidelines on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines.* Circulation*. 2014;130:2215–2245. Copyright © 2014 American Heart Association, Inc.*)

Many vascular surgery patients are unable to undergo

exercise stress testing because of limitations presented by their cardiac, pulmonary, or peripheral vascular disease. A dipyridamole-thallium stress test or a dobutamine stress echocardiogram is a pharmacologic test to assess ischemic potential. Dipyridamole causes vasodilation of normal coronary arteries. This results in a "steal" of blood flow from the area beyond a coronary stenosis. Blood flow redistributes as the drug dissipates.

Positive results on preoperative stress testing may not always necessitate revascularization. There is evidence to suggest that vascular patients who undergo coronary revascularization have an increased risk of periprocedural and long-term complications. The decision to perform coronary revascularization procedures, rather than employ medical management, should be undertaken in close consultation with a cardiologist and a cardiac surgeon. Recent evidence also suggests that patients at significant risk for ischemic heart disease may benefit from an endovascular approach, if anatomically feasible.

Perioperative cardiovascular care for noncardiac surgery is clearly evolving with the publication of large-scale clinical trials, and the focus on determining the value of different assessment and treatment strategies to patient clinical outcome and long-term improvement in quality of life can be better determined. Although there is a growing trend to move from extensive preoperative testing to more targeted surveillance and treatment, the key question will be ensuring that patients make the most informed decision regarding the indication for surgery given the patient's trajectory for recovery, including returning to baseline or improved functional status and health.

Fleisher LA. The value of preoperative assessment before noncardiac surgery in the era of value-based care. *Circulation*. 2017;136:1769–1771.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients

undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130:2215–2245.

Glance LG, Faden E, Dutton RP, et al. Impact of the choice of risk model for identifying low-risk patients using the 2014 American College of Cardiology/American Heart Association perioperative guidelines. *Anesthesiology*. 2018;129:889–900.

Hertzer NR, Beven EG, Young JR, et al. Coronary artery disease in peripheral vascular patients. A classification of 1000 coronary angiograms and results of surgical management. *Ann Surg*. 1984;199:223–233.

Kertai MD. Preoperative coronary revascularization in high-risk patients undergoing vascular surgery: a core review. *Anesth Analg*. 2008;106:751–758.

Troisi N, Dorigo W, Lo Sapio P, et al. Preoperative cardiac assessment in patients undergoing aortic surgery: analysis of factors affecting the cardiac outcomes. *Ann Vasc Surg*. 2010;24:733–740.

B.3. Is it necessary to evaluate this patient's pulmonary status?

The patient's smoking history and the chronic changes present on his chest radiograph are evidence of chronic obstructive pulmonary disease (COPD). Provided the patient is minimally symptomatic and has good functional status, a detailed history and thorough physical exam can provide significant information regarding pulmonary status. A chest radiograph can be particularly useful at detecting underlying lung infection. If the radiograph displays the absence of acute pulmonary processes, as in this patient, further pulmonary testing may not be indicated. In the patient with severe signs and symptoms of COPD, ABG analysis can evaluate the patient's ability to oxygenate and ventilate. Patients with severe COPD tend may be chronically hypercarbic and hypoxic. A preoperative ABG can guide perioperative ventilatory management and predicting the likelihood of postoperative mechanical ventilation in these patients.

In those patients with severe disease, particularly those with poor functional status and significant findings on physical exam

and chest radiograph, pulmonary function testing may be indicated. Preoperative pulmonary function testing evaluates baseline forced vital capacity (VC) and FEV_1. Maximum midexpiratory flow rate (MMEFR) is an effort-independent value that is a sensitive index of small airway obstruction. Peak expiratory flow rate is related to the FEV_1 and MMEFR, although often it is less reproducible. These tests should be performed before and after bronchodilator therapy to assess reversibility of airway obstruction. A 15% improvement is considered a positive response.

This patient is a 2-pack-per-day smoker with dyspnea on exertion, and the anticipated surgery required an upper abdominal incision. These factors likely affect his baseline pulmonary function and presage postoperative ventilatory problems. A VC less than 50% of predicted, or less than 2 L total, is an indicator of increased risk of pulmonary complications as a VC at least 3 times the tidal volume is necessary for an effective cough. FEV_1 less than 2 L, maximum breathing capacity less than 50% of predicted, and MMEFR less than 50% of predicted are also values associated with increased risk of postoperative mechanical ventilation.

Discontinuation of smoking for 48 hours preoperatively increases oxygen tissue availability and, if stopped 4 to 6 weeks before surgery, may decrease postoperative complications. Pulmonary function tests should be viewed as a management tool to optimize preoperative pulmonary function should not be the sole means of assessing risk. Functional status, severity of illness, and comorbid medical conditions also have significant predictive value.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:237–264.

Niewoehner DE. Clinical practice. Outpatient management of severe COPD. *N*

Engl J Med. 2010;362(15): 1407–1416.

Warner DO. Preventing postoperative pulmonary complications: the role of the anesthesiologist. *Anesthesiology*. 2000;92:1467–1472.

B.4. Preoperative arterial blood gas (ABG) measurement shows pH, 7.35; $PaCO_2$, 47 mmHg; and PaO_2, 68 mmHg on room air. What is the significance of this result?

The normal value for Pao_2 in young adults ranges from 85 to 100 mmHg with an average of about 95 mmHg. This value falls steadily with aging to an average Pao_2 of 80 mmHg at age 60 years. One formula for estimating Pao_2 is $Pao_2 = 100 - (\text{age in years} / 3)$. The normal range for $PaCO_2$ is 37 to 43 mmHg and is unaffected by aging. For every 10 mmHg increase in $PaCO_2$, pH decreases by 0.05. For every 10 mmHg decrease in $PaCO_2$, pH increases by 0.1.

The main causes of arterial hypoxemia are hypoventilation, diffusion impairment, shunting, and ventilation/perfusion ($\dot{V}/\dot{Q}$) mismatch. The major causes of hypercarbia or carbon dioxide retention are hypoventilation and $\dot{V}/\dot{Q}$ mismatch. Mild $\dot{V}/\dot{Q}$ mismatch does not necessarily cause an increase in arterial CO_2. This is due to the fact that CO_2 is a highly diffusible gas and central chemoreceptors compensate for increasing CO_2 tension by causing an increase in ventilation. The same is not true of arterial oxygenation, however, as even mild degrees of $\dot{V}/\dot{Q}$ mismatch can lead to hypoxemia.

The assessment of this patient's blood gas analysis reveals moderate hypoxemia with a mildly elevated CO_2 tension. The pH is consistent with a mild respiratory acidosis. The most likely reason for this patient's blood gas abnormality is $\dot{V}/\dot{Q}$ mismatch, secondary to COPD, which is likely the result of his extensive smoking history.

West JB. *West's Respiratory Physiology: The Essentials*. 10th ed. Baltimore: Wolters Kluwer; 2016:63–86.

B.5. How would you measure creatinine clearance in this patient, and what is its value in this case?

Preoperative renal dysfunction indicates potential postoperative impairment. Despite maximal medical management, including hemodialysis, acute renal failure (ARF) after aortic reconstruction carries a mortality of greater than 30% postoperatively. Maintenance of intravascular volume and adequate blood pressure are the best means of avoiding postoperative renal failure. This complication is more likely in patients requiring a suprarenal cross-clamp but also occurs with infrarenal clamping.

Operative mortality is 19% when aortic reconstruction is performed on patients with a creatinine greater than 2 mg per dL, but mortality is only 4.6% if the levels are lower. Therefore, if the creatinine is greater than 2 mg per dL, reversible factors, such as renal stenosis, should be investigated. The most direct measurement of glomerular filtration rate (GFR) is the measurement of creatinine clearance. Although BUN and serum creatinine are related to renal function, they are altered by such nonrenal factors as protein metabolism, diet, liver dysfunction, or skeletal muscle mass. A 24-hour collection of urine is measured, and the following equation is used to calculate GFR: $GFR = U \times V / P$. U, urine concentration of creatinine (mg per dL); V, volume of urine measured (mL per minute); P, plasma concentration of creatinine (mg per dL). A 2-hour sample collected through a Foley catheter has been shown to correlate well with a 24-hour sample collection.

In spite of the widespread use of creatinine clearance to detect renal impairment, it should be noted that as much as 50% of functional nephron mass may be lost before changes in creatinine concentration become apparent. As a result, patients

with lower baseline creatinine concentration can have acute kidney injury (AKI) despite normal creatinine clearance. Several novel biomarkers are being studied now that may be able to detect AKI earlier than traditional markers such as urinary output and serum creatinine. Neutrophil gelatinase-associated lipocalin (NGAL) is a protein found in excess in urine and plasma in patients with AKI as many as 48 hours prior to increase in serum concentration. Serum cystatin C, a protease inhibitor that is less affected by sex, age, muscle mass, and diet than creatinine, also allows earlier detection of AKI.

Borthwick E, Ferguson A. Perioperative acute kidney injury: risk factors, recognition, management, and outcomes. *BMJ*. 2010;340:c3365.

Sheinbaum R, Ignacio C, Safi H. Contemporary strategies to preserve renal function during cardiac and vascular surgery. *Rev Cardiovasc Med*. 2003;4(suppl 1):S21–S28.

Sladen RN. Anesthetic considerations for the patient with renal failure. *Anesthesiol Clin North Am*. 2000;18:863–882.

B.6. Describe the blood flow to the spinal cord. What is its relevance to surgery involving the abdominal aorta?

The spinal cord has a system of longitudinal arteries and a system of transverse arteries as shown in **Figure 10.3**. Anatomic studies have shown that the most important longitudinal arteries are a single anterior spinal artery supplying 75% of the cord and a pair of posterior spinal arteries supplying 25% of the cord. Although in humans the anterior spinal artery is a continuous vessel, modern anatomy has emphasized the reinforcing transverse arteries rather than the meager longitudinal vessels. The territory supplied by the anterior spinal artery is divided into three functionally distinct levels: cervicodorsal, intermediate or midthoracic, and thoracolumbar. The cervicodorsal region receives its blood supply from the vertebral, subclavian, thyrocervical, and costocervical arteries. The midthoracic region is supplied by a meager left or right intercostal artery arising

between the fourth and the ninth thoracic vertebrae. The thoracolumbar region of the anterior spinal artery receives the bulk of blood supply from one of the intercostal arteries—the *arteria radicularis magna* or the *artery of Adamkiewicz*. It arises at the level of T5–T8 in 15%, T9–T12 in 60%, L1 in 14%, and L2 in 10% of patients. The *arteria radicularis magna* is often involved in the surgical repair.

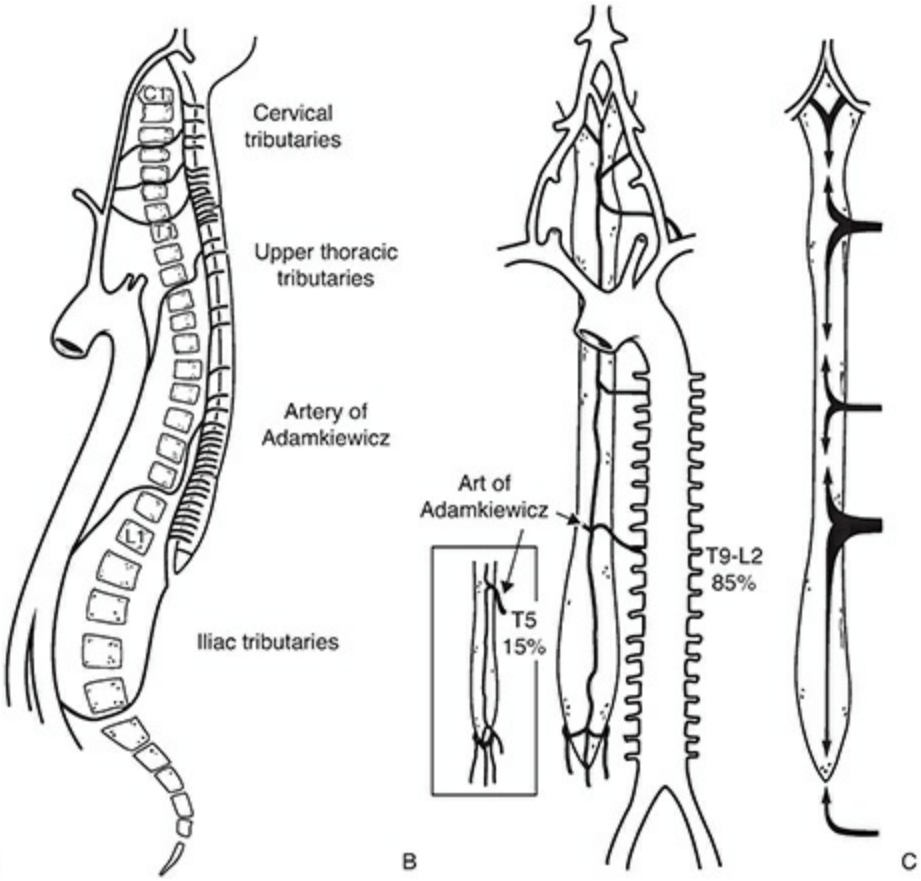

FIGURE 10.3. Diagram to show components of the anterior spinal artery. A. Arterial view. **B.** Anterior-posterior view showing origins of artery of Adamkiewicz. **C.** Schematic representation of direction and volume of flow from nutrient vessels supplying the anterior spinal artery. Size of arrows is proportional to flow contribution. (*Adapted from Bromage PR.* Epidural Anesthesia*. Philadelphia, PA: WB Saunders; 1978:50–54. Copyright © 1978 Elsevier. With permission.*)

The anterior spinal artery is smaller above than below the entry of the *arteria radicularis magna*. Resistance to blood flow is 51.7 times greater going up the anterior spinal artery as compared with coming down the artery. Therefore, distal aortic

perfusion during thoracic aortic cross-clamping protects the spinal cord below the *arteria radicularis magna* but not above it. This is why paraplegia still occurs in approximately 2% to 15% of patients having thoracic aortic surgery with distal aortic perfusion. However, reimplantation of intercostal arteries during surgery has been shown to reduce the incidence of neurologic injury.

Spinal cord ischemia can develop during aortic cross-clamping as a result of one of two mechanisms: decreased blood flow through critical intercostal arteries (important in infrarenal cross-clamping) and hypotension in the aorta distal to the cross-clamp, leading to a "steal" phenomenon through the collateral circulation to the distal aorta (important in thoracic cross-clamping). There are many strategies to prevent spinal cord ischemia: moderate hypothermia (local and systemic), cerebrospinal fluid drainage, and femoral–femoral bypass. The only definitive methods of preservation are expeditious surgery and maintenance of cardiac output.

Ling E, Arellano R. Systematic overview of the evidence supporting the use of cerebrospinal fluid drainage in thoracoabdominal aneurysm surgery for prevention of paraplegia. *Anesthesiology*. 2000;93:1115–1122.

Rickenbacher J, Landolt AM, Theiler K. *Applied Anatomy of the Back*. Berlin, Germany: Springer-Verlag; 1985:268–280.

B.7. How do you detect spinal cord ischemia?

Evoked potential is used in thoracoabdominal surgery to detect spinal cord ischemia. Two varieties of evoked potential are used in thoracoabdominal aortic aneurysm repair. SSEPs travel through the dorsal root ganglia to the posterior columns of the spinal cord. The potentials continue along the lemniscal pathways on to the thalamus and the cortex. Comparison of the latency and amplitude of the potentials, tested minutes apart, define the degree of change in the SSEP. Temperature,

anesthetic depth, and changes in blood flow can alter the evoked potentials. Changes in blood flow through the anterior spinal artery are not reflected in the posterior columns. It is possible, therefore, to have paralysis with normal SSEPs.

Ischemia of the spinal cord is indicated by increases in latency and/or decreases in amplitude of evoked potential tracing. The typical SSEP trace is shown in **Figure 10.4**, and its response to aortic cross-clamping is shown in **Figure 10.5**. The latency increases as early as 4 minutes following aortic cross-clamping, with progress to cessation of spinal cord conduction within 7 minutes of cross-clamping. Return of spinal cord conduction occurs 47 minutes following distal aortic reperfusion, with return to normal spinal cord conduction within 24 hours after operation. It has been shown that the loss of SSEP signals for longer than 14 to 30 minutes was associated with postoperative neurologic deficit.

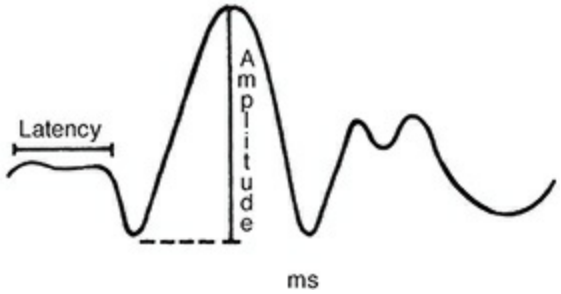

FIGURE 10.4. Typical SSEP trace. (*Reprinted with permission from Cunningham JN Jr, Laschinger JC, Merkin HA, et al. Measurement of spinal cord ischemia during operations upon the thoracic aorta: initial clinical experience.* Ann Surg. *1982;196[3]:285–296.*)

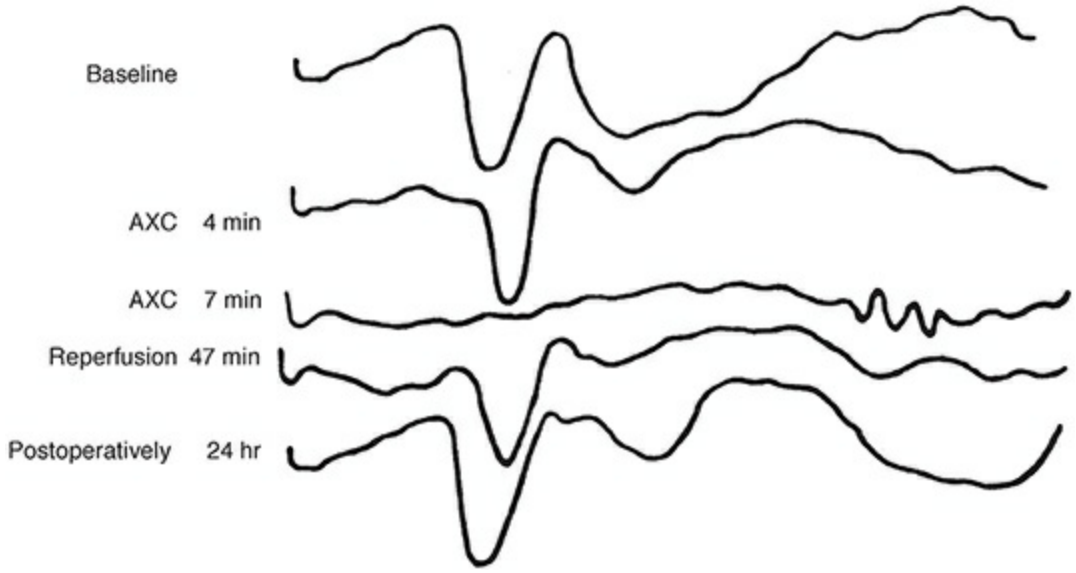

FIGURE 10.5. SSEP response to aortic cross-clamping (AXC). (*Reprinted with permission from Cunningham JN Jr, Laschinger JC, Merkin HA, et al. Measurement of spinal cord ischemia during operations upon the thoracic aorta: initial clinical experience.* Ann Surg. *1982;196[3]:285–296.*)

Motor evoked potentials (MEPs) relate monitor areas of the cord supplied by the anterior spinal artery. To assess MEP, patients require partial paralysis and light plane of anesthesia. Both of these requirements are suboptimal anesthetic options for a thoracoabdominal aortic aneurysm repair.

Finally, the signal-to-noise ratio of evoked potentials make interpretation of the data in the operating room more difficult and less reliable.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1112–1143.

Ginsbury HH, Shetter AG, Raudzens PA, et al. Postoperative paraplegia with preserved intraoperative somatosensory evoked potentials. *J Neurosurg*. 1985;63:296–300.

Jacobs MJ, Mess WH. The role of evoked potential monitoring in operative management of type I and type II thoracoabdominal aortic aneurysms. *Semin Thorac Cardiovasc Surg*. 2003;15(4):353–364.

B.8. What are the various surgical approaches to repair an AAA?

The classic approach to the abdominal aorta is through a vertical

anterior midline incision with a transperitoneal approach to the retroperitoneal space. This gives access to all major arteries in the abdomen and pelvis. A transverse abdominal incision (supraumbilical) is also adequate for a transperitoneal approach. Although the entry is slower, there is less pain and pulmonary impairment postoperatively. The transperitoneal approach, with the necessary exposure of the abdominal organs, causes major heat and fluid loss and prolonged postoperative ileus.

The retroperitoneal approach is performed through a left flank incision with the patient in the right lateral decubitus position. In some studies, this approach has been shown to have less respiratory and wound complications, less postoperative ileus, less blood loss, lower fluid requirements, and earlier discharge from the hospital. Monitoring and line placement must take the lateral position into consideration.

A less invasive approach to aortic aneurysm repair is endovascular aneurysm repair (EVAR) surgery. The EVAR technique has the advantage of a shorter length of stay (LOS) relative to open repair and a shortened recovery period. Due to the cost of the stent grafts and imaging equipment, this does not necessarily translate to overall cost reduction. Anatomic issues can significantly complicate stent placement. A common problem is iliac and common femoral arteries that are of insufficient caliber. Successful aneurysm exclusion has been achieved in 50% to 90% of selected cases. Problems of the procedure include vessel perforation, inability to seal the aneurysm (endoleaks), and inability to advance the device past the iliac artery, ultimately necessitating the conversion to an open repair.

In the EVAR-1 and Dutch Randomized Endovascular Aneurysm Management (DREAM) randomized clinical trials, reinterventions were required in 2 to 3 times as many patients in the endovascular group as in those who had open repair.

Endovascular leaks are one of the leading causes of postoperative complications necessitating reintervention in up to 15% of patients. The various types of endovascular leaks are shown in **Figure 10.6**. In the EVAR-1 trial, postoperative complications were 5 times more frequent with endovascular repair when compared to the open repair group. This highlights the importance of close follow-up in these patients and necessitates periodic reimaging for the remainder of these patients' lives. It is also worthy to note that endovascular repair has not been shown to improve survival in patients who have medical contraindication to open repair.

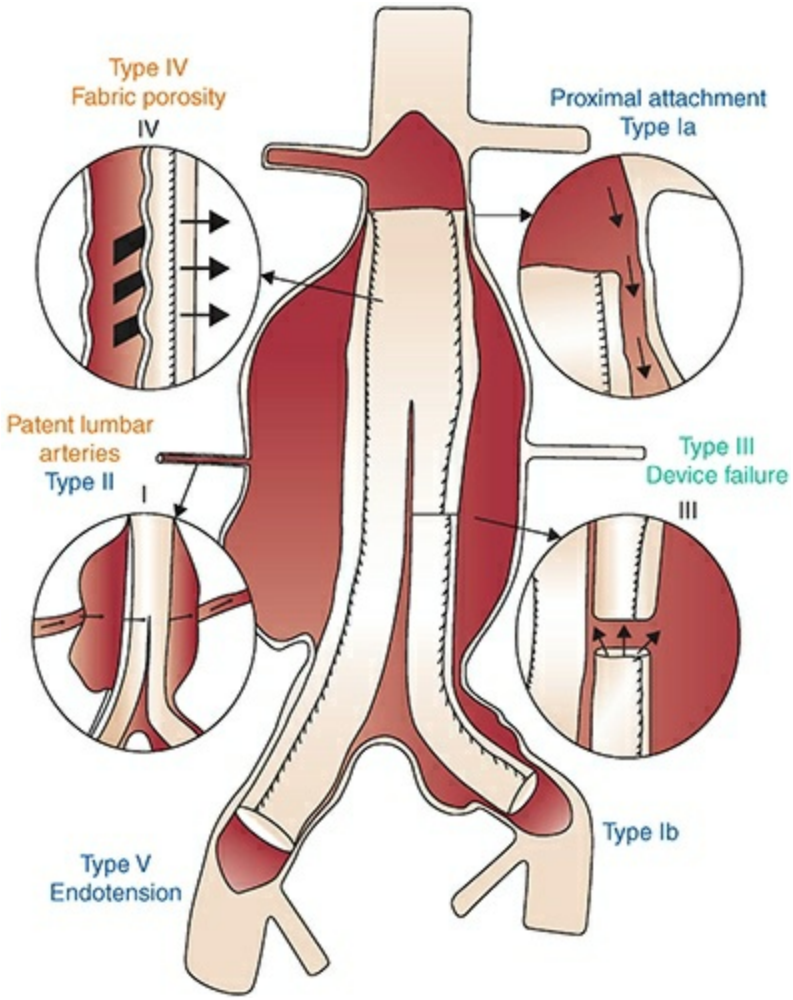

FIGURE 10.6. Types of endovascular leaks. (*Illustrations courtesy of the Society for Vascular Surgery ©.*)

In contrast, when compared with open abdominal repair in the perioperative period, endovascular surgery is associated with 60% less blood loss, and decreased ventilator days, decreased ICU LOS and decreased hospital LOS. Currently, overall mortality of the procedures appears similar, with slightly a slight decrease in morbid cardiac events (6% in the open repair group vs. 4.8% in the endovascular group).

Ballard JL, Yonemoto H, Killeen JD. Cost-effective aortic exposure: a retroperitoneal experience. *Ann Vasc Surg*. 2001;14(1):1–5.

Endovascular Aneurysm Repair (EVAR) Trial Participants. Comparison endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomized controlled trial. *Lancet*. 2004;364:843–848.

Endovascular Aneurysm Repair (EVAR) Trial Participants. Endovascular aneurysm repair and outcome in patients unfit for open repair of abdominal aortic aneurysms (EVAR trial 2): randomized controlled trial. *Lancet*. 2005;365:2179–2186.

Huang Y, Gloviczki P, Oderich GS, et al. Outcome after open and endovascular repairs of abdominal aortic aneurysms in matched cohorts using propensity score modeling. *J Vasc Surg*. 2015;62(2):304–311.e2.

Prinssen M, Verhoeven EL, Buth J, et al; for Dutch Randomized Endovascular Aneurysm Management (DREAM) Trial Group. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N Engl J Med*. 2004;351:1607–1618.

Sampram ES, Karafa MT, Mascha EJ, et al. Nature, frequency, and predictors of secondary procedures after endovascular repair of abdominal aortic aneurysm. *J Vasc Surg*. 2003;37:930–937.

B.9. How does the choice of surgical technique affect the anesthetic management?

Debate exists over the advantages of general anesthesia compared with regional anesthesia or combined approaches to the management of patients with CAD. Meticulous control of heart rate and blood pressure should be the goals regardless of technique. Regional anesthesia blunts sympathetic tone, potentially decreasing coronary perfusion pressure; general

anesthesia increases in sympathetic stimulation with intubation and emergence. Regional anesthesia may decrease hypercoagulability and thrombotic events in patients undergoing vascular surgery, and confers significant postoperative pain control.

The goals for the management of patients with CAD include prevention and mitigation of sympathetic stimulation. This can be achieved by using β-antagonists, narcotics, or volatile anesthetics during the perioperative period. Coronary perfusion pressure, defined as aortic diastolic pressure minus left ventricular end diastolic pressure, should be meticulously maintained. Myocardial contractility and heart rate should not be increased as this will increase oxygen demand.

De Virgilio C, Romero L, Donayre C, et al. Endovascular aortic aneurysm repair with general versus local anesthesia: a comparison of cardiopulmonary morbidity and mortality rates. *J Vasc Surg*. 2002;36:988–991.

Ellis JE, Roizen MF, Youngberg JA. Anesthesia for abdominal aortic revascularization. In: Youngberg JA, Lake CL, Roizen MF, et al, eds. *Cardiac, Vascular, and Thoracic Anesthesia*. Philadelphia, PA: Churchill Livingstone; 2000:336–337.

Warltier DC, Pagel PS, Kersten JR. Approaches to the prevention of perioperative myocardial ischemia. *Anesthesiology*. 2000;92:253–259.

B.10. How would you premedicate this patient?

Typically, a low-dose anxiolytic is likely to be sufficient premedication for most patients. Any other preoperative medications can be given intravenously upon arrival to the operating room. If oral medications are used, they may be taken with a sip of water 1 hour prior to the procedure.

Additional specific pharmacologic regimens should be tailored to individual patient needs. Various medications and combinations have been used, including narcotics, anticholinergics, barbiturates, and benzodiazepines. No single agent or combination has been demonstrated to be superior to

others. Respiratory depressants should be avoided in patients with chronic hypercapnia).

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1112–1143.

C. Intraoperative Management

C.1. Would you use an arterial line? What are the complications of arterial line placement?

Arterial pressure monitoring is exceedingly important in this case, from induction of anesthesia through emergence. In this patient with a history of CAD, an arterial line is particularly important for blood pressure management during induction and should be placed prior to the institution of anesthesia.

Vascular insufficiency and infection are the two major complications of arterial line placement. Catheter size and duration of cannulation are implicated in vascular occlusion. The causes of most vascular injuries are embolic. Radial artery cannulation is a low-risk, high-benefit method that can be used to closely monitor blood pressure in this patient. Open AAA repair is frequently associated with blood pressure lability, particularly on clamping and unclamping, and arterial blood pressure monitoring is particularly helpful in this situation. In addition, frequent sampling of ABGs to assess hematocrit, ventilation, perfusion, electrolyte levels, glucose, and level of anticoagulation may be necessary. If a radial artery catheter cannot be placed, cannulation attempts can be made at the brachial and axillary arteries. Concerns have been raised that brachial artery cannulation might be inadvisable given the lack of adequate collateral supply to the forearm and hand. In practice, however, complications from brachial artery cannulation have been reported rarely and the risk of vascular

insufficiency appears to be no different from that of radial cannulation. Axillary artery cannulation, however, may carry an added risk of vascular insufficiency and nerve injury from thrombosis and hematoma formation. This added risk is likely due to the fact that the axillary neurovascular bundle travels in the confined space of the axillary sheath.

Handlogten KS, Wilson GA, Clifford L, et al. Brachial artery catheterization: an assessment of use patterns and associated complications. *Anesth Analg*. 2014;118(2);288–295.

C.2. What various monitors are available for myocardial ischemia? Is a pulmonary artery catheter (PAC) helpful in determining the occurrence of ischemia?

Monitoring of the patient undergoing aortic reconstruction surgery should be aimed at preserving myocardial, pulmonary, and renal function as well as maintaining intravascular volume. Therefore, it is mandatory, particularly in this patient with known CAD, to monitor for myocardial ischemia and maintain volume status in the face of fluid shifts. Monitoring of the ST segments of the V_5 and II leads of the ECG is the most common method used to assess for intraoperative myocardial ischemia. However, in some studies, this alone was insufficient to recognize from 40% to 75% of intraoperative ischemic events detected by wall-motion abnormalities seen with a two-dimensional transesophageal echocardiogram.

Monitoring the pulmonary artery (PA) pressure tracing for the appearance of V waves and increasing PCWP with decreasing cardiac output are other methods of detecting intraoperative myocardial ischemia. Unfortunately, the PAC is not a particularly sensitive technique for detecting ischemic events. Wall-motion abnormalities, detected by transesophageal echocardiography (TEE), are highly sensitive markers of myocardial ischemia and appear earlier than either ST segment

or PAC waveform changes.

A microcomputer-based ECG reader (ST-segment trend monitor) also has been advocated as a monitor of myocardial ischemia. These systems can pick up more subtle changes in ST segments than by simple observation. Multilead ECG systems are most helpful. The most sensitive means for monitoring patients to determine the development of myocardial ischemia at its earliest presentation is, in fact, wall-motion abnormalities demonstrated by two-dimensional TEE. As yet, no improvement in outcome has been demonstrated by the use of any of these monitors.

American Society of Anesthesiologists and Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. Practice guidelines for perioperative transesophageal echocardiography. An updated report by the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. *Anesthesiology*. 2010;112(5):1084–1096.

American Society of Anesthesiologists Task Force on Pulmonary Artery Catheterization. Practice guidelines for pulmonary artery catheterization: an updated report by the American Society of Anesthesiologists Task Force on Pulmonary Artery Catheterization. *Anesthesiology*. 2003;99:998–1014.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1112–1143.

C.3. What additional monitors would you employ?

An invasive monitor of volume status is recommended in patients undergoing open AAA repair. The choice of invasive monitoring, central venous pressure (CVP) or PAC can be based on the level of aortic cross-clamping and the severity of the patient's underlying cardiac disease. The CVP is informative at low and high extremes. As the right side of the heart is usually a compliant system, large shifts of intravascular volume may occur without significant CVP alteration. The PCWP, obtained by a PAC, may be more accurate in determining intravascular volume status. In addition, the PAC allows for measurement of

cardiac output, helpful during aortic cross-clamp in the patient with left ventricular dysfunction. In this situation, CVP may not accurately represent left-sided pressures reflected by the PCWP. This is also true of the patient with significant pulmonary disease. The decision of PAC placement can also be influenced by the level at which the cross-clamp is applied. Suprarenal and supraceliac cross-clamping are associated with greater hemodynamic lability than infrarenal clamp application. Thus, PAC insertion may be of greater utility during proximal procedures, particularly if cardiac dysfunction is also present.

The American Society of Anesthesiologists (ASA) practice guidelines support the prudent use of a PAC in select situations. PAC should be employed in high-risk procedures (cardiac, aortic reconstruction, anticipated hemodynamic instability, and large-volume fluid shifts), used in patients with a minimal risk of complication from catheter placement, and used when appropriate staff (familiar with PAC troubleshooting) is available. Furthermore, when such monitoring is employed, it should only be utilized by those who are trained to appropriately interpret and intervene on the data.

TEE is another monitoring modality that is being increasingly utilized in aortic reconstruction procedures. TEE has several potential benefits over other invasive monitors such as the PAC and the CVP. Currently, TEE is the most sensitive modality for detecting myocardial ischemia. It is able to detect regional wall motion abnormalities well before changes appear on other heart monitors such as the ECG or PAC. In addition, TEE allows for detailed analysis of valvular dysfunction, which may significantly alter perioperative anesthetic management. The ASA practice guidelines state the use of perioperative TEE may be appropriate when the nature of the planned surgery or the patient’s cardiovascular pathology might result in severe hemodynamic, pulmonary, or neurologic compromise. In

addition, TEE should be used when unexplained life-threatening circulatory instability persists despite corrective therapy.

Another useful measure of intravascular volume status, as well as renal blood flow, is the collection of urine through a Foley catheter. Urine output will diminish with decreasing glomerular filtration caused by decreased renal blood flow. Assessment of urine output, provided kidney function is unimpaired, can be an accurate and cost-effective measure of volume status.

Temperature monitoring should also be employed as with any case under general anesthesia. Body temperature should be closely monitored and aggressively maintained. These patients can undergo tremendous heat and insensible fluid loss as a result of the enormous incisional surface area exposed to room air. If forced hot air thermal blankets are used, they are contraindicated on the lower extremities when an aortic cross-clamp is applied. They may, however, be used on the upper body throughout the procedure, along with fluid warmers, to maintain temperature.

Finally, pulse oximetry, capnography, and mass spectral analysis of inhaled agents also should be utilized. This data combined with ABG analysis, will permit efficient ventilatory management and accurate delivery of anesthetic gases.

American Society of Anesthesiologists and Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. Practice guidelines for perioperative transesophageal echocardiography. An updated report by the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. *Anesthesiology*. 2010;112(5):1084–1096.

American Society of Anesthesiologists Task Force on Pulmonary Artery Catheterization. Practice guidelines for pulmonary artery catheterization: an updated report by the American Society of Anesthesiologists Task Force on Pulmonary Artery Catheterization. *Anesthesiology*. 2003;99:998–1014.

Ansley DM, Ramsay JG, Whalley DG, et al. The relationship between central venous pressure and pulmonary capillary wedge pressure during aortic surgery. *Can J Anaesth*. 1987;34:594–600.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1112–1143.

C.4. Is there a role for somatosensory evoked potential (SSEP) monitoring during aortic clamping?

SSEPs can be used during aortic reconstruction surgery to monitor spinal cord function. For thoracic aortic surgery, SSEPs remain stable if the distal aortic pressure is maintained above 60 mmHg. At lower pressures, SSEPs gradually disappear. In one study, paraplegia occurred in 5 of 6 patients whose SSEPs remained absent for more than 30 minutes. Patients should be monitored for SSEP changes if they are at higher risk of spinal cord ischemia. SSEPs are most commonly altered in patients with baseline risk for neurologic complications. Proximal (especially thoracic) or prolonged cross-clamp placement increases risk for neurologic embarrassment. With a conduction block in place, such as epidural or spinal anesthesia, SSEPs will be ablated.

Ellis JE, Roizen MF, Youngberg JA. Anesthesia for abdominal aortic revascularization. In: Youngberg JA, Lake CL, Roizen MF, et al, eds. *Cardiac, Vascular, and Thoracic Anesthesia*. Philadelphia, PA: Churchill Livingstone; 2000:336–337.

Nuwer MR, Emerson RG, Galloway G, et al; for American Association of Neuromuscular and Electrodiagnostic Medicine. (2012). Evidence-based guideline update: intraoperative spinal monitoring with somatosensory and transcranial electrical motor evoked potentials. *J Clin Neurophysiol*. 2012;29(1):101–108.

C.5. How would you anesthetize this patient for an open repair of the aorta? What techniques could be used for an endovascular aortic aneurysm repair? Discuss the various anesthetic techniques that can be employed for this surgery.

All anesthetic techniques have been used and advocated for abdominal aortic surgery. General anesthesia, regional blockade,

or combined general and regional techniques, have all have been described. Outcome studies are equivocal among the various techniques, affording flexibility in the anesthetic approach to these patients. Tailoring this plan to each patient's medical condition is the most effective strategy. The primary goals in the anesthetic management of patients undergoing aortic reconstruction include protection of myocardial, neurologic, and renal function.

When combined regional (epidural) and general anesthesia techniques are employed, fluid requirements may be increased in order to maintain hemodynamic stability. Typically, this additional fluid requirement can be up to 2 L per case. In addition, neuroaxial sympathectomy can predispose to hypotension upon clamp removal. The use of α-agonist vasoconstriction, will counteract the vasodilatory effects of epidural anesthesia and may reduce fluid requirements. In addition, the placement of an epidural catheter will afford optimal postoperative pain management of the patient.

Anesthesia for endoluminal repair has ranged from general, general combined with epidural anesthesia, lumbar epidural with sedation, or sedation with local anesthesia. Considerations for choice of anesthesia include the need for patient immobility, the need for systemic anticoagulation (heparin), the possibility of exsanguination, and prevention of heat loss. Blood pressure stability is imperative during aortic balloon occlusion, to prevent distal migration of the stent. If neuraxial techniques are used, coagulation status must be carefully monitored in the perioperative period.

Baler AB, Lloyd G, Fraser TA, et al. Retrospective review of 100 cases of endoluminal aortic stent-graft surgery from an anaesthetic perspective. *Anaesth Intensive Care*. 1997;25:378–384.

Norris EJ, Beattie C, Perler BA, et al. Double-masked randomized trial comparing alternate combinations of intraoperative anesthesia and

postoperative analgesia in abdominal aortic surgery. *Anesthesiology*. 2001;95:1054–1067.

Rupert V, Leurs LJ, et al. Influence of anesthesia type on outcome after endovascular aortic aneurysm repair: an analysis based on EUROSTAR data. *J Vasc Surg*. 2006;44:16–21.

Yaeger MP, Burns AK. Regional versus general anesthesia for major vascular surgery. In: Kaplan JA, Lake CL, Murray MJ, eds. *Vascular Anesthesia*. 2nd ed. New York: Churchill Livingstone; 2004:165–186.

C.6. This patient is to be heparinized intraoperatively, and anticoagulation may be continued postoperatively. Is this a contraindication to the preoperative placement of either an epidural or intraspinal catheter? What if the patient is receiving anticoagulants in the preoperative period?

Epidural catheter placement in the setting of anticoagulation increases the risk of an epidural hematoma and subsequent neurologic deficit. Procedural risk of spinal cord ischemia will confound the diagnosis of neuroaxial hematoma and may preclude the placement of an epidural catheter. However, an epidural catheter can be placed with a relative degree of confidence in patients who are not anticoagulated at the time of the puncture but who will receive anticoagulation later. Current guidelines suggest administration of intravenous heparin at least 1 hour after neuraxial catheter placement. Furthermore, in patients who have undergone systemic heparinization, heparin should be discontinued for at least 2 to 4 hours prior to epidural catheter removal. Coagulation status must be assessed prior to catheter manipulation, and frequent lower extremity neurologic assessment must continue for at least 12 hours after catheter removal.

Low molecular weight heparins (LMWHs), which are increasingly being employed for thromboprophylaxis, pose a significant potential for increased risk of neuraxial hematoma. In

patients receiving these drugs, needle placement should occur at least 12 hours after the last dose of LMWH. If higher doses have been used (e.g., enoxaparin 1 mg per kg twice daily), needle placement should be delayed at least 24 hours. It is currently recommended that indwelling catheters be removed prior to initiation of LMWH thromboprophylaxis. In addition, the first dose should be administered at least 2 hours after catheter removal.

In those patients who are on chronic anticoagulation with oral warfarin, several recommendations are applicable with regard to perioperative management of neuraxial anesthesia. Oral warfarin should be discontinued at least 4 to 5 days prior to surgery. International normalized ratio (INR) should be measured at least 24 hours prior to the procedure. Neuraxial manipulation must commence only when INR has normalized. Neurologic testing of sensory and motor function should be performed routinely during epidural analgesia for patients on warfarin therapy. The type of analgesic solution should also be tailored to minimize the degree of sensory and motor blockade so as to allow frequent neurologic monitoring. As thromboprophylaxis with warfarin is reinitiated in the postsurgical period, neuraxial catheters should be removed while the INR is less than 1.5.

Fibrinolytic and thrombolytic drugs predispose to a high risk of hematoma formation in conjunction with neuraxial technique. Recent American Society of Regional Anesthesia and Pain Medicine (ASRA) practice guidelines, addressing regional anesthesia in the anticoagulated patient, recommend avoidance of all neuraxial manipulation in patients who have received thrombolytic or fibrinolytic therapy. There appears to be no clear data detailing the length of time neuraxial puncture should be avoided after discontinuation of these drugs.

Although the use of antiplatelet agents such as aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) do not

contraindicate the use of neuraxial techniques, care should be exercised when combinations of anticoagulants and antiplatelet drugs are used. Such combinations increase the risk of hemorrhagic complications in the perioperative period. Neurologic testing of sensory and motor function should be routinely performed on patients with indwelling catheters undergoing simultaneous anticoagulation.

Horlocker TT, Wedel DJ, Rowlingson JC, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine evidence-based guidelines (third edition). *Reg Anesth Pain Med*. 2010;35:64–101.

Rao TL, El-Etr AA. Anticoagulation following placement of epidural and subarachnoid catheters: an evaluation of neurologic sequelae. *Anesthesiology*. 1981;55:618–620.

C.7. What are your plans for fluid and blood replacement during surgery?

Fluid replacement should maintain the patient's intravascular filling pressures. Isotonic crystalloid should be used because there is little evidence to suggest that colloid administration poses any advantage over crystalloid administration.

There has been much controversy in recent literature regarding the use of "liberal" versus "restrictive" fluid protocols during open abdominal procedures. Most of this data has been gathered on patients undergoing bowel procedures but applicable to the patient undergoing open AAA repair. There is a lack of consensus regarding the optimal fluid management protocol. What has emerged from this data is the use of fluid therapy to optimize tissue perfusion rather than predefined volume replacement.

Current paradigm suggests a shift away from the classic model of calculation of nothing by mouth (NPO) fluid deficit, intraoperative insensible losses, and third-space losses. Increasingly, most clinicians are employing "demand-related"

regimens with the goal of maximizing tissue blood flow while minimizing interstitial edema. Surrogates for intravascular losses include visual blood loss, vital signs, urinary output, hematocrit, acid–base status, and invasive hemodynamics (as available). Insensible losses are replaced at 0.5 to 1 mL/kg/hr, a significantly lower rate than what has previously been utilized. The traditional concept of a third-space compartment is increasingly being abandoned. Instead, it is now recognized that fluid shift into the interstitium is a function of crystalloid overload and deterioration of vascular integrity.

The concurrent use of an autotransfuser (e.g., Cell Saver) decreases the need for exogenous blood transfusions. Liberal blood product administration should be avoided due to increased risk of immune suppression, hemolytic transfusion reactions, infectious vector transmission, and lung injury.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1112–1143.

Chappell D, Jacob M, Hofmann-Kiefer K, et al. A rational approach to perioperative fluid management. *Anesthesiology*. 2008;109:723–740.

Grocott MP, Mythen MG, Gan TJ. Perioperative fluid management and clinical outcome in adults. *Anesth Analg*. 2005;100:1093–1106.

C.8. What are the hemodynamic changes of aortic cross-clamp placement? What efforts can be made to minimize these changes both before and during cross-clamping? If the patient develops ST-segment depressions with a rising pulmonary capillary wedge pressure (PCWP) during cross-clamp, what maneuvers should be taken?

The systemic hemodynamic response to aortic cross-clamping is shown in **Figure 10.7**.

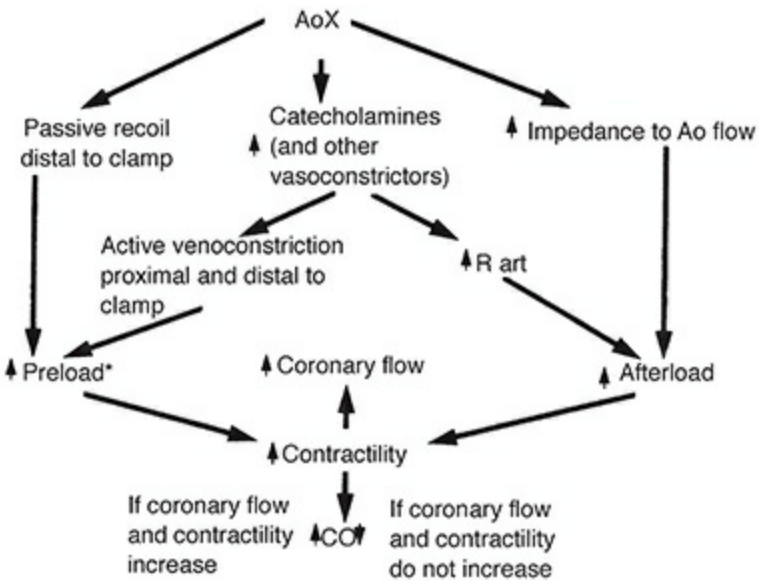

FIGURE 10.7. Systemic hemodynamic response to aortic cross-clamping (AoX). Ao, aortic; R art, arterial resistance; ↑ and ↓, increase and decrease, respectively. *Different patterns are possible. (*Reprinted with permission from Gelman S. The pathophysiology of aortic cross-clamping and unclamping.* Anesthesiology. *1995;82:1026–1060.*)

Arterial hypertension is the most dramatic and consistent result of the application of an aortic cross-clamp. This is the result of sudden increases in afterload and left ventricular end-diastolic wall stress. Usually, these changes are accompanied by decreased cardiac output. Some of these changes may also be due to redistribution of blood volume from the venous vasculature to the upper part of the body. All of the previously stated factors are more profound in the case of supraceliac or thoracic cross-clamp placement. Variations in blood volume status or splanchnic vascular tone are affected anesthetic depth, anesthesia technique, and intravascular volume status. These factors all determine the pattern of blood volume redistribution.

A sudden increase in afterload can lead to left ventricular failure, particularly in the patient with a noncompliant left ventricle. Ideally, the patient should have lower filling pressures for the half hour prior to cross-clamp placement. This mitigates the adverse response to sudden increased afterload. The PAC is helpful in accurately assessing and maintaining preclamp values

for the left side of the heart. A potent anesthetic agent and/or a vasodilator such as nicardipine is used to revert afterload to near normal. This also helps increase the cardiac output and decrease stress on the left ventricle. If this is insufficient to reverse left ventricular failure, the addition of an inotrope may be necessary.

The increase in afterload, following cross-clamp placement, may also result in myocardial ischemia. Ischemia, reflected as a rising PCWP and ST-segment depressions, can be managed with intravenous nitroglycerin, a potent dilator of the capacitance vessels. This drug is used to decrease left ventricular end-diastolic volume and left ventricular end-diastolic pressure. Decreasing left ventricular end-diastolic pressure also decreases the transluminal pressure across the coronary vasculature and augments blood flow to the myocardium.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1112–1143.

Gelman S. The pathophysiology of aortic cross-clamping and unclamping. *Anesthesiology*. 1995;82:1026–1060.

C.9. Because this case involves an infrarenal aneurysm, is renal blood flow affected with the placement of the cross-clamp? If an endovascular repair is chosen, what are the risks to the kidneys? Are there any treatment maneuvers that can be taken to minimize these risks in either repair?

ARF after aortic aneurysm repair is associated with a mortality of greater than 30%. Decreased renal function is observed in many patients after aortic cross-clamping, even when the clamp is placed distal to the renal arteries. Although it is clear that a suprarenal cross-clamp will decrease renal blood flow up to 80%, an infrarenal cross-clamp also causes a decrease in renal cortical blood flow with an associated decrease in GFR. The degree of decrease in urine output does not correlate with the

decrease in GFR nor does it predict postoperative renal failure. The most dangerous complication of alteration in renal blood flow is acute tubular necrosis and ARF.

The maintenance of cardiac output and adequate circulating blood volume is of cardinal importance in sustaining renal blood flow and in the prevention of renal failure. Low-dose dopamine (2 to 3 μg/kg/min) increases renal blood flow and may improve urine output, although decreased incidence of postoperative renal failure has not been proven. Renal protection may, however, be provided by the administration of mannitol (0.25 g per kg). The use of mannitol attenuates the reduction of renal cortical blood flow—before, during, and after renal ischemia—increases glomerular ultrafiltration flow, and is a hydroxyl free radical scavenger. Fenoldopam and furosemide may be utilized during aortic reconstruction procedures to minimize nephrotoxicity. Unfortunately, strong clinical evidence is currently lacking for any of these measures.

During endovascular repair, radiocontrast material may cause further insult to the kidneys. There is some suggestion that the use of a bicarbonate infusion or pretreatment with N-acetyl cysteine may be protective. It is prudent to minimize exposure to nonionic contrast or replace with gadolinium dimeglumine.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1112–1143.

Merten GJ, Burgess WP, Gray JV, et al. Prevention of contrast-induced nephropathy with sodium bicarbonate: a randomized clinical trial. *JAMA*. 2004;291(19):2328–2334.

Miller DC, Myers BD. Pathophysiology and prevention of acute renal failure associated with thoracoabdominal or abdominal aortic surgery. *J Vasc Surg*. 1987;5:518–523.

Paul MD, Mazer CD, Byrick RJ, et al. Influence of mannitol and dopamine on renal function during elective infrarenal aortic clamping in man. *Am J Nephrol*. 1986;6:427–434.

C.10. What are the hemodynamic consequences of aortic cross-clamp removal? What can be done to minimize the effects of removing the aortic cross-clamp? If the systemic blood pressure remains depressed after removal of the cross-clamp, what is the differential diagnosis? How would you diagnose and correct the problem?

The hemodynamic response to aortic unclamping is shown in **Figure 10.8**.

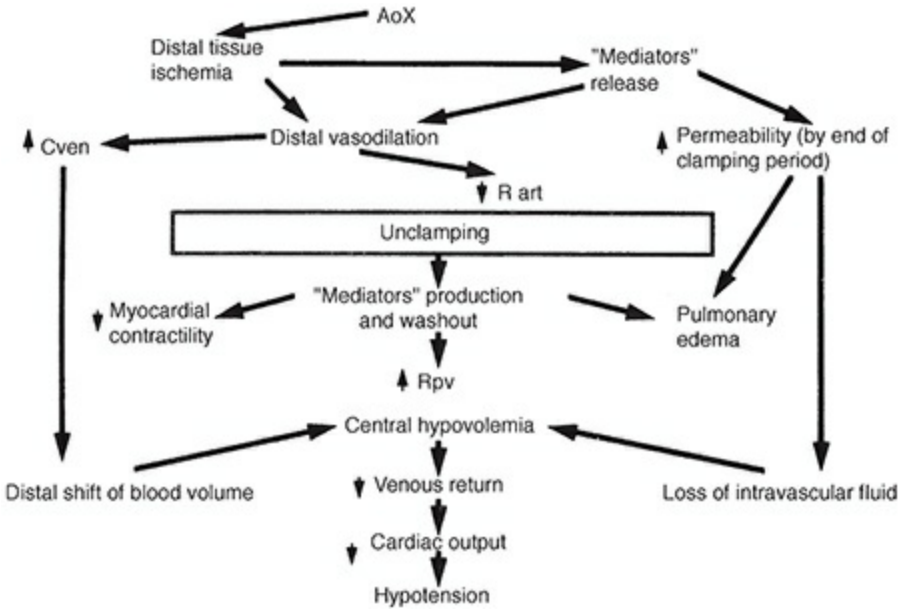

FIGURE 10.8. Systemic hemodynamic response to aortic unclamping. AoX, aortic cross-clamping; Cven, venous capacitance; R art, arterial resistance; Rpv, pulmonary vascular resistance; ↑ and ↓, increase and decrease, respectively. (*Reprinted with permission from Gelman S. The pathophysiology of aortic cross-clamping and unclamping.* Anesthesiology. *1995;82:1026–1060.*)

During cross-clamping, blood flow to the lower extremities is grossly decreased. Metabolism switches from aerobic to anaerobic as ischemia develops. This results in maximal vasodilation and lactic acid production. When the cross-clamp is released, systemic vascular resistance and arterial blood pressure decreases dramatically. Peripheral vasodilation can result in relative volume depletion and hypotension. Vasodilation may

become systemic as the lactic acid is washed out of the extremities into the central circulation. This condition is sometimes known as “declamping shock.”

To minimize the hypotensive response, volume loading in the period prior to cross-clamp release is suggested to raise filling pressures to slightly above normal. Vasodilators such as nitroprusside and/or nitroglycerin during this period allow additional volume loading with maintenance of filling pressures. In addition, gradual release of the clamp allows time for adjustments in volume, pressors, and correction of acidosis.

Sometimes, even in the face of adequate volume loading, the blood pressure remains low following cross-clamp removal. Proximal cross-clamping is associated with a higher incidence of hypotension. In this situation, it is advisable to ask the surgeon to reapply the aortic cross-clamp to varying degree depending on the severity of hypotension. Such maneuvers allow more time for correction of blood volume or acidosis.

Other causes of sustained hypotension in the face of adequate management include a continued site of hemorrhage and myocardial ischemia and/or failure. Measurement of filling pressures or use of TEE can particularly help in the differentiation of the etiology of sustained hypotension. Ischemia or failure can be detected by wall motion abnormalities or elevated filling pressures accompanying systemic hypotension. In contrast, hemorrhage is diagnosed by low filling pressures and increased systemic vascular resistance (due to reflex vasoconstriction).

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1112–1143.

Gelman S. The pathophysiology of aortic cross-clamping and unclamping. *Anesthesiology*. 1995;82:1026–1060.

D. Postoperative Management

D.1. What are the parameters used to extubate this patient?

The following ventilatory criteria can be used to assess suitability for extubation: The patient is awake and alert, has an adequate gag reflex, displays signs of adequate reversal of neuromuscular blockade, and meets minimum respiratory parameters for extubation. The typical respiratory parameters used to assess suitability for extubation are shown in **Table 10.1**.

TABLE 10.1 Typical Respiratory Parameters Used to Determine Suitability for Extubation

Vital capacity greater than 15 mL/kg
pH greater than 7.30
PaO_2 greater than 60 mmHg at FIO_2 less than 50%
$PaCO_2$ less than 50 mmHg
Maximal negative inspiratory force greater than −20 cm H_2O
Stable hemodynamic status
Respiratory rate less than 30 breaths per minute

FIO_2, fraction of inspired oxygen

It is important to recognize that such parameters should serve merely as a guide in the clinical assessment of suitability for extubation. The decision to extubate should be ultimately guided by assessment of the patient's overall status and clinical judgment. Extubation may need to be delayed in those patients who display labored breathing on physical exam, inadequate pain control, or hemodynamic instability.

Perioperative fluid management also should be carefully considered when assessing a patient's suitability for extubation. For shorter cases with minimal anticipated fluid shifts, the patient can be extubated in the immediate postoperative period. For longer cases, instances of large volumes of fluid

replacement and significant blood product administration, extubation should be delayed until the hemodynamics are stabilized and temperature is normalized. In these cases, airway swelling also can be a significant concern and may lead to ventilatory failure in the postoperative period. A "cuff leak" test may be somewhat indicative of the degree of airway edema. It is performed by occluding the endotracheal tube of a spontaneously breathing patient and auscultating for breath sounds with the cuff deflated.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:237–264.

D.2. What are the anticipated changes in postoperative pulmonary function in these patients? How does the surgical technique affect postoperative pulmonary function? Are there any postoperative maneuvers that can improve respiratory parameters?

The transabdominal approach to the aorta involves an upper abdominal incision. Total lung capacity and its subdivisions decrease after upper abdominal surgery. VC decreases 25% to 50% and returns to normal in 1 to 2 weeks, and residual volume increases 13%. Functional residual capacity declines 30% and recovers over 3 to 4 days. Expiratory reserve volume declines 20% after lower abdominal surgery and up to 60% after upper abdominal and thoracic incisions. Tidal volume decreases 20% on the first postoperative day and gradually returns to normal. The retroperitoneal approach to the aorta involves a flank incision, which leads to far less respiratory compromise.

In a series of adult men undergoing abdominal surgery, postoperative pulmonary complications occurred more frequently than cardiac complications (9.6% vs. 5.7%) and were associated with significantly greater length of hospitalization. In

addition, the effects of surgical trauma are most pronounced after upper abdominal surgery. Lower abdominal and thoracic incisions impact the respiratory muscles to a lesser degree. This occurs through surgical disruption of the respiratory muscles, postoperative pain, and abdominal contents, preventing normal diaphragm excursion. The patient follows a rapid shallow breathing pattern without sighs.

The overall effect of postoperative regional analgesia on the breathing mechanics is complex, but epidural analgesia may decrease the risk for postoperative pulmonary complications. Ambulation and control of postoperative pain diminish splinting and help maximize respiratory parameters. Maneuvers to encourage deep breathing are of proven benefit.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1112–1143.

Warner DO. Preventing postoperative pulmonary complications: the role of the anesthesiologist. *Anesthesiology*. 2000;92:1467–1472.

D.3. How would you control postoperative pain? What are the alternatives in the management of this patient's postoperative pain?

The goal of effective postoperative pain relief is to produce a high quality of pain control with the fewest number of side effects and complications. Neuraxial analgesia in the immediate postoperative period is the preferred method of pain management in this high-risk patient population. The ideal opiate, its concentration, and combination with local anesthetic have yet to be defined. (For suggested protocols, see **Table 10.2**.)

TABLE 10.2 Epidural Opioid/Bupivacaine Combinations Administered by Continuous Infusion[a]

	Bolus Dose

Drug Combinations	Solution[b] of Bupivacaine	Basal Infusion[c]	Breakthrough Doses	Increments Breakthrou
Morphine	0.01%	6–8 mL/hr	1–2 mL every 10–15 min	1 mL of the solu
Bupivacaine[e]	0.05%–0.1% 0.5%–0.25%			
Hydromorphone	0.0025%–0.005%	6–8 mL/hr	1–3 mL every 10–15 min	1 mL of the solu
Bupivacaine[f]	0.05%–0.1% 0.5%–0.25%			
Fentanyl	0.001%	0.1–0.15 mL/kg/hr	1–1.5 mL every 10–15 min	1 mL of the solu
Bupivacaine[g]	0.05%–0.1% 0.5%–0.25%			
Sufentanil	0.0001%	0.1–0.2 mL/kg/hr	1–1.5 mL every 10–15 min	1 mL of the solu
Bupivacaine[h]	0.05%–0.1% 0.5%–0.25%			

[a]Catheter insertion site is the dermatome corresponding to the middle of the surgical incision. Administer a bolus dose of 0.5% bupivacaine or 2% lidocaine to establish surgical anesthesia or 0.25% bupivacaine to induce postoperative analgesia in 5-mL aliquots.

[b]Due to infectious control, a total volume of 150 mL is recommended.

[c]Initial basal infusion rates will depend on the age, general condition, and weight of the patient.

[d]If analgesia is inadequate after 1 hour, increase the breakthrough dose by the recommended amount. If analgesia is inadequate after one additional hour, decrease the lockout interval by 5 minutes.

[e]Prepare this solution by mixing 75–150 mg of bupivacaine with 15 mg of preservative-free morphine in a total volume of 150 mL of preservative-free normal saline.

[f]Prepare this solution by mixing 75–150 mg of bupivacaine with 3.75–7.5 mg of hydromorphone in a total volume of 150 mL of preservative-free normal saline.

[g]Prepare this solution by mixing 75–150 mg of bupivacaine with 1,500 μg of fentanyl in a total volume of 150 mL of preservative-free normal saline.

[h]Prepare this solution by mixing 75–150 mg of bupivacaine with 150–300 μg of sufentanil in a total volume of 150 mL of preservative-free normal saline.

Reprinted with permission from de Leon-Casasola OA, Lema MJ. Postoperative epidural opioid analgesia: what are the choices? *Anesth Analg*. 1996;83:867–875.

Complications of the epidural route of analgesia include dural puncture, epidural hematoma, and epidural abscess. The risk of epidural hematoma is small in patients receiving appropriate doses of anticoagulation postoperatively but is prohibitively high in patients receiving thrombolytic treatment or LMWHs. Careful consideration should be given to the timing of insertion

and removal of the catheter. The risk of complications is similar whether the catheter is placed at the thoracic or lumbar level. Other complications include pruritus, nausea, urinary retention, and delayed respiratory depression. The latter is less than 1% when epidural morphine is used, similar to the oral and parenteral route. Difficulty ambulating and orthostatic hypotension are minimized when catheters are placed in the thoracic region with low infusion rates and bupivacaine concentrations used are less than 0.08%.

Systemic narcotic analgesia can be used to provide effective postoperative pain control. Intravenous narcotics are commonly administered by a patient-controlled analgesia (PCA) pump after this type of procedure, allowing the patient to titrate the dose of narcotic to achieve adequate pain control. These modified infusion pumps are able to administer infusions of narcotics, small preprogrammed bolus doses on patient demand, and larger bolus doses by prescription. The PCA technique allows the patients to self-titrate narcotic doses to achieve optimal analgesic doses while avoiding the toxic side effects that result from high peak serum levels.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1112–1143.

de Leon-Casasola OA, Lema MJ. Postoperative epidural opioid analgesia: what are the choices? *Anesth Analg*. 1996;83:867–875.

Mann C, Pouzeratte Y, Boccara G, et al. Comparison of intravenous or epidural patient-controlled analgesia in the elderly after major abdominal surgery. *Anesthesiology*. 2000;92:433–441.

11 Hypertension

Christopher W. Tam and Fun-Sun F. Yao

A 70-year-old man with cholelithiasis was scheduled for a cholecystectomy. His blood pressure (BP) was 230/120 mmHg; pulse, 60 beats per minute. Hematocrit was 38%; serum sodium, 140 mEq per L; and serum potassium, 2.7 mEq per L. His medications included metoprolol, aspirin, atorvastatin (Lipitor), and hydrochlorothiazide.

A. Medical Disease and Differential Diagnosis

1. Define hypertension and categorize its severity.
2. What is the prevalence of hypertension?
3. What is the general classification of hypertension? Enumerate the causes of each type of hypertension.
4. What are the clinical patterns of hypertension encountered?
5. What is the pathophysiology of essential hypertension?
6. What is the pathophysiology of isolated systolic hypertension (ISH) and of pulse pressure hypertension (PPH)?
7. What are the end-organ damages caused by long-standing hypertension?
8. Are hypertensive patients at an increased risk for perioperative cardiac morbidity?
9. Perioperative cerebral and renal complications are mostly associated with which subtype of hypertension?

10. Would you employ a controlled hypotensive technique for hypertensive patients? How much would you safely lower the BP?
11. What are the BP goals for patients with hypertension and when should antihypertensive drugs be initiated?
12. What is the mechanism of action of antihypertensive drugs?
13. Does the choice of antihypertensive therapy influence hemodynamic responses to induction, laryngoscopy, and intubation?
14. Does chronic angiotensin-converting enzyme (ACE) inhibition influence anesthetic induction?

B. Preoperative Evaluation and Preparation

1. How would you evaluate this patient preoperatively?
2. Would you postpone the surgery? Why? What BP would you like the patient to achieve before surgery?
3. Should all or any of the chronic medications be discontinued before the operation?
4. Should hypokalemia be treated before anesthesia? Why?
5. Should hypomagnesemia be treated before anesthesia? Why?
6. Does an asymptomatic carotid bruit increase the risk in these patients?
7. The surgery was postponed for 6 weeks. The patient was on metoprolol, aspirin, atorvastatin, captopril, hydrochlorothiazide, and potassium chloride. His BP was 160/60 mmHg and potassium 4.0 mEq per L. How would you premedicate this patient?
8. If the patient is an untreated hypertensive patient with BP 170/70 mmHg, would you treat the patient preoperatively with an antihypertensive agent?

C. Intraoperative Management

1. How would you monitor this patient?
2. What are the anesthetic goals for hypertensive patients?

3. How would you induce anesthesia for the hypertensive patient?
4. How does tracheal intubation produce hypertension?
5. What happens to the left ventricular ejection fraction during and immediately following intubation?
6. What other measures can prevent hypertension and tachycardia at the time of intubation?
7. After induction and intubation, the BP decreased to 70/40 mmHg. What would you do?
8. What is your choice of agents for maintenance of anesthesia? Why?
9. How would you manage fluid therapy for hypertensive patients?
10. During the surgery, BP increased to 220/120 mmHg. How would you treat the hypertension?
11. What could you do to prevent hypertension during extubation and emergence?
12. Would you consider regional anesthesia for this patient?

D. Postoperative Management

1. The patient developed hypertension, BP 210/110 mmHg, in the postanesthesia care unit. What would you do?

A. Medical Disease and Differential Diagnosis

A.1. Define hypertension and categorize its severity.

Systemic hypertension is the leading cause of cardiovascular death in the United States among modifiable risk factors and the second leading preventable cause of death. According to the seventh report on classification and characterization of BP by the Joint National Committee (JNC) on Evaluation, Detection, and Prevention of High Blood Pressure in 2003, hypertension is defined as an average systolic BP greater than 120 mmHg and a

diastolic pressure greater than 80 mmHg. The classification stages of hypertension have been updated since 2003 with tightened guidelines for diagnosis of hypertension. According to the American College of Cardiology (ACC)/American Heart Association (AHA) recommendations from 2017, hypertension is classified as normal, elevated, stage 1 hypertension, and stage 2 hypertension. The term "pre-hypertension" as seen in the JNC 7 report has been replaced by "elevated blood pressure" in the current guidelines. The current recommended BP ranges for each category can be seen on **Table 11.1**. The tightened BP classification is expected to increase the prevalence of hypertension by 14% in the United States and about 2% increase in antihypertensive therapy usage.

TABLE 11.1 Categories of Blood Pressure in Adults

BP Category	SBP	DBP
Normal	<120 mmHg and	<80 mmHg
Elevated	120–129 mmHg and	<80 mmHg
Hypertension		
Stage 1	130–139 mmHg or	80–89 mmHg
Stage 2	≥140 mmHg or	≥90 mmHg

BP, blood pressure; DBP, diastolic BP; SBP, systolic BP.

Reprinted with permission from Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018;71:e13–e115. Copyright © 2018 American Heart Association, Inc.

The definition of hypertension in children and adolescents has also been updated by the American Academy of Pediatrics in 2017. Similar to the adult recommendations, the pediatric definition for hypertension has also been tightened in the most current updated guidelines. According to American Association of Pediatrics (AAP), pediatric hypertension is classified as

normal, elevated, stage 1 hypertension, and stage 2 hypertension. As in the adult update, the term "pre-hypertension" has been replaced by "elevated blood pressure" in the current guidelines. The current recommended BP ranges can be seen on **Table 11.2**.

TABLE 11.2 Categories of Blood Pressure in Pediatrics

BP Category	Children Aged 1–<13 Years Old	Children Aged ≥13 Years Old
Normal	<90th percentile	<120/<80 mmHg
Elevated	≥90th percentile to <95th percentile or 120/80 mmHg to <95th percentile (whichever is lower)	120/<80–129/<80 mmHg
Stage 1 hypertension	≥95th percentile to <95 percentile + 12 mmHg or 130/80–139/89 mmHg (whichever is lower)	130/80–139/89 mmHg
Stage 2 hypertension	≥95th percentile + 12 mmHg or ≥140/90 mmHg (whichever is lower)	≥140/90 mmHg

Reproduced with permission from Flynn JT, Kaelber DC, Baker-Smith CM, et al. Clinical practice guideline for screening and management of high blood pressure in children and adolescents. *Pediatrics*. 2017;140(3):e20171904. Copyright © 2017 by the American Academy of Pediatrics.

It is important to note that the classification of hypertension defines and specifies hypertension according to systolic and/or diastolic limits, each representing different pathophysiologic processes. Systolic hypertension is a marker of macrovascular disease and large arterial stiffening (atherosclerosis), and diastolic hypertension is a consequence of microvascular disease involving typically vessels less than 1 mm in size.

Uncontrolled hypertension can escalate to a hypertensive crisis defined as systolic BP greater than 180 mmHg or diastolic BP greater than 120 mmHg and categorized as urgent and emergent. According to the ACC/AHA guidelines 2017, hypertensive emergency is defined as elevated BP (usually >180/120 mmHg) complicated by evidence of impending or progressive end-organ damage, whereas hypertensive urgency is

severe elevation of BP without progressive end-organ damage.

Flynn JT, Kaelber DC, Baker-Smith CM, et al. Clinical practice guideline for screening and management of high blood pressure in children and adolescents. *Pediatrics*. 2017;140(3):e20171904.

Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2018;138:e484–e594.

A.2. What is the prevalence of hypertension?

The prevalence of hypertension depends on both the racial composition of the population and the criteria used to define hypertension. In a white suburban population like that in the Framingham study, nearly one-fifth has a BP greater than 160/95 mmHg and almost one-half has a BP greater than 140/90 mmHg. A higher prevalence of hypertension has been found in the non-white population. The frequency increases with the age of the population with nearly two-thirds of hypertensive patients being older than 50 years, and by the age of 75 years, almost 90% will have hypertension. According to the JNC 7, the overall prevalence of hypertension was 32%. In the United States, however, with the updated ACC/AHA definition of hypertension, the prevalence increases to 46%. The highest prevalence is found in the non-Hispanic black population with an overall prevalence of close to 60% with the current updated definition. However, the prevalence of pharmacologic therapy has not increased with this updated definition because for the percentage of population where patients are now considered hypertensive, the recommended therapy is conservative lifestyle changes. The number of hypertensive persons in the United States in 1983 was estimated to be 57.7 million—more than double the estimate made in 1960 to 1962. Currently, approximately 1 in 3 or 75 million Americans suffer from

hypertension.

Franklin SS, Larson MG, Khan SA, et al. Does the relation of blood pressure to coronary heart disease risk change with aging? The Framingham Heart Study. *Circulation*. 2001;103:1245–1249.

Merai R, Siegel C, Rakotz M, et al. CDC grand rounds: a public health approach to detect and control hypertension. *MMWR Morb Mortal Wkly Rep*. 2016;65(45):1261–1264.

Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2018;138:e484–e594.

A.3. What is the general classification of hypertension? Enumerate the causes of each type of hypertension.

Hypertension is classified according to its subtypes: systolic, diastolic, and pulse pressure (**Table 11.3**). Historically, only diastolic hypertension—essential hypertension—was recognized, but more recently, there has been increasing emphasis and recognition of systolic hypertension, namely, ISH. ISH is the most common subtype of hypertension affecting predominantly individuals older than 60 years of age. In fact, approximately 70% of hypertensive patients have ISH with approximately half of these individuals having very wide pulse pressure (>65 mmHg) or PPH. Isolated diastolic hypertension is most prevalent in individuals younger than 50 years and is an important marker of coronary heart disease and mortality in this age group. Some hypertensive patients have both systolic and diastolic hypertension categorized as *combined systolic and diastolic hypertension*. The ranges of systolic, diastolic, and pulse pressure that define each subtype of hypertension are presented in **Table 11.1**.

TABLE 11.3 Classification of Hypertension

Systolic and diastolic hypertension
- Essential
- Renal
- Endocrine
- Neurogenic
- Miscellaneous

Systolic hypertension with wide pulse pressure
- Increased cardiac output
- Rigidity of aorta

Etiology of Hypertension

- *Essential hypertension*. Unknown etiology
- *Renal*. Acute and chronic glomerulonephritis, chronic pyelonephritis, polycystic kidney, diabetic nephropathy, hydronephrosis, renovascular stenosis, renin-producing tumors, primary sodium retention
- *Endocrine*. Adrenal—Cushing syndrome, primary aldosteronism, congenital adrenal hyperplasia, pheochromocytoma, acromegaly, hypothyroidism, carcinoid, hyperthyroidism, oral contraceptives, corticosteroids
- *Neurogenic*. Psychogenic, increased intracranial pressure, spinal cord section, familial dysautonomia, lead poisoning, Guillain-Barré syndrome, sleep apnea
- *Miscellaneous*. Coarctation of aorta, increased intravascular volume, pregnancy-induced hypertension, polyarteritis nodosa, acute porphyria, hypercalcemia, alcohol and drug use, acute stress including surgery

Jameson J, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:1895–1900.

Sesso HD, Stampfer MJ, Rosner B, et al. Systolic and diastolic blood pressure, pulse pressure, and mean arterial pressure as predictors of cardiovascular disease risk in men. *Hypertension*. 2000;36:801–807.

Zipes DP, Libby P, Bonow RO, et al, eds. *Braunwald's Heart Disease*. 11th ed. Philadelphia, PA: Elsevier; 2018:910–927.

A.4. What are the clinical patterns of hypertension

encountered?

- "Vasoconstricted" hypertension—in medical patient with chronic renovascular hypertension, characterized by diastolic hypertension and systemic vascular resistant with normal or even decreased cardiac output and heart rate
- "Hyperdynamic" hypertension—in postoperative surgical patient, characterized by acute systolic hypertension; widened pulse pressure; and increased cardiac output, heart rate, and systemic vascular resistant

Jameson J, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:1893–1894.

Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2018;138:e484–e594.

Zipes DP, Libby P, Bonow RO, et al, eds. *Braunwald's Heart Disease*. 11th ed. Philadelphia, PA: Elsevier; 2018:910–927.

A.5. What is the pathophysiology of essential hypertension?

The underlying mechanism of essential hypertension is unknown. A variety of abnormalities, including heredity, fetal undernutrition, abnormal sympathetic nervous system activity, cell membrane defects, renal retention of excess salt, microcirculatory alterations, endothelial cell dysfunction, hyperinsulinemia secondary to insulin resistance, vascular hypertrophy, and altered renin–angiotensin system regulation are implicated. There is increasing evidence that "local renin–angiotensin" paracrine factors may be involved in the development of hypertension. However, characteristic hemodynamic changes are present as follows:

- Increased systemic vascular resistance with normal cardiac

output

- Markedly increased sympathetic response to stress such as endotracheal intubation
- A greater increase in BP with vasoconstriction and a greater decrease in BP with vasodilation because of the increased thickening of arterial wall and high ratio of wall thickness to internal diameter

The higher the level of BP, the more likely that various cardiovascular diseases will develop prematurely through acceleration of arteriosclerosis. If untreated, approximately 50% of hypertensive patients die of coronary heart disease or congestive heart failure (CHF), approximately 33% of stroke, and 10% to 15% of renal failure.

Kotchen TA. Hypertensive vascular disease. In: Jameson J, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:1891–1894.

Zipes DP, Libby P, Bonow RO, et al, eds. *Braunwald's Heart Disease*. 11th ed. Philadelphia, PA: Elsevier; 2018:910–959.

A.6. What is the pathophysiology of isolated systolic hypertension (ISH) and of pulse pressure hypertension (PPH)?

ISH is a manifestation of atherosclerotic disease involving predominantly the aorta and its major branches. Both ISH and PPH reflect arterial stiffening and represent the pulsatile component of BP, whereas the mean arterial pressure (MAP) represents the static state. Systole, then, is directly influenced by the ventricular contractile state, the ejected volume, heart rate, and, importantly, compliance of the aorta and pulse wave velocity. With increasing age and factors such as diabetes, smoking, and increased cholesterol as well as some genetic factors, compliance of the aorta diminishes markedly (**Fig. 11.1**). The net result is stiffening of the arterial tree and inability

to absorb the pulsatile load, causing the systolic pressure to rise sharply. Pulse wave velocity has gained much attention lately because it may be a richer substrate for characterizing the physiology of blood flow and pressure. Under normal physiologic conditions, the ejected blood volume is transmitted peripherally as a propagated wave. After reaching the periphery, in particular, at the bifurcation sites, a reflected wave or a retrograde wave is generated from the encountered impedance. Under normal conditions, wave reflection arrival coincides with the beginning of diastole, thereby augmenting the diastolic pressure. However, with stiffening of the aorta as occurs with aging, both the propagated and the reflected waves travel much more rapidly, and early return of the reflected arterial wave during late systole augments the systolic component, effectively increasing afterload. The ensuing loss of diastolic augmentation results in a disproportionate increase in the systolic BP and lower diastolic BP—a hallmark of ISH and of PPH.

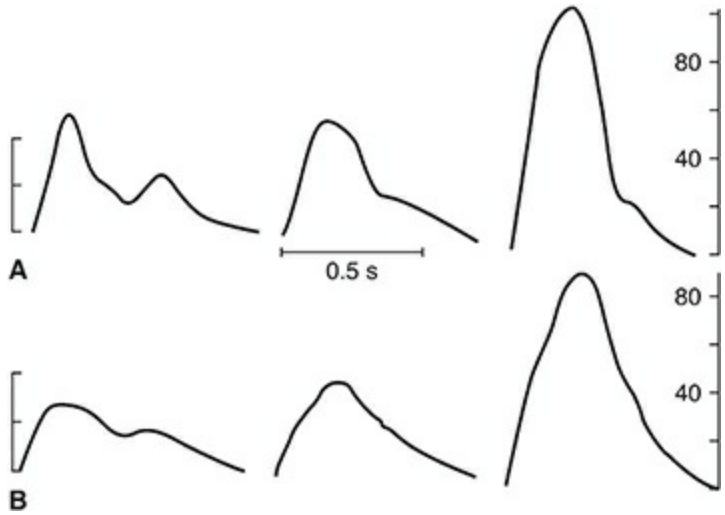

FIGURE 11.1. Change in amplitude and contour of the upper limb (A) and ascending aortic (B) pressure wave with age, as recorded in three female members of a family: at age 18 (left), at age 48 (center), and at age 97 years (right). Upper limb pulse pressure was just more than twice as high in the old compared with the young subject (102 vs. 46 mmHg), whereas aortic pulse pressure was more than three times higher (104 vs. 27 mmHg). (*Reprinted with permission from O'Rourke MF, Nichols WW. Aortic diameter, aortic stiffness, and wave reflection increase with age and isolated systolic hypertension.* Hypertension*. 2005;45[4]:652–658.*)

Mechanistically, pulse pressure is also an index of the stiffness of conduit vessels and the rate of pressure wave propagation and reflection within the arterial tree. Approximately half of patients with ISH also have wide pulse pressure; however, both individuals who are normotensive (systolic, <120 mmHg) with a low diastolic pressure or persons with combined systolic and diastolic hypertension (systolic >130 mmHg and diastolic >80 mmHg) can have wide pulse pressure (normal values being ≤40 mmHg).

Dart AM, Kingwell BA. Pulse pressure—a review of mechanism and clinical relevance. *J Am Coll Cardiol*. 2001;37:975–984.

O'Rourke MF, Nichols WW. Aortic diameter, aortic stiffness, and wave reflection increase with age and isolated systolic hypertension. *Hypertension*. 2005;45(4):652–658.

Schiffrin EL. Vascular stiffening and arterial compliance. Implications for systolic blood pressure. *Am J Hypertens*. 2004;17:39S–48S.

A.7. What are the end-organ damages caused by long-standing hypertension?

The end-organ damages caused by long-standing hypertension are as follows:

Cardiac Involvement

Left ventricular hypertrophy (LVH)
Angina or myocardial infarction (MI)
Arrhythmias
Congestive failure

Eye Involvement

Vascular changes in the fundus reflect hypertensive retinopathy and arteriosclerotic retinopathy.

Renal Involvement

Nephropathy

Cerebral Involvement

Stroke or transient ischemic attack

Complications of hypertension to vascular disease probably involve three interrelated processes: pulsatile flow, endothelial cell dysfunction, and smooth muscle cell hypertrophy. These three interrelated processes are probably responsible for the arteriolar and arterial sclerosis that is the usual consequence of long-standing hypertension. Large vessels such as the aorta may be directly affected and be at risk for aneurysms and dissection. As discussed previously, the consequences of long-standing hypertension need be addressed according to the subtypes of hypertension; for the associated risks for cerebral, cardiac, and renal vascular complications differ according to systolic, diastolic, and PPH. For example, diastolic hypertension being a better predictor of coronary heart disease in younger patients, whereas systolic and PPH being associated with greater risk of stroke, coronary heart disease, and mortality in persons older than 60 years.

Aronson S, Fontes ML. Hypertension: a new look at an old problem. *Curr Opin Anaesthesiol*. 2006;19:59–64.

Zipes DP, Libby P, Bonow RO, et al, eds. *Braunwald's Heart Disease*. 11th ed. Philadelphia, PA: Elsevier; 2018:910–959.

A.8. Are hypertensive patients at an increased risk for perioperative cardiac morbidity?

Hypertensive patients are at increased risk for coronary artery disease, silent myocardial ischemia, CHF, and stroke. However, whether preoperative hypertension is predictive of perioperative major cardiac morbidity remains controversial. Some investigators have shown that patients with untreated, poorly controlled, or labile preoperative hypertension are at increased risk for perioperative BP lability, dysrhythmias, myocardial

ischemia, and transient neurologic complications. Some suggested that preoperative hypertension predicted perioperative MI. However, Goldman and Caldera demonstrated that mild-to-moderate hypertension did not increase the risk of major morbid events. Instead, preoperative hypertension may predict several intermediates of outcome, such as BP lability and myocardial ischemia. The controversy may be due to the wide variability in the hypertensive population. Hypertension may affect perioperative morbidity through the extent of end-organ damage and not the manifestation of the disease itself. LVH, which signifies long-standing poorly controlled hypertension, can increase the risk of myocardial ischemia from imbalances of myocardial oxygen (O_2) supply and demand regardless of the presence or absence of coronary artery disease.

ISH (systolic BP >140 mmHg and diastolic BP <90 mmHg) has been identified as a risk factor for cardiovascular complications in the general population, and treatment reduces the future risk of stroke. Aronson et al. and Fontes et al. found that among the various components of BP, preoperative PPH was independently and significantly associated with postoperative stroke, renal failure, and mortality in patients undergoing coronary artery bypass. Neither ISH nor isolated diastolic hypertension was predictive of vascular complications. This finding is consistent with results of longitudinal studies finding that increase in pulse pressure is a better predictor of major vascular complications than increase in either systolic or diastolic BP. Interestingly, rises in pulse pressure as few as 10 mmHg in both normotensive and hypertensive individuals are associated with 20% or more increase risk of renal, coronary, and cerebral events.

Aboyans V, Frank M, Nubret K, et al. Heart rate and pulse pressure at rest are major prognostic markers of early postoperative complications after coronary bypass surgery. *Eur J Cardiothorac Surg*. 2008;33:971–976.

Aronson S, Fontes ML, Miao Y, et al; for the Investigators of the Multicenter Study of Perioperative Ischemia Research Group and the Ischemia Research and Education Foundation. Risk index for perioperative renal dysfunction/failure: critical dependence on pulse pressure hypertension. *Circulation*. 2007;115(6):733–742.

Casadei B, Abuzeid H. Is there a strong rationale for deferring elective surgery in patients with poorly controlled hypertension? *J Hypertens*. 2005;23(1):19–22.

Fontes ML, Aronson S, Mathew JP, et al; for the Multicenter Study of Perioperative Ischemia (McSPI) Research Group and the Ischemia Research and Education Foundation (IREF) Investigators. Pulse pressure and risk of adverse outcome in coronary bypass surgery. *Anesth Analg*. 2008;107:1122–1129.

Goldman L, Caldera DL. Risks of general anesthesia and elective operation in the hypertensive patient. *Anesthesiology*. 1979;50:285–292.

A.9. Perioperative cerebral and renal complications are mostly associated with which subtype of hypertension?

Both systolic hypertension and high pulse pressure are strongly associated with risk for perioperative cerebrovascular accidents and acute renal failure. The brain and the kidneys as well as the heart differ from most organs in that they receive large amount of blood flow and have very low resistance. As such, the pulsatile load (pulse pressure) tends to be very high. Over a period of many years of poorly or untreated hypertension, endothelial injury and vascular remodeling changes can promote both arteriosclerosis and atherosclerosis, which are known risk factors for cerebral and renal vascular complications. The pulsatile stress also can cause dislodgment of plaques from the aorta and its major branches, resulting in embolic stroke.

In hypertensive patients, autoregulation of cerebral blood flow is reset to a higher range than normal, and although it protects the brain against sudden increases in pressure, it makes it more vulnerable to hypotension. Therefore, when BP is lowered acutely, hypertensive patients will show signs of

cerebral ischemia at a higher level of BP than normotensive patients.

Hypertension may accelerate cognitive decline with age. Hypertension, particularly systolic, is a major risk factor for initial and recurrent stroke and for transient ischemia attacks caused by extracranial atherosclerosis.

Chronic renal insufficiency is a common sequela of hypertension. Patients with hypertension should have a measurement of baseline serum creatinine. In the original Cardiac Risk Index, an elevated serum creatinine level (>3.0 mg per dL [>265.2 mmol per L]) was one of the independent risk factors for perioperative cardiovascular morbidity and mortality. This has been confirmed in the revised Cardiac Risk Index in which a preoperative serum creatinine level greater than 2.0 mg per dL (176.8 mmol per L) was one of six independent factors that predicted increased cardiovascular risk.

Aronson S, Fontes ML, Miao Y, et al; for the Investigators of the Multicenter Study of Perioperative Ischemia Research Group and the Ischemia Research and Education Foundation. Risk index for perioperative renal dysfunction/failure: critical dependence on pulse pressure hypertension. *Circulation*. 2007;115(6):733–742.

Benjo A, Thompson RE, Fine D, et al. Pulse pressure is an age-independent predictor of stroke development after cardiac surgery. *Hypertension*. 2007;50:630–635.

Finnerty FA Jr, Witkin L, Fazekas JF. Cerebral hemodynamics during cerebral ischemia induced by acute hypotension. *J Clin Invest*. 1954;33:1227–1232.

A.10. Would you employ a controlled hypotensive technique for hypertensive patients? How much would you safely lower the BP?

Uncontrolled or untreated severe hypertension is a contraindication to controlled hypotension. However, controlled hypotension may be used with caution in treated hypertensive patients. Because cerebral autoregulation is shifted to the right

with chronic hypertension, the lower limit of controlled hypotension should be higher for hypertensive patients. However, with long-term treatment, the autoregulation curve shifts leftward to approach that in normals. Strandgaard found that the lower limit of autoregulation was 113 mmHg in severe untreated or uncontrolled hypertensives; 96 mmHg in formerly severe, now-treated hypertensives; and 73 mmHg in normotensive patients. The lowest level of mean BP tolerated without symptoms of hypoperfusion was 65 mmHg in severe hypertensives, 53 mmHg in treated hypertensives, and 43 mmHg in normal patients. However, although the autoregulation may shift toward normal with treatment, in many patients, the autoregulation did not shift toward normal even after 12 months of treatment. Because one cannot measure patients' autoregulation, a useful clinical guide is that a 25% decrease in MAP reaches the lower limit of autoregulation and a 55% decrease in MAP reaches symptomatic cerebral hypoperfusion. Another suggested rule is that the systolic pressure of controlled hypotension should not be lower than the diastolic pressure of the patient's usual pressure. It is important to note that peripherally measured BP do not match central aorta BP, which is more reflective of actual cerebral BP.

Recently, noninvasive cerebral oximeter using near-infrared spectroscopy has been used to monitor O_2 saturations of the cerebral cortex. The values of cerebral O_2 saturations correspond with those of a mixture of 85% jugular venous O_2 saturation and 15% of arterial O_2 saturation. It reflects the balance between cerebral O_2 delivery and O_2 demand. In a steady state of anesthesia, the cerebral O_2 demand does not change significantly. Therefore, cerebral O_2 saturations will not decrease until the BP falls below its autoregulation range. Therefore, the cerebral oximeter may be employed to determine

the lower limit of autoregulation and to ensure adequate cerebral oxygenation. Unfortunately, there is wide variability in measured cerebral saturations with some individual's baseline oximetric saturation values being near 50% at baseline. Furthermore, the measured value is reflective of regional saturation such that distant areas that may be ischemic are not detected.

It should be mentioned that neither the threshold for upper nor lower limits of systolic and diastolic BP have been established. Frequently, these limits have been chosen arbitrarily and the relation of perioperative hypertension to outcomes has been inconsistent among the studies that have addressed this question. In part, the limitation comes from grouping all types of hypertension together. Moreover, available vasoactive agents are not selective in lowering or raising systolic BP, and diastolic BP without a concomitant increase or fall in the other component. Undermining the broad-based reliance on systolic BP and diastolic BP are a number of studies in humans over the past several decades that clearly show that both morbidity and mortality do not always linearly correlate with rises or fall in BP. In individuals with demonstrable coronary disease, namely, those with previous infarcts, coronary mortality was significantly related to diastolic pressure in a U-shaped configuration—occurring more frequently in those with very high or very low diastolic BP. Unfortunately, the emphasis on BP management perioperatively has been to control the systolic component with no attention paid to the diastolic component. This is particularly concerning in patients with ISH and with very wide pulse pressure where the diastolic BP is already critically low. By reducing the systolic component, further lowering of the diastolic BP can result in ischemic complications in most sensitive vascular beds such as the brain, the heart, and the kidneys. Lastly, it is critical to recognize that

peripheral arterial pressures do not necessarily reflect central pressures with exception of the MAP. In a subset of hypertensive individuals, both the systolic and the pulse pressures are grossly higher peripherally as compared to central aortic pressures, such that lowering of the peripheral BP may result in critical reduction in perfusion pressure.

Fontes ML, Aronson S, Mathew JP, et al; for the Multicenter Study of Perioperative Ischemia (McSPI) Research Group and the Ischemia Research and Education Foundation (IREF) Investigators. Pulse pressure and risk of adverse outcome in coronary bypass surgery. *Anesth Analg*. 2008;107:1122–1129.

Strandgaard S. Autoregulation of cerebral blood flow in hypertensive patients. The modifying influence of prolonged antihypertensive treatment on the tolerance to acute, drug-induced hypotension. *Circulation*. 1976;53(4):720–727.

Yao FS, Tseng CC, Ho CY, et al. Cerebral oxygen desaturation is associated with early postoperative neuropsychological dysfunction in patients undergoing cardiac surgery. *J Cardiothorac Vasc Anesth*. 2004;18:552–558.

A.11. What are the BP goals for patients with hypertension and when should antihypertensive drugs be initiated?

The current ACC/AHA guidelines outline the BP treatment goals based on systematic review of the literature. According to the current ACC/AHA guidelines 2017, it is a class Ia recommendation to treat patients with antihypertensive drug therapy in addition to lifestyle modification as secondary prevention if patients currently have cardiovascular disease and an average systolic BP ≥130 mmHg or diastolic BP ≥80 mmHg or as primary prevention in patients with no history of cardiovascular disease but with an estimated 10-year cardiovascular disease risk of <10% and systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg. Cardiovascular disease includes coronary heart diseases, CHF, and stroke. For patients in the elevated BP category, lifestyle modification alone is the recommended treatment modality.

Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2018;138:e484–e594.

A.12. What is the mechanism of action of antihypertensive drugs?

Antihypertensive drugs are categorized by their mechanism of action as follows.

Diuretics

They include thiazides (e.g., hydrochlorothiazide), loop diuretics (e.g., furosemide, ethacrynic acid), and potassium-sparing agents (e.g., spironolactone, triamterene). All diuretics initially lower the BP by increasing urinary sodium excretion and by reducing plasma volume, extracellular fluid volume, and cardiac output. Within 6 to 8 weeks, the cardiac output returns to normal. The lowered BP is related to a fall in peripheral resistance. Diuretics may cause hypokalemia, hypomagnesemia, hyperuricemia, hyperlipidemia, hypercalcemia, and hyperglycemia. For patients with ST-segment changes and evidence of pulmonary edema and hypertension or with increased intracranial cerebral pressure and hypertension, intravenous furosemide may be appropriate.

Antiadrenergic Agents

- *Centrally acting drugs*. Clonidine, dexmedetomidine, and mivazerol. These drugs and their metabolites are primarily α_2-receptor agonists. Stimulation of α_2 receptors in the vasomotor centers of the brain reduces sympathetic outflow.
- *Peripherally acting drugs*
  - α-Receptor blockers
    α_1 and α_2 Receptors—phenoxybenzamine (Dibenzyline),

phentolamine (Regitine)
α_1 Receptor—prazosin (Minipress), doxazosin (Cardura)
By blocking α-mediated vasoconstriction, these drugs induce a fall in peripheral resistance with both arteriolar and venous dilation.

- β-Receptor blockers—atenolol (Tenormin), metoprolol (Lopressor), nadolol (Corgard), pindolol (Visken), propranolol (Inderal), esmolol (Brevibloc). These drugs lower the BP by decreasing heart rate, contractility, cardiac output, and renin levels. BP is decreased without reflex tachycardia or widening of the pulse pressure. They also have antiarrhythmic activity and suppress both ventricular and supraventricular ectopic rhythms.
- α- and β-Receptor blockers—labetalol (Trandate)
- Endothelin receptor antagonists—act on endothelin A and B receptors to block the effect of endothelin-1, which is the most potent vasoconstrictor that is secreted primarily from vascular smooth muscle and endothelial cells. Bosentan (receptor A and B antagonist) and sitaxsentan (receptor A antagonist) are examples of a few of this class of agents used in the management of pulmonary hypertension and less so for hypertension-related heart failure.

Direct Vasodilators

They include hydralazine, nitroprusside, nitroglycerin, and calcium channel blockers. These drugs directly relax the smooth muscle of resistance and capacitance vessels to different degrees.

Dopaminergic Agonists

Dopaminergic agonists (DAs) are classified into DA_1 and DA_2 subtypes.

Stimulation of DA_1 receptors causes vasodilation, and inhibition of active sodium transport in the proximal tubule, leading to natriuresis.

Stimulation of DA_2 receptors inhibits norepinephrine release and promotes peripheral vasodilation.

Fenoldopam, a dopamine receptor (DA_1 selective) agonist and a systemic and renal vasodilator, offers significant advantages as a parenterally administered agent for the management of BP in hypertensive emergencies and in the perioperative setting. Parenteral fenoldopam has a rapid onset and offset of effect, with an elimination half-time of approximately 10 minutes. Prepared in concentration of 10 mg in 250 mL (40 μg per mL), the recommended starting dose is 0.05 μg/kg/min. This should be titrated to effect by 0.025 μg/kg/min every 10 to 15 minutes to a maximum dose of 0.5 to 0.8 μg/kg/min. The drug should not be administered in boluses; the incidence of reflex tachycardia is related to rapidity of upward titration. Unlike dopamine, it has no β- or α-adrenergic activity, and increasing doses result in increasing vasodilation without tachycardia or tachyarrhythmias.

Calcium Channel Blockers

The cardiovascular effects of calcium antagonists are listed in **Table 11.4**. These drugs decrease BP mainly by peripheral vasodilation. Renin and aldosterone secretion may be reduced as well.

TABLE 11.4 Cardiovascular Effects of Calcium Channel Blockers

	Verapamil	Diltiazem	Nifedipine	Nicardipine	Clevidipine
Heart rate	↓	↓	↓ or –	↑ or –	–
Nodal conduction	↓↓	↓	↓ or –	–	–
Myocardial depression	↑↑	↑	–	–	–
Vasodilation	↑	↑	↑↑	↑↑	↑↑

↑↑, more increase; ↓↓, more decrease; ↑, increase; ↓, decrease; −, no change.

Angiotensin-Converting Enzyme Inhibitors

They include captopril, enalapril, lisinopril, quinapril, and ramipril. The renin–angiotensin system may be inhibited in four ways as shown in **Figure 11.2**. These drugs inhibit the conversion of the inactive decapeptide angiotensin I to the active octapeptide angiotensin II. Lower levels of angiotensin II may decrease BP by reducing angiotensin II–induced vasoconstriction and by decreasing aldosterone synthesis. ACE inhibitors also retard the degradation of a potent vasodilator (bradykinin), alter prostaglandin production (most notably with captopril), and can modify the activity of the adrenergic nervous system.

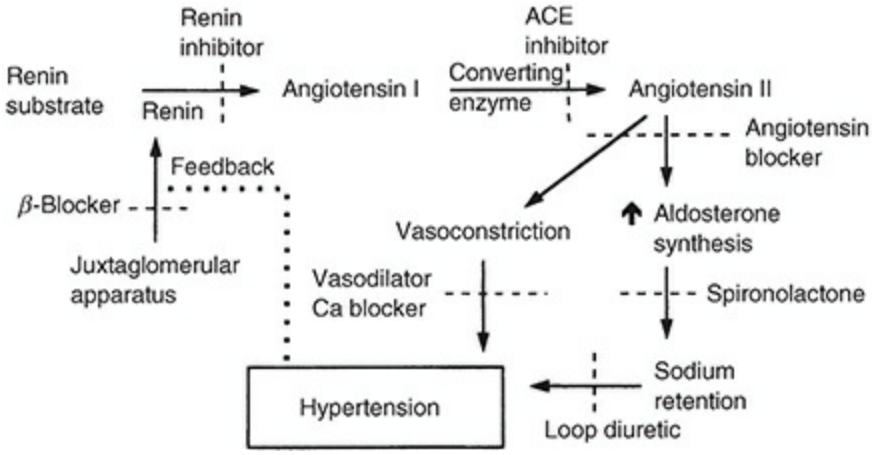

FIGURE 11.2. The renin–angiotensin system and the mechanism of action of antihypertensive drugs. ACE, angiotensin-converting enzyme.

ACE inhibitors provide predominantly arterial vasodilation and have become primary therapy for the treatment of CHF by afterload reduction. Cardiac output is increased without excessive decrease in preload, with a favorable effect on survival.

Angiotensin II Receptor Blockers

Angiotensin II receptor antagonists or blockers (ARBs)

represent the third class that antagonizes the renin–angiotensin–aldosterone system. Blockade of the action of angiotensin II leads to elevations in plasma levels of renin, angiotensin I, and angiotensin II. However, this build-up of precursors does not overwhelm the receptor blockade, as evidenced by a persistent fall in both BP and plasma aldosterone levels. There are several possible differences between ACE inhibitors and angiotensin II receptor antagonists. These include the following:

- ACE is a kininase. Therefore, inhibiting this enzyme, which normally degrades bradykinin, with an ACE inhibitor leads to increased kinin levels, an effect not seen with an angiotensin II receptor antagonist. High bradykinin levels may also provide additional vasodilation and other benefits not observed with angiotensin II receptor antagonists.
- ACE inhibitors, by decreasing angiotensin II production, reduce the effect of both angiotensin II receptor type 1 (AT1) and type 2 (AT2); only the former are inhibited by the ARBs. Chronic stimulation of the AT2 receptor may be beneficial.
- In the heart, kidney, and perhaps the blood vessels, the production of angiotensin II may be catalyzed by enzymes other than ACE, such as chymase. The effect of the angiotensin II produced by this reaction can be inhibited by the angiotensin II receptor antagonists but not by ACE inhibitors.

There is evidence that ARBs are more effective in treating ISH and PPH particularly in combination with ACE inhibitors and with endothelin receptor blockers.

Other Vasodilators

They include brain natriuretic peptides such as nesiritide that is primarily used in acute exacerbation of heart failure to improve forward flow and reduce symptoms and signs of heart failure. There has been recent controversy about the clinical efficacy of

these agents. Importantly, there have been several reports suggesting that the renal outcome is worsened in patients receiving nesiritide.

Doerschug KC, Delsing AS, Schmidt GA, et al. Renin-angiotensin system activation correlates with microvascular dysfunction in a prospective cohort study of clinical sepsis. *Crit Care*. 2010;14:R24.

Ferrari R, Guardigli G, Ceconi C. Secondary prevention of CAD with ACE inhibitors: a struggle between life and death of the endothelium. *Cardiovasc Drugs Ther*. 2010;24:331–339.

Spinler SA, Cziraky M, Miller A. ACE inhibitors versus ARBs: comparison of practice guidelines and treatment selection considerations. *Formulary*. 2006;41:274–284.

Zipes DP, Libby P, Bonow RO, et al, eds. *Braunwald's Heart Disease*. 11th ed. Philadelphia, PA: Elsevier; 2018:928–959.

A.13. Does the choice of antihypertensive therapy influence hemodynamic responses to induction, laryngoscopy, and intubation?

The pressor responses to induction, laryngoscopy, and intubation differ little whether patients with mild-to-moderate hypertension receive a β-blocker, a calcium channel blocker, an ACE inhibitor, or a diuretic. Even changes of a similar magnitude are also observed in untreated hypertensive patients. On the other hand, hypotensive responses may be magnified in those patients with poorly controlled hypertension following induction—generally due to a reduced intravascular volume in the face of increased vascular sympathetic tone. As mentioned previously, attention should be directed not only to the systolic but also to pulse and diastolic pressures.

Sear JW, Jewkes C, Tellez JC, et al. Does the choice of antihypertensive therapy influence haemodynamic responses to induction, laryngoscopy and intubation? *Br J Anaesth*. 1994;73:303–308.

A.14. Does chronic angiotensin-converting enzyme (ACE) inhibition influence anesthetic induction?

Coriat et al. reported that, in hypertensive patients chronically treated with ACE inhibitors, therapy until the day of surgery is a major factor influencing BP responsiveness to anesthetic induction for vascular surgery. If enalapril (a long-acting ACE inhibitor) treatment is continued, a very low plasma-converting enzyme activity will be observed and an exaggerated hypotensive response may occur at induction. If captopril (a short-acting ACE inhibitor) treatment is continued, the magnitude of the decrease in BP in response to induction, although lower than with enalapril, is enhanced compared with that noted in patients in whom captopril had been stopped. All of the hypotensive episodes in patients who received ACE inhibitors until the day of surgery were easily corrected by administration of an α agonist. The temporary withdrawal of these two ACE inhibitors attenuated the hypotensive response to induction but did not lead to an abnormal BP response to induction and intubation. However, Ryckwaert and Colson reported that ACE inhibitor treatment in patients with infarction-induced myocardial dysfunction does not increase the incidence of severe hypotension after induction of anesthesia. Additionally, a retrospective analysis of patients who underwent shoulder surgery in the sitting position by Trentman et al. showed that timing of the last dose of ACE inhibitors or angiotensin receptor antagonists had no impact on intraoperative hypotensive episodes. Hollmann et al. published in 2018 in *Anesthesia and Analgesia* a meta-analysis where they found that ACE inhibitors and ARBs did not demonstrated to have an increased incidence of perioperative mortality even though there was an increased association with intraoperative hypotension. In all, the overwhelming opinion is to continue all antihypertensive medication including the day of surgery and resumption of such therapy postoperatively. A number of studies have shown an improvement in outcome when therapy is continued versus a

worsening in outcome when either ACE inhibitors or β-blockers have been withdrawn.

Benedetto U, Sciarretta S, Roscitano A, et al. Preoperative angiotensin-converting enzyme inhibitors and acute kidney injury after coronary artery bypass grafting. *Ann Thorac Surg*. 2008;86:1160–1165.

Coriat P, Richer C, Douraki T, et al. Influence of chronic angiotensin-converting enzyme inhibition on anesthetic induction. *Anesthesiology*. 1994;81:299–307.

Hollmann C, Fernandes NL, Biccard BM. A systematic review of outcomes associated with withholding or continuing angiotensin-converting enzyme inhibitors and angiotensin receptor blockers before noncardiac surgery. *Anesth Analg*. 2018;127(3);678–687.

Kwapisz MM, Müller M, Schindler E, et al. The effect of intravenous quinaprilat on plasma cytokines and hemodynamic variables during cardiac surgery. *J Cardiothorac Vasc Anesth*. 2004;18:53–58.

Ryckwaert F, Colson P. Hemodynamic effects of anesthesia in patients with ischemic heart failure chronically treated with angiotensin-converting enzyme inhibitors. *Anesth Analg*. 1997;84:945–949.

Trentman TL, Fassett SL, Thomas JK, et al. More hypotension in patients taking antihypertensives preoperatively during shoulder surgery in the beach chair position. *Can J Anaesth*. 2011;58(11):993–1000.

B. Preoperative Evaluation and Preparation

B.1. How would you evaluate this patient preoperatively?

In addition to the routine systemic preoperative physical and history, special attention should be paid to the following: etiology and severity of hypertension, the subtype of hypertension, current therapy, and the end-organ damage from chronic hypertension.

The underlying cause of hypertension should be clear. Surgical mortality is relatively high in patients with renovascular hypertension. Moreover, failure to diagnose a pheochromocytoma preoperatively, albeit a rare finding, may prove fatal because anesthetic agents are well known to precipitate a crisis in such patients. Meanwhile, the severity of

hypertension alters anesthetic risk.

Antihypertensive drugs have different anesthetic implications. Diuretics frequently cause chronic hypokalemia and hypomagnesemia, which may increase the risk of arrhythmia. Therefore, serum electrolytes should be checked preoperatively.

The presence of target-organ damage in the brain, heart, and kidney signifies long-standing, poorly controlled hypertension. Unfortunately, markers of organ damage become demonstrable only after significant end-organ damage has occurred.

For cardiac evaluation, electrocardiogram and chest x-ray film serve as minimal tests. The echocardiogram will be helpful. LVH can increase the risk of perioperative myocardial ischemia from imbalances of myocardial O_2 supply and demand regardless of the presence or absence of coronary artery disease. There is a very high correlation between LVH, ISH, and PPH—it is uncertain which comes first. Some authorities believe that hypertensive patients without evidence of LVH or other risk factors are at a lower perioperative cardiac risk and do not require further evaluation for most operations. Patients with severe hypertension are also at an increased risk for diastolic dysfunction causing CHF.

For renal evaluation, urinalysis, serum creatinine, and blood urea nitrogen should be measured to define the presence and extent of renal parenchymal disease. If chronic renal failure exists, hyperkalemia and elevated plasma volume may be of concern. Normal saline crystalloid intravenous solution is recommended for such cases.

For cerebrovascular evaluation, a history of cerebrovascular accidents and transient ischemic attacks and the presence of hypertensive retinopathy should be looked for.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:585–611.

Fleisher LA. Preoperative evaluation of the patient with hypertension. *JAMA*. 2002;287:2043–2046.

Fontes M, Heerdt PM. Systemic and pulmonary arterial hypertension. In: Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:188–189.

B.2. Would you postpone the surgery? Why? What BP would you like the patient to achieve before surgery?

It is prudent to postpone elective surgery with a BP of 230/120 mmHg. This patient should be considered to have hypertensive emergency if additional end-organ sequelae are present, in which case he needs to be admitted for intravenous control of BP. Otherwise, for hypertensive urgency, it is recommended that the patient be placed in a quiet environment and managed with rest and oral antihypertensives. The patient should be discharged and instructed to follow-up with his internist for management and control of hypertension. Prior to rescheduling for surgery, if time permits, the BP should be gradually lowered over 6 to 8 weeks to less than 140/90 mmHg. Acute control within several hours is inadvisable before elective surgery because this practice may put the cerebral or other circulations at risk for ischemia.

In moderate hypertensive patients with severe end-organ involvement, preoperative BP should be normalized as much as possible, although in asymptomatic patients with mild-to-moderate hypertension (diastolic BP <110 mmHg), elective surgery may proceed without increased cardiovascular risks. Goldman found that patients with mild and moderate hypertension were not at increased risk of vascular complications unless they had other risks of coronary heart disease. In all, the thresholds being recommended apply only in part to today's surgical population. Most hypertensive patients presenting for surgery are elderly patients who suffer almost exclusively from ISH and PPH. It is uncertain what acute changes in BP preoperatively will have on outcome giving that

the pathologic changes are chronic and unlikely to normalize with treatment. In patients with medically refractory coronary disease requiring coronary artery bypass grafting (CABG) surgery, PPH was associated with an increased risk of major vascular complication.

Fleisher LA. Preoperative evaluation of the patient with hypertension. *JAMA*. 2002;287:2043–2046.

Fontes ML, Aronson S, Mathew JP, et al; for the Multicenter Study of Perioperative Ischemia (McSPI) Research Group and the Ischemia Research and Education Foundation (IREF) Investigators. Pulse pressure and risk of adverse outcome in coronary bypass surgery. *Anesth Analg*. 2008;107:1122–1129.

Goldman L. Cardiac risk in noncardiac surgery: an update. *Anesth Analg*. 1995;80:810–820.

Nikolov NM, Fontes ML, White WD, et al. Pulse pressure and long-term survival after coronary artery bypass graft surgery. *Anesth Analg*. 2010;110:335–340.

B.3. Should all or any of the chronic medications be discontinued before the operation?

Current opinion generally favors continuation of antihypertensive medications, especially β-blockers, up to the time of surgery. There is concern that acute withdrawal of these medications may precipitate ischemic myocardial events. Because β-blockade does not impair the hemodynamic response to hemorrhage and does not adversely affect responses to hypoxia, the medications should be continued. The withdrawal syndrome is characterized by an enhanced sensitivity to sympathetic stimulation and has been attributed to various factors, including sympathetic overactivity and increased triiodothyronine levels, but most probably, it is a result of increased β-receptor density.

The safety of β-blockers and their benefits (prevention of hypertensive responses, dysrhythmias, and myocardial ischemia) have been long established. Similarly, treatment with calcium

channel blockers, ACE inhibitors, statins, and diuretics can be maintained. Indeed, the responses to induction of anesthesia, laryngoscopy, and intubation differ little whether patients receive a β-blocker, a calcium channel blocker, an ACE inhibitor, or a diuretic. Withdrawal of clonidine has been associated with rebound hypertension.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:585–611.

Fleisher LA. Preoperative evaluation of the patient with hypertension. *JAMA*. 2002;287:2043–2046.

Sear JW, Jewkes C, Tellez JC, et al. Does the choice of antihypertensive therapy influence haemodynamic responses to induction, laryngoscopy and intubation? *Br J Anaesth*. 1994;73:303–308.

B.4. Should hypokalemia be treated before anesthesia? Why?

Hypokalemia is a frequent finding in hypertensive patients treated with the diuretic thiazides. It is important to maintain normal electrolyte balance in patients with heart or coronary artery disease. A low value of potassium (3.0 to 3.5 mEq per L) in these patients may cause arrhythmias, increase sensitivity to digitalis, and depress neuromuscular function. In patients without risk of cardiac complications of surgery and anesthesia, this modest reduction (3.0 to 3.5 mEq per L) should not prompt postponement of surgery or immediate potassium replacement. Patients with more severe potassium depletion ($\leq$2.9 mEq per L) should be treated and/or undergo workup for such profound hypokalemia. For those patients, at least 1 week before surgery, supplemental potassium should be given if renal function is not impaired. In surgical emergencies, potassium may be given at a rate not to exceed 0.5 mEq per kg of body weight per hour. Administration should be stopped during surgery and restarted postoperatively, depending on serial potassium determinations. Vitez et al. concluded that chronic hypokalemia per se is not

associated with a higher incidence of intraoperative arrhythmia.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:384–418.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:407–424.

Vitez TS, Soper LE, Wong KC, et al. Chronic hypokalemia and intraoperative dysrhythmias. *Anesthesiology*. 1985;63:130–133.

B.5. Should hypomagnesemia be treated before anesthesia? Why?

The normal level of magnesium is between 1.5 and 2.5 mEq per L. Magnesium ion is essential for the proper function of most enzyme systems. Depletion is characterized by neuromuscular and central nervous system hyperexcitability. These signs are similar to those of calcium deficiency. Cardiovascular abnormalities include coronary artery spasm, cardiac failure, and dysrhythmias. When severe, hypomagnesemia may induce seizures, confusion, and coma. Replacement should be done only in cases of severe depletion. Magnesium should not be given to the oliguric patient and should be given very carefully to patients with renal insufficiency. Small intravenous doses should be used, with careful observation for toxicity (lethargy, weakness, and loss of deep tendon reflexes).

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:384–418.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:407–424.

B.6. Does an asymptomatic carotid bruit increase the risk in these patients?

Yes. The incidence of stroke is increased in such patients, although the stroke may not be thrombotic or related to the carotid artery in which the bruit was heard. Bruits are general predictors of vascular disease and may be predictors of

perioperative strokes. It is important to note that in patients who are asymptomatic from their carotid stenosis, endarterectomy is no longer recommended. Nevertheless, there continues to be much debate on this topic.

De Feo M, Renzulli A, Onorati F, et al. The risk of stroke following CABG: one possible strategy to reduce it? *Int J Cardiol*. 2005;98(2):261–266.

Wolf PA, Kannel WB, Sorlie P, et al. Asymptomatic carotid bruit and risk of stroke. The Framingham study. *JAMA*. 1981;245:1442–1445.

Yatsu FM, Hart RG. Asymptomatic carotid bruit and stenosis: a reappraisal. *Stroke*. 1983;14:301–304.

B.7. The surgery was postponed for 6 weeks. The patient was on metoprolol, aspirin, atorvastatin, captopril, hydrochlorothiazide, and potassium chloride. His BP was 160/60 mmHg and potassium 4.0 mEq per L. How would you premedicate this patient?

Because half or more of hypertensive patients still have elevated BP despite treatment, the anesthesiologist should determine the anxiety level of the patient. With this knowledge, the premedication with diazepam, lorazepam, or midazolam can be regulated to have the patient arrive in the operating room sedated. However, due to a high occurrence of delirium in the elderly receiving benzodiazepines, premedication with such agents is being discouraged. This will help to prevent a starting BP well above the optimal level. All the antihypertensive medications are continued up to the day of surgery.

Lepousé C, Lautner CA, Liu L, et al. Emergence delirium in adults in the post-anaesthesia care unit. *Br J Anaesth*. 2006;96(6):747–753.

B.8. If the patient is an untreated hypertensive patient with BP 170/70 mmHg, would you treat the patient preoperatively with an antihypertensive agent?

Yes. The preoperative administration of clonidine, β-blockers, or

ACE inhibitors has been advocated to reduce the intraoperative hemodynamic lability and myocardial ischemia in hypertensive patients. Clonidine, a central α_2-agonist, decreases sympathetic outflow and reduces plasma catecholamines, aldosterone levels, and renin activity. A single dose of clonidine, 5 μg per kg orally, 2 hours before surgery significantly decreases anesthetic requirements and hemodynamic lability in patients with mild-to-moderate hypertension. However, preoperative clonidine did not decrease BP lability during aortic operation. Perioperative use of clonidine also has been shown to have short- and long-term benefits related to cardiac morbidity and survival.

The best treatment may be cardioselective β-blocker therapy. A single small oral dose of a β-adrenergic blocking agent such as labetalol, atenolol, or metoprolol given preoperatively to untreated, asymptomatic, mildly hypertensive patients effectively attenuated tachycardia with tracheal intubation and emergence. The incidence of myocardial ischemia was reduced from 28% in the control group to 2% in the β-blocker groups. An oral-dose ACE inhibitor such as enalapril given preoperatively also attenuates the hemodynamic responses to intubation and surgical stimulation.

Fleisher LA. Preoperative evaluation of the patient with hypertension. *JAMA*. 2002;287:2043–2046.

Stone JG, Foëx P, Sear JW, et al. Myocardial ischemia in untreated hypertensive patients: effect of a single small oral dose of a beta-adrenergic blocking agent. *Anesthesiology*. 1988;68:495–500.

Wallace AW, Galindez D, Salahieh A, et al. Effect of clonidine on cardiovascular morbidity and mortality after noncardiac surgery. *Anesthesiology*. 2004;101(2):284–293.

C. Intraoperative Management

C.1. How would you monitor this patient?

- *Electrocardiogram*. Simultaneous leads V_5 and II, multiple-lead ST-segment analysis, if possible, are essential because hypertensive patients are at increased risk for myocardial ischemia regardless of the presence or absence of coronary disease.
- *BP*. A continuous monitoring of BP is essential because of lability of BP in these patients. Direct intra-arterial measurement of BP permits beat-to-beat observation. However, noninvasive automatic oscillometric techniques usually are sufficient.
- *Pulmonary artery catheter (PAC)*. Only for those hypertensive patients with a history of CHF or a recent MI, a PAC may be helpful in managing fluid replacement and monitoring ventricular function. Of note, there is a strong correlation between hypertension and LVH, which results in poor ventricular compliance reflected by elevated pulmonary artery occlusion pressure in the face of low or normal ventricular volumes and normal contractility. Presence of CHF in hypertensive patients is frequently a marker of diastolic dysfunction and *not* systolic dysfunction.
- *Pulse oximeter*. This should be used to monitor peripheral blood flow and oxygenation.
- *End-tidal CO_2 analyzer*. This monitor will help maintain normocarbia.

C.2. What are the anesthetic goals for hypertensive patients?

The anesthetic goal is to minimize wide lability of BP in response to anesthetic and surgical stimuli to prevent the following:

- Myocardial ischemia from tachycardia or less common from either hypertension or hypotension
- Cerebral hypoperfusion from hypotension

- Cerebral hemorrhage and hypertensive encephalopathy resulting from hypertension or embolic stroke from rupture of plagues either locally or from the aorta and the neck vessels
- Renal failure from renal hypoperfusion

Particular attention to diastolic BP is strongly recommended while attempting to reduce systolic BP. It is unfortunate that clinical practice perioperatively hinges on manipulation of the systolic BP without attention to the diastolic component. This is particularly troublesome in most elderly patients who suffer from ISH and/or wide pulse pressure. In both subtypes of hypertension, the already lower diastolic pressure can easily be reduced further—predisposing to myocardial hypoperfusion and ischemia.

Lee et al. showed that patients with wide pulse pressure have an increased risk for thrombogenesis marked by elevated levels of D-dimers, von Willebrand factor, and platelet activation. This along with extensive atherosclerotic disease of the aorta, carotid, and renal arteries, which is also common in patients with ISH, provides a pathophysiologic basis for the increase incidence of perioperative stroke, MI, and renal dysfunction observed in hypertensive patients.

Lastly, careful control of the hemodynamic responses to noxious stimuli such as endotracheal intubation, surgical incision and manipulation, and emergence from anesthesia is essential in the hypertensive patient.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:183–198.

Lee KW, Blann AD, Lip GY. High pulse pressure and nondipping circadian blood pressure in patients with coronary artery disease: relationship to thrombogenesis and endothelial damage/dysfunction. *Am J Hypertens*. 2005;18:104–115.

Lovett JK, Howard SC, Rothwell PM. Pulse pressure is independently associated with carotid plaque ulceration. *J Hypertens*. 2003;21:1669–1676.

C.3. How would you induce anesthesia for the hypertensive patient?

While the patient is being preoxygenated, fentanyl, 2 to 5 μg per kg, is given slowly to achieve drowsiness. Then, either thiopental in 50-mg increments or propofol in 30- to 50-mg increments is titrated to produce unconsciousness, followed by succinylcholine, 1 mg per kg, or nondepolarizing muscle relaxants to facilitate tracheal intubation.

All anesthetic agents are acceptable with the possible exception of ketamine, which may produce significant hypertension and tachycardia. However, deeper anesthesia with potent inhalation agents to attenuate tachycardia and hypertension should be done with caution because of higher incidence of hypotension arising from both vasodilation and cardiac depression.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:183–198.

Martin DE, Rosenberg H, Aukburg SJ, et al. Low-dose fentanyl blunts circulatory responses to tracheal intubation. *Anesth Analg*. 1982;61:680–684.

C.4. How does tracheal intubation produce hypertension?

Translaryngeal intubation of the trachea stimulates laryngeal and tracheal receptors, resulting in marked increase in the elaboration of sympathomimetic amines. This sympathetic stimulation results in tachycardia and a rise in BP. In normotensive patients, this rise is approximately 20 to 25 mmHg; it is much greater in hypertensive patients. This increase in BP results from vasoconstriction because of unopposed α stimulation in hypertensive patients taking α-blocking drugs.

Prys-Roberts C, Greene LT, Meloche R, et al. Studies of anaesthesia in relation to hypertension. II. Haemodynamic consequences of induction and endotracheal intubation. *Br J Anaesth*. 1971;43:531–547.

C.5. What happens to the left ventricular ejection fraction during and immediately following intubation?

During and immediately following intubation associated with tachycardia and hypertension, there is a decrease in the left ventricular ejection fraction. This is particularly marked in patients with coronary artery disease. Nevertheless, such hemodynamic perturbations can be anticipated and treated accordingly with β-blockade, narcotic, and titration of hypnotic and/or inhalation agents.

Giles RW, Berger JH, Barash PG, et al. Continuous monitoring of left ventricular performance with the computerized nuclear probe during laryngoscopy and intubation before coronary artery bypass surgery. *Am J Cardiol*. 1982;50:735–741.

C.6. What other measures can prevent hypertension and tachycardia at the time of intubation?

The rise in BP and heart rate occurs approximately 14 seconds after the start of laryngoscopy and becomes maximal after 30 to 45 seconds of direct laryngoscopy. If possible, laryngoscopy time should be 15 seconds or less to minimize BP elevation. Simultaneous administration of fentanyl, 5 μg per kg with the induction dose of thiopental or propofol, can blunt the cardiovascular response to tracheal intubation. Other measures are described as follows:

- Lidocaine, 1.5 mg per kg, is given 2 minutes before intubation.
- Esmolol, up to 2 mg per kg, appears to be especially effective in providing consistent and reliable protection against hypertension and tachycardia with intubation. It is easy to titrate and does not exacerbate postintubation hypotension because of its short duration of action.
- Labetalol, 0.15 to 0.45 mg per kg, is comparable to esmolol, 1.5 to 4.5 mg per kg, in attenuating hemodynamic effects.

However, the half-lives of intravenous esmolol and labetalol are 9 minutes and 5 hours, respectively. Additionally, labetalol has minimal effects on heart rate, and through its action on α receptors, it acts similar to a vasodilator, particularly with chronic use.

- Nicardipine, 1 mg intravenously, 2 minutes before tracheal intubation maintained hemodynamic stability during the intraoperative period. Both doses of 0.015 and 0.03 mg per kg attenuated BP but not heart rate responses during emergence and extubation. Greater BP control occurred with the larger nicardipine dose of 0.03 mg per kg.

It is important to remember that all the previously mentioned doses are used with a single agent only. If a combination of different agents or anesthetics is used, doses should be decreased accordingly. Otherwise, severe hypotension may ensue.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:585–611.

Gold MI, Sacks DJ, Grosnoff DB, et al. Use of esmolol during anesthesia to treat tachycardia and hypertension. *Anesth Analg*. 1989;68:101–104.

Helfman SM, Gold MI, Delisser EA, et al. Which drug prevents tachycardia and hypertension associated with tracheal intubation: lidocaine, fentanyl, or esmolol? *Anesth Analg*. 1991;72:482–486.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:183–198.

Kapnoudhis P, Vaghadia H, Jenkins LC, et al. Esmolol versus fentanyl for preventing haemodynamic response to intubation in cardiovascular disease. *Can J Anaesth*. 1990;37:S145.

Kovac AL, McKinley C, Tebbe CJ, et al. Comparison of nicardipine versus placebo to control hemodynamic responses during emergence and extubation. *J Cardiothorac Vasc Anesth*. 2001;15:704–709.

Martin DE, Rosenberg H, Aukburg SJ, et al. Low-dose fentanyl blunts circulatory responses to tracheal intubation. *Anesth Analg*. 1982;61:680–684.

C.7. After induction and intubation, the BP decreased to 70/40 mmHg. What would you do?

Hypotension after induction of anesthesia is usually due to combination of vasodilation, hypovolemia, and cardiac depression. Vasodilation can be caused by inducing agents such as thiopental, propofol, or midazolam; moderate-to-high doses of narcotics; and potent inhalation agents. Hypertensive patients are in relative hypovolemia because of chronic vasoconstriction and/or diuretic therapy. Preoperative bowel preparation and nothing by mouth further contribute to hypovolemia. Barbiturates, benzodiazepines, and inhalation agents can cause a mild-to-moderate degree of cardiac depression.

Hypotension after induction of anesthesia usually can be easily corrected by volume replacement and simultaneous titration of vasopressors such as ephedrine 5 to 10 mg or phenylephrine in 0.1-mg increments.

Coriat P, Richer C, Douraki T, et al. Influence of chronic angiotensin-converting enzyme inhibition on anesthetic induction. *Anesthesiology*. 1994;81:299–307.

C.8. What is your choice of agents for maintenance of anesthesia? Why?

No particular anesthetic technique or specific drug combinations have been demonstrated to be superior to others in hypertensive patients. Potent inhalation anesthetics or narcotics should be titrated to the desired level of central nervous system depression while the BP is monitored continuously.

Narcotics and nitrous oxide provide an anesthetic with less overall lability of BP, but commonly, intraoperative hypertension is difficult to control by moderate doses of narcotics. High doses of narcotics are not suitable for early extubation. Likewise, use of nitrous oxide is debatable in open cholecystectomy given its propensity to increase bowel distention—the severity being related to higher concentration of nitrous oxide and to longer duration of use. This concern is less

pertinent for laparoscopic cholecystectomy whereby insufflation of gas to pressurize the abdomen should counteract the distensible property of nitrous oxide (also see Chapter 26, section C.4).

Potent inhalation agents provide greater control of hypertension but seem to produce less stability. Isoflurane, desflurane, and sevoflurane possess the advantage of more peripheral vasodilation and less cardiac depression.

Akca O, Lenhardt R, Fleischmann E, et al. Nitrous oxide increases the incidence of bowel distension in patients undergoing elective colon resection. *Acta Anaesthesiol Scand*. 2004;48(7):894–898.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:183–198.

Taylor E, Feinstein R, White PF, et al. Anesthesia for laparoscopic cholecystectomy. Is nitrous oxide contraindicated? *Anesthesiology*. 1992;76(4):541–543.

C.9. How would you manage fluid therapy for hypertensive patients?

Patients with essential hypertension are usually hypovolemic because of vasoconstriction and diuretic therapy. Hydration of the hypertensive patient should be started before induction of anesthesia to minimize the "roller coaster" often seen with hypertension. However, overhydration should be avoided because it may contribute to postoperative hypertension when the vasodilating effects of anesthetics are gone. Therefore, careful estimation of fluid intake and output is essential. Foley catheter and central venous pressure monitor are indicated for major surgery with extensive fluid exchange.

As discussed previously, presence of LVH in hypertensive patients shifts the left ventricular compliance curve upward and leftward such that for the same ventricular volume, a higher left ventricular diastolic pressure is attained as compared to a nonhypertrophied ventricle. When managing these patients with

a PAC, higher pulmonary artery occlusion pressure (sometimes >20 mmHg) is necessary to achieve normovolemia. Cardiac output also must be checked frequently during volume challenges.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:183–198.

C.10. During the surgery, BP increased to 220/120 mmHg. How would you treat the hypertension?

Intraoperative control of hypertension is outlined in **Table 11.5**. Severe hypertension that occurs during a surgical procedure is most frequently due to inadequate anesthesia. Inadequate blockade of sensory input from the surgical procedure stimulates the elaboration of sympathomimetic amines, resulting in hypertension and tachycardia. If a potent inhalation anesthetic is being used, the level of anesthesia should be deepened by increasing the inspired concentration of the anesthetic. A narcotic may not control the rise in BP, and it may be necessary to switch to a potent inhalation anesthetic.

TABLE 11.5 Intraoperative Control of Hypertension

Anesthetics
Narcotics, inhalation agents, butorphanol, lidocaine
Antihypertensives
Adrenergic blockers
α-Blocker: phentolamine
β-Blocker: propranolol, metoprolol
α- and β-Blocker: labetalol
Calcium channel blockers
Diltiazem, nicardipine, verapamil
ACE inhibitors
Enalapril
Direct vasodilators
Hydralazine, nitroglycerin, nitroprusside
Dopaminergic agonists
Fenoldopam

ACE, angiotensin-converting enzyme.

Hydralazine, 5-mg increments, may be titrated to decrease BP safely with little chance of excessive reduction. The onset of action is in 10 to 15 minutes with 1 to 2 hours duration.

Labetalol, 5- to 10-mg increments, is very useful in controlling hypertension and tachycardia. It makes the most sense to use β-blockers after a significant rise in BP because these agents act directly to antagonize the effects of the catecholamines. Although other agents may lower the BP, it is highly possible that the excessive availability of both norepinephrine and epinephrine will continue to exert their effects at the receptor site—compromising tissue perfusion from microcirculatory vasoconstriction. This view may explain the broad anti-ischemic effects of perioperative β-blockers on the brain, the heart, and the kidneys.

Rarely, continuous infusion of nicardipine, nitroglycerin, or nitroprusside, direct arteriolar vasodilators, is needed to control hypertension during anesthesia.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:183–198.

Lindenauer PK, Pekow P, Wang K, et al. Perioperative beta-blocker therapy and mortality after major noncardiac surgery. *N Engl J Med*. 2005;353(4):349–361.

C.11. What could you do to prevent hypertension during extubation and emergence?

It is logical to use antihypertensive agents during extubation and emergence because the patient is awakened at the end of surgery. Many drugs or combinations are effective, including intravenous lidocaine, esmolol, labetalol, verapamil, or diltiazem 2 minutes before extubation. If BP goes over desired levels after extubation, additional doses may be titrated to control BP.

Mikawa K, Nishina K, Maekawa N, et al. Attenuation of cardiovascular responses to tracheal extubation: verapamil versus diltiazem. *Anesth Analg*.

1996;82:1205–1210.

C.12. Would you consider regional anesthesia for this patient?

Certainly, regional anesthesia can avoid marked increases in sympathetic tone and hemodynamic changes that occur with intubation and extubation. Spinal or epidural anesthesia may be used for lower abdominal surgery. For cholecystectomy, higher levels of regional anesthesia are needed and may compromise respiratory function or unmask hypovolemia. In addition, prolonged surgery in a nonsedated patient can cause anxiety and irritability that may induce hypertension and tachycardia.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:183–198.

D. Postoperative Management

D.1. The patient developed hypertension, BP 210/110 mmHg, in the postanesthesia care unit. What would you do?

The management of postoperative hypertension depends on the etiology of the hypertension, the clinical scenario, and the level of hypertension. First, the cause of hypertension should be determined and treated accordingly. Hypertension per se should also be treated by an antihypertensive agent. The causes of postoperative hypertension include pain, emergence excitement, hypoxemia, hypercarbia, reaction to endotracheal tube, full bladder, hypothermia, relative hypervolemia from intraoperative administration of excess fluid, and chronic medication and withdrawal. The most common cause of postoperative hypertension is incisional pain. As the patient awakens, pain triggers an outpouring of catecholamines. The extreme lability of BP in many hypertensive patients makes this rapid increase

critical to control. Depending on the cause of hypertension, intravenous analgesics and antihypertensives or diuretics should be titrated to control hypertension. If both tachycardia and hypertension occurred postoperatively, calcium channel blockers such as verapamil, diltiazem, or nicardipine and β-blocking agents such as propranolol, esmolol, labetalol, or metoprolol are preferred agents. Hypertension resulting from pain can be preventable or attenuated by asking the surgeon to inject a long-lasting local anesthetic along the incision or to perform a local nerve block.

Barash PG, Cullen BF, Stoelting RK, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1562–1606.

Cardiac Tamponade

June M. Chan

12

Four days after a two-vessel coronary artery bypass graft procedure with a mitral valve replacement, a 69-year-old, 90 kg, 167-cm tall woman presents with shortness of breath, orthopnea, oliguria, and overt weakness. On examination, she is sitting fully upright and appears anxious; her skin is cold and clammy. Her vital signs are as follows: heart rate (HR), 120 beats per minute (sinus tachycardia); respiratory rate, 38 breaths per minute; and systemic blood pressure, 115/66 mmHg.

A pulmonary artery catheter (PAC) is inserted and reveals: pulmonary artery (PA) pressure, 55/21 mmHg; pulmonary artery occlusion pressure (PAOP), 14 mmHg; central venous pressure (CVP), 23 mmHg; and cardiac output (CO), 2.7 L per minute.

A. Medical Disease and Differential Diagnosis

1. What is the differential diagnosis of low CO following cardiac surgery?
2. Describe the pathophysiology of cardiac tamponade.
3. What are the common etiologies of cardiac tamponade?
4. What is the difference between acute and delayed cardiac tamponade?
5. What is regional cardiac tamponade?
6. Describe the ventricular interaction in cardiac tamponade.

7. How is coronary blood flow affected in cardiac tamponade?
8. What is the Beck triad? Describe the typical signs and symptoms of cardiac tamponade.
9. Define pulsus paradoxus and describe its pathophysiology.
10. What is Kussmaul sign? Is this finding consistent with tamponade physiology?
11. Which medical conditions mimic cardiac tamponade?

B. Preoperative Evaluation and Preparation

1. Interpret and explain the pathophysiologic basis for this patient's hemodynamic findings.
2. How would you optimize this patient's cardiovascular status prior to definitive diagnosis and treatment?
3. What are the radiographic findings in tamponade?
4. A limited bedside transthoracic echocardiogram is performed, demonstrating a layer of clotted blood anterior to the right atrium (RA) and ventricle. What echocardiographic findings support the diagnosis of tamponade?
5. What additional information should be obtained from a limited echocardiographic study?
6. Describe the procedures for treating cardiac tamponade. What are the clinical indications for each approach?
7. Having made the diagnosis of tamponade, what additional investigations are required prior to surgery?
8. Explain the technical and physiologic principles behind rotational thromboelastometry.
9. A rotational thromboelastometry was performed, and a 10-minute analysis reveals the following results (see **Fig. 12.9** and **Table 12.8**). How do you interpret this information?
10. Given the ROTEM® findings and high clinical suspicion for occult postsurgical bleeding, what hemostatic products would you arrange to have in the operating room?
11. How would you organize and conduct the transport of this

patient to the operating room?

C. Intraoperative Management

1. What are the cardiovascular effects of commonly used intravenous anesthetic and coinduction agents?
2. What is the effect of supine positioning and positive pressure ventilation on the hemodynamics of a patient with tamponade?
3. Describe the induction process for cardiac tamponade.
4. Following induction and intubation, the systemic blood pressure decreases to 55/30 mmHg. Describe your management.
5. What hemodynamic changes are frequently associated with opening the pericardial space?
6. Following the removal of approximately 500 mL of dark blood and clots from the mediastinum, the patient's CO remains low. What are your differential diagnoses?
7. What is pericardial decompression syndrome (PDS)?

D. Postoperative Management

1. A pericardial drain is placed following mediastinal decompression. How should this drainage tube be managed?
2. How would you manage hypertension in the intensive care unit?

A. Medical Disease and Differential Diagnosis

A.1. What is the differential diagnosis of low CO following cardiac surgery?

CO is the product of stroke volume (SV) and HR:

$$CO = HR \times SV$$

A prima facie interpretation of this relationship is that a low SV and/or low HR will cause a low CO state. However, fast HR of either ventricular or atrial origin (i.e., atrial fibrillation) may

also cause a low CO state because the diastolic filling time is decreased or the atrial contribution to the ventricular filling is altered. Preload, afterload, and contractility all contribute to SV and their alterations can also result in a decrease in CO (**Table 12.1**). A decrease in preload will decrease SV if the ventricle becomes underfilled. An increase in preload can also decrease SV if it causes ventricular overdistension, thereby stretching the ventricular myocytes beyond the working limits of the length-tension relationship. A decrease in myocardial contractility can compromise CO. Finally, in a ventricle with systolic dysfunction, an increase in afterload can further impair ejection and SV. A combination of different hemodynamic disturbances can coexist in the same patient. For example, a patient can have both a decrease in contractility and a reduced preload to account for the low CO state. Therefore, correcting one problem alone may not produce the optimal hemodynamic condition.

TABLE 12.1 Differential Diagnoses of a Low Cardiac Output

Parameter	Change	Examples
Heart rate	Decrease	Bradycardia
		Heart block causing loss of AV synchrony
	Increase	Atrial fibrillation
		Ventricular tachyarrhythmias
Preload	Decrease	Hypovolemia
		Mitral stenosis
	Increase	Ventricular overdistension and systolic dysfunction
		Mitral regurgitation
Afterload	Increase	Embolism
		Outflow tract obstruction
Contractility	Direct decrease	Right and/or left ventricle • Ischemia/infarction • Stunning/hibernation
	Indirect decrease	Tamponade
		Embolism

	Negative inotropic agents
	Toxins (endotoxin, inflammatory cytokines)

AV, atrioventricular.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia: For Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:143–178.

Tung A. Critical care of the cardiac patient. *Anesthesiol Clin*. 2013;31:421–432.

A.2. Describe the pathophysiology of cardiac tamponade.

The pericardium is a two-layered blind sac surrounding the atria, ventricles, proximal great vessels, and distal venae cava and pulmonary veins. Normally, 10 to 50 mL of fluid exist within the pericardial space. This plasma-like fluid is produced by the serous pericardium and is drained by the lymphatic system. The serous pericardium consists of a visceral portion, which is adherent to the epicardium, and a parietal layer, which is adherent to the outer, fibrous pericardium. The relatively noncompliant fibrous pericardium constrains the heart within the thoracic cavity. The normal physiologic functions of this pericardial constraint include limiting acute ventricular dilatation with increases in preload, preserving the "optimal" ventricular shape for mechanical efficiency, and maintaining the normal coupling of right (RV) and left ventricular (LV) function.

Cardiac tamponade may be defined as a pathologic increase in intrapericardial pressure causing a decrease in CO. In normal conditions, intrapericardial pressure is very close to intrathoracic pressure, being slightly negative relative to atmosphere at rest. In tamponade, intrapericardial pressure increases and approaches atrial and ventricular diastolic pressures. This forms a Starling resistor system that progressively impairs diastolic cardiac filling and SV, eventually causing hypotension and

shock depending on the rate of pericardial pressure increase relative to intracardiac filling pressures and the compliance of the pericardial sac (**Table 12.2**).

TABLE 12.2 Three Phases of Cardiac Tamponade

Phase	Pathophysiologic Events	Pressure Relationship
I	Pericardial fluid increases ventricular stiffness, increasing filling pressures.	LVEDP > RVEDP > IPP
II	Pericardial pressure approaches right-sided filling pressures, exerts Starling resistor forces on RV filling. Respirophasic variation in stroke volume appears.	LVEDP > IPP = RVEDP
III	Pericardial pressure approaches left-sided filling pressures. Hemodynamic instability is prominent.	IPP = LVEDP = RVEDP

IPP, intrapericardial pressures; LVEDP, left ventricular end-diastolic pressure; RVEDP, right ventricular end-diastolic pressure.

In defining tamponade as a state where intrapericardial pressure approaches cardiac diastolic pressures, it is important to note that tamponade can result from a decrease in cardiac filling pressures in the presence of modest elevations in intrapericardial pressure. This has been described as "low pressure cardiac tamponade."

Ariyarajah Y, Spodick DH. Cardiac tamponade revisited: a postmortem look at a cautionary case. *Tex Heart Inst J*. 2007;34(3):347–351.

Hayes SN, Freeman WK, Gersh BJ. Low pressure cardiac tamponade: diagnosis facilitated by Doppler echocardiography. *Br Heart J*. 1990;63:136–140.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia: For Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:143–178.

Reddy PS, Curtiss EI, Uretsky BF. Spectrum of hemodynamic changes in cardiac tamponade. *Am J Cardiol*. 1990;66:1487–1491

Saito Y, Donohue A, Attai S, et al. The syndrome of cardiac tamponade with "small" pericardial effusion. *Echocardiography*. 2008;25:321–327.

A.3. What are the common etiologies of cardiac tamponade?

Common causes of increased intrapericardial pressure include blood, exudate, transudate, and air (**Table 12.3**). In the United States, the most common cause of pericardial effusions complicated by tamponade are due to malignancies, followed by iatrogenesis from interventional cardiologic procedures and surgical cardiotomy.

TABLE 12.3 Causes of Cardiac Tamponade

Category	Differential Diagnoses
Blood	• Iatrogenic/postcardiotomy • Trauma • Aortic dissection • Anticoagulation
Exudate	• Locoregional inflammation – Infectious: viral, bacterial, tuberculous – Postmyocardial infarction – Dressler syndrome • Systemic inflammation – Systemic lupus erythematosus – Rheumatoid arthritis – Sarcoidosis – Malignancy
Transudate	• Congestive heart failure • Uremia • Hypothyroidism • Radiation • Pulmonary hypertension • Hypoalbuminemia
Air	• Iatrogenic/postsurgical • Trauma • Mechanical ventilation

Adler Y, Charron P, Imazio M, et al. 2015 ESC guidelines for the diagnosis and management of pericardial diseases: the Task Force for the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology (ESC) endorsed by: the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J*. 2015;36(42):2921–2964.

Ariyarajah Y, Spodick DH. Cardiac tamponade revisited: a postmortem look at a cautionary case. *Tex Heart Inst J*. 2007;34(3):347–351.

Mathew J, Swaminathan M, Ayoub C, eds. *Clinical Manual and Review of*

Transesophageal Echocardiography. 2nd ed. New York: McGraw-Hill; 2010:351–369.

Meltser H, Kalaria VG. Cardiac tamponade. *Catheter Cardiovasc Interv*. 2005;64:245–255.

Spodick DH. Pathophysiology of cardiac tamponade. *Chest*. 1998;113:1372–1378.

A.4. What is the difference between acute and delayed cardiac tamponade?

Normal adult pericardial reserve is limited to acute increases in volume of approximately 150 to 250 mL. Beyond this point, further increases will cause dramatic changes in intrapericardial pressure. In slowly accumulating effusions, the pericardium is able to remodel and stretch, thereby increasing its capacitance (**Fig. 12.1**). Massive, slowly accumulating pericardial effusions therefore can exist with little to no clinical evidence of tamponade.

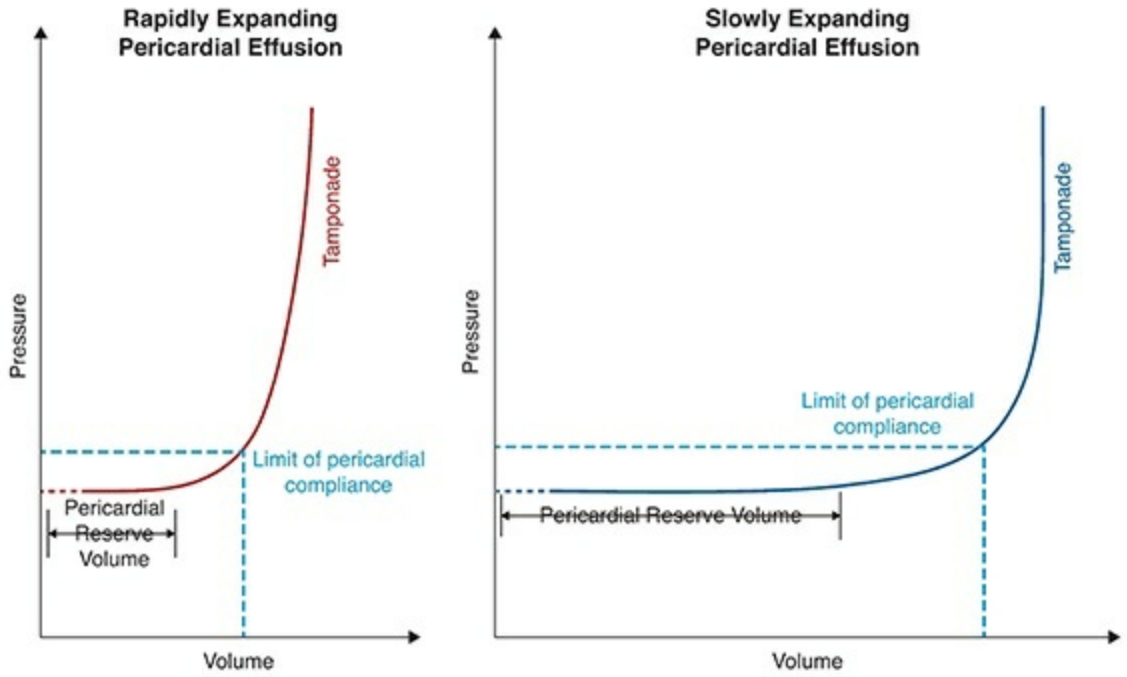

FIGURE 12.1. Acute versus delayed tamponade. In acute effusions, normal pericardium has a reserve volume of approximately 150 to 250 mL. Until this volume is exceeded, intrapericardial pressure remains relatively stable. Beyond this reserve, pericardial pressure rises until the limit of pericardial compliance is met. Once this inflection point is reached, pericardial pressure rises rapidly,

which clinically corresponds to tamponade as cardiac structures become compressed. In slowly accumulating effusions, the pericardium remodels and increases its mass and surface area, thereby increasing its overall compliance. This increases its pericardial reserve volume relative to rapidly growing effusions. (*From Imazio M, Adler Y. Management of pericardial effusion.* Eur Heart J. *2013;34[16]:1186–1197. Copyright © 2012 The Author. Adapted by permission of Oxford University Press.*)

Imazio M, Adler Y. Management of pericardial effusion. *Eur Heart J*. 2013;34(16):1186–1197.

LeWinter MM. Pericardiectomy to treat heart failure with preserved ejection fraction: unrestrained enthusiasm? *Circ Heart Fail*. 2017;10(4):e003971.

Russo AM, O'Connor WH, Waxman HL. Atypical presentations and echocardiographic findings in patients with cardiac tamponade occurring early and late after cardiac surgery. *Chest*. 1993;104:71–78.

A.5. What is regional cardiac tamponade?

In contrast to typical cardiac tamponade, where pericardial volume and pressure is evenly distributed around the heart, regional tamponade describes localized cardiac compression due to a loculated intrapericardial collection. This can occur as a result of hematoma formation in a postcardiotomy patient or subacutely from effusions developing around adhesions and septation of the pericardial space (**Figs. 12.2** and **12.3**).

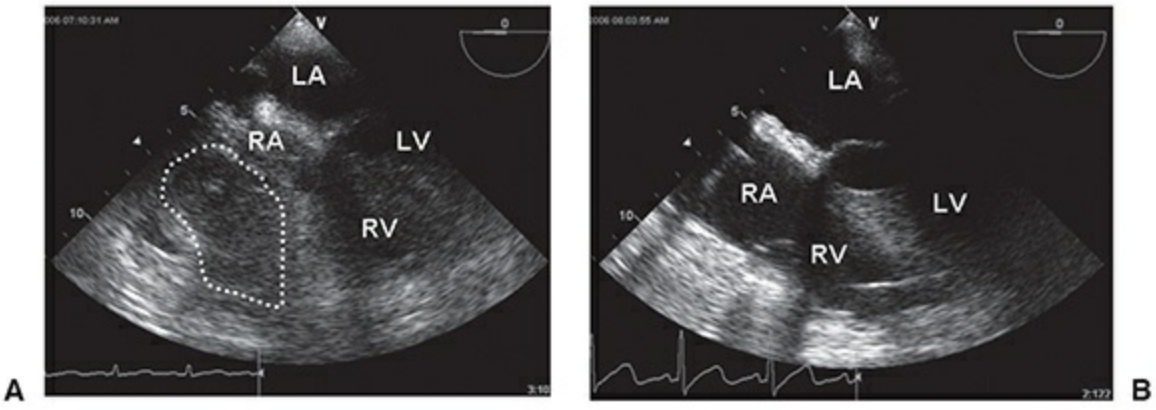

FIGURE 12.2. Acute regional pericardial effusion, right atrial compression. The heart is viewed in the midesophageal four-chamber view. In **A**, a loculated pericardial clot *(dotted line)* is seen around the right atrium (RA), almost obliterating its cavity and partially compressing the right ventricle (RV). **B** shows the same heart following decompression. LA, left atrium; LV, left ventricle.

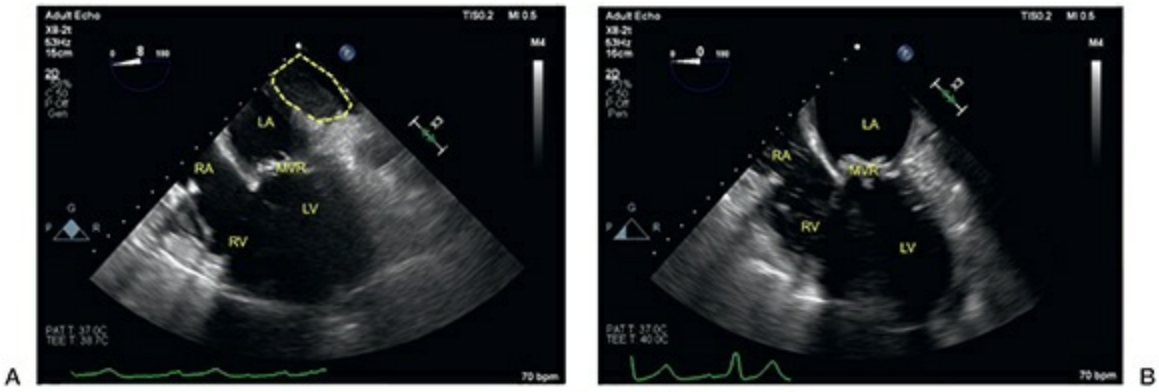

FIGURE 12.3. Acute regional pericardial effusion, left atrial compression. A and **B** show an example of regional pericardial effusion posterior to the heart, compressing the left atrium (LA). The heart is shown in a midesophageal four-chamber view, with **A** rotated leftward to center the view on the localized pericardial effusion *(dotted line)*. In both views, the left ventricle (LV) is partially obscured by shadowing artifact from a bioprosthetic mitral valve replacement (MVR). In **A**, the LA is partially compressed by the effusion. **B** shows the same heart following decompression, showing restoration of LA size. Agitated blood can be seen in the right atrium (RA) and right ventricle (RV) during intravenous fluid administration.

The low-pressure RA, right ventricle, and left atrium (LA) are most susceptible to postcardiotomy regional tamponade. Clot arising from right atrial bleeding typically localizes anteriorly and along the right lateral pericardial recess. Clot can also settle posteriorly behind the LA within the oblique sinus. In postcardiac surgery patients, the majority of effusions are anterior (especially after coronary artery bypass surgery), whereas posterolateral effusions are more commonly seen in valve replacement patients. Clinical signs and symptoms in regional tamponade can be subtle and atypical, corresponding to the discontinuous compression of cardiac chambers. Regional tamponade has been mistaken for congestive heart failure, acute ventricular dysfunction, septic shock, or pulmonary embolism.

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Ionescu A, Wilde P, Karsch KR. Localized pericardial tamponade: difficult echocardiographic diagnosis of a rare complication after cardiac surgery. *J Am Soc Echocardiogr*. 2001;14(12):1220–1223.

Pepi M, Muratori M, Barbier P, et al. Pericardial effusion after cardiac surgery: incidence, site, size, and haemodynamic consequences. *Br Heart J*. 1994;72:327–331.

Russo AM, O'Connor WH, Waxman HL. Atypical presentations and echocardiographic findings in patients with cardiac tamponade occurring early and late after cardiac surgery. *Chest*. 1993;104:71–78.

Saito Y, Donohue A, Attai S, et al. The syndrome of cardiac tamponade with "small" pericardial effusion. *Echocardiography*. 2008;25:321–327.

A.6. Describe the ventricular interaction in cardiac tamponade.

RV and LV function are interdependent due to their shared septum and pericardial constraint, sometimes termed *parallel ventricular interdependence*. Under normal conditions, there is sufficient compliance in the cardiac chambers and pericardium to accommodate the distension that results from diastolic filling of one ventricle with minimal change in the filling and function of the other. In tamponade, this shared septum becomes the figurative battleground for optimal diastolic filling in the face of increasing pericardial constraint. Pericardial fluid competes with the cardiac chambers for a portion of a relatively fixed pericardial volume. Furthermore, increasing pericardial pressure increases filling pressures of all the cardiac chambers. Under these conditions, instead of free wall distension, RV filling during inspiration shifts the interventricular septum toward the left ventricle; this accommodates the diastolic volume augmented by negative pressure inspiration but at the expense of LV cavity size and compliance (**Fig. 12.4**).

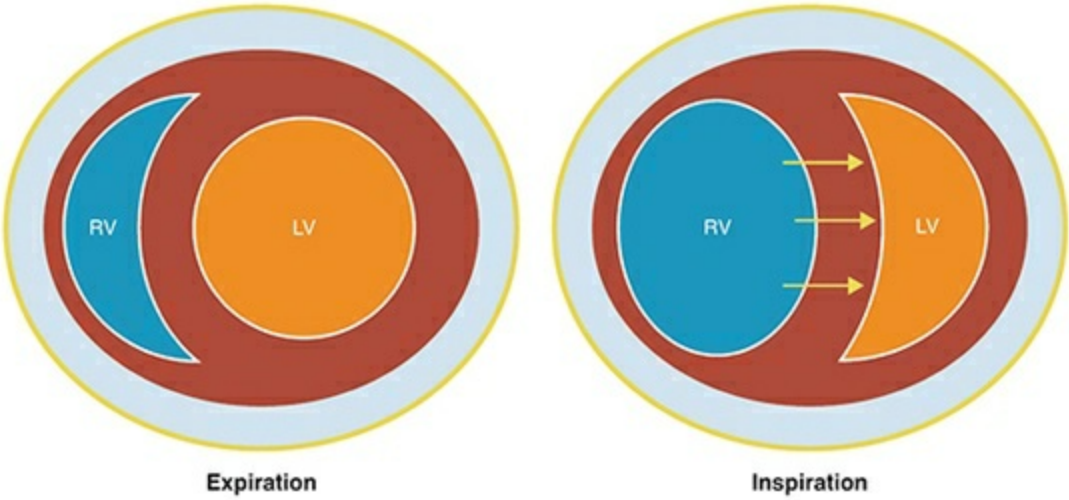

FIGURE 12.4. Parallel ventricular interdependence. In tamponade, diastolic ventricular filling is constrained by increased pericardial pressure. To accommodate increased right ventricular diastolic volume during inspiration, the interventricular septum shifts toward the left ventricle (LV). This alters LV compliance and mechanics, leading to a decrease in LV SV during inspiration. RV, right ventricle.

Series ventricular interdependence refers to the dependence of LV filling on RV output. Changes in RV SV will affect LV diastolic volume, albeit with a delay of several seconds as it crosses the pulmonary circulation to the left heart. This pulmonary transit time is highly variable, lasting 5 to 10 seconds in normal subjects at rest. In tamponade, the increasing dependence of RV filling on intrathoracic pressure will result in similar respirophasic changes in pulmonary venous return and LV SV.

Taken together, tamponade causes an exaggeration of both parallel and series ventricular interdependence: in order to fill the right ventricle, LV filling and SV becomes compromised, and LV filling is decreased if RV SV is impaired. This augmented variability in ventricular filling can be measured with Doppler echocardiography of the transmitral and transtricuspid inflow velocities, demonstrating an increase in one while simultaneously showing a decrease in the other.

Depending on the chronicity, size, and etiology of tamponade (i.e., fluid vs. clot, regional vs. global tamponade), exaggerated

atrioventricular interdependence can develop as they become subject to worsening pericardial constraint and pressure. Normally, venous return to the atria is maximal during ventricular systole and early diastole (corresponding to the *x*-descent, *v*-wave, and *y*-descent). With tamponade, the atria fill more readily when the ventricles are small (i.e., during ventricular systole) and passive atrioventricular filling becomes increasingly influenced by intrapericardial pressure as a Starling resistor. This leads to a deep *x*-descent as atrial filling occurs almost solely during ventricular systole and the loss of the early diastolic *y*-descent, both characteristic findings in cardiac tamponade (**Fig. 12.5**). Eventually, pericardial pressure increases sharply as pericardial compliance becomes exhausted. This pressure first compresses the thin-walled atria, followed by the low-pressure right ventricle, and finally the left ventricle.

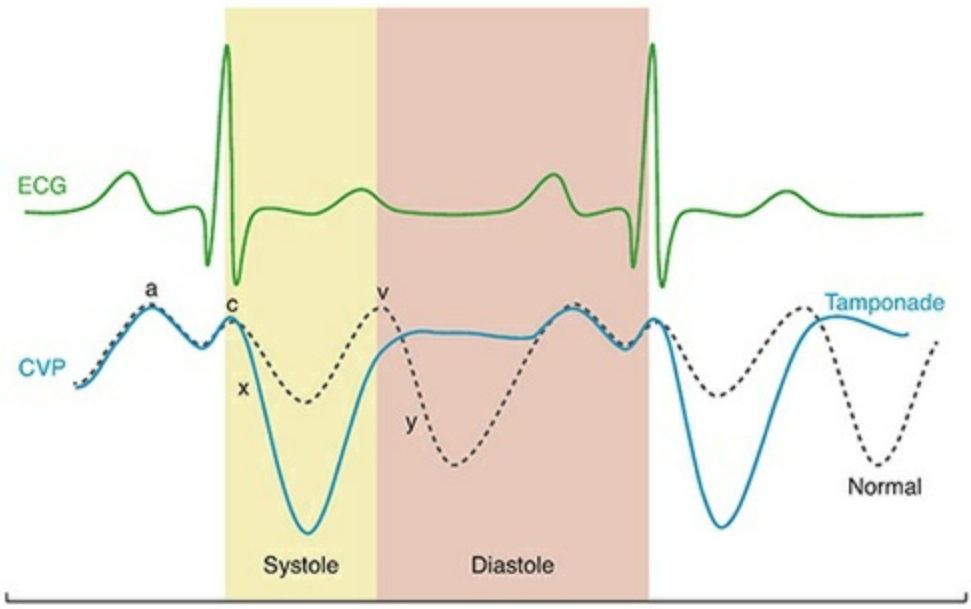

FIGURE 12.5. Central venous pressure (CVP) waveform abnormalities in tamponade. Compared with normal conditions, the CVP trace in tamponade is characterized by a deep x-descent, signaling increased atrial filling during ventricular systole (i.e., when the ventricles are small) and a loss of the y-descent. The y-descent normally coincides with opening of the tricuspid and mitral valves. During this period of diastole, the atrium acts as a conduit between the large central veins and the ventricle with venous return travelling down its hydrostatic pressure gradient to the ventricle. In tamponade, pericardial pressure acts as a Starling resistor to venous return on the atrium, dampening and eventually

eliminating the y-descent as a result. ECG, electrocardiogram.

Buckberg G, Hoffman JIE. Right ventricular architecture responsible for mechanical performance: unifying role of ventricular septum. *J Thorac Cardiovasc Surg*. 2014;148(6): 3166.e4–3171.e4.

Hamzaoui O, Monnet X, Teboul JL. Pulsus paradoxus. *Eur Respir J*. 2013;42:1696–1705.

Hoit BD. Pathophysiology of the pericardium. *Prog Cardiovasc Dis*. 2017;59(4):341–348.

Spodick DH. Pathophysiology of cardiac tamponade. *Chest*. 1998;113:1372–1378.

A.7. How is coronary blood flow affected in cardiac tamponade?

In the absence of coronary artery disease, coronary blood flow can be reduced in tamponade due to the direct effect of pericardial pressure on the epicardium and extracardiac epicardial vessels. Although it has been argued that this reduction is not sufficient to add an ischemic insult to the heart because of a proportionate decrease in ventricular preload, the compensatory sympathetic outflow leading to tachycardia and increased contractility shifts the balance toward increasing myocardial demand. More recent reports have demonstrated a marked decline in coronary blood flow due to increased coronary vascular resistance with increasing pericardial pressures, with direct coronary arterial flow studies demonstrating decreased diastolic coronary blood flow and increased retrograde flow in systole.

Abusaid GH, Khalife WI. Reduced coronary blood flow in cardiac tamponade: mystery solved. *J Invasive Cardiol*. 2012;24(12):E328–E329.

Reddy PS, Curtiss EL, O'Toole JD, et al. Cardiac tamponade: hemodynamic observations in man. *Circulation*. 1978;58:265–272.

Skalidis EI, Kochiadakis GE, Chrysostomakis SI, et al. Effect of pericardial pressure on human coronary circulation. *Chest*. 2000;117(3):910–912.

A.8. What is the Beck triad? Describe the typical signs

and symptoms of cardiac tamponade.

The eponymous Beck triad was described in 1935 by Claude Beck, the American cardiac surgeon. In fact, he reported two characteristic triads for acute and chronic cardiac compression.

In acute tamponade, the presence of the full classic triad of distended neck veins, diminished heart sounds, and hypotension is quite uncommon occurring in only 10% to 40% of patients. The individual components are seen with varying frequency. Hypotension is present in 14% to 35% of patients, diminished heart sounds in 24% to 34%, and elevated jugular venous pressure in 53% to 88%. The most common presenting symptom in patients with symptomatic pericardial effusions requiring drainage is dyspnea (87% to 88% sensitive), and the most sensitive and specific physical finding is pulsus paradoxus (98% sensitive, 83% specific with a >12 mmHg change in pressure). Other signs and symptoms are listed in **Table 12.4**. It should be noted that patients with loculated effusions or regional tamponade may present with very few or with an atypical constellation of these signs and symptoms.

TABLE 12.4 Signs and Symptoms of Cardiac Tamponade

Symptoms	Dyspnea
	Fatigue
	Weakness
	Palpitations
	Orthopnea
Signs	Tachycardia
	Tachypnea
	Hypotension
	Diminished heart sounds
	Jugular venous distension
	Narrow pulse pressure
	Pulsus paradoxus
	“Unable to lie flat”

The second of the Beck triads, that of chronic cardiac

compression, is characterized by elevated jugular venous pressures, ascites, and diminished heart sounds. Beck described this triad most commonly in patients with tuberculous, idiopathic pericarditis, or constrictive pericarditis without effusion. The shift in symptomatology from hypotension to ascites reflects the longer-term restriction of venous return to the RA and right ventricle, leading to chronic passive hepatic congestion.

Hypertensive tamponade is an unusual variant thought to be a result of an exuberant sympathetic response to impaired cardiac filling in patients who develop tamponade over days to weeks. These patients challenge the classic aphorism of tamponade being a clinical diagnosis, with average systolic pressures of between 127 and 144 mmHg at presentation from six retrospective reviews encompassing 239 patients. These patients all had features of supportive echocardiographic criteria for tamponade, including right atrial and RV collapse and exaggerated respiratory variation of RV and LV inflow velocities. Draining the effusion leads to the normalization of blood pressure.

Argulian E, Herzog E, Halpern DG, et al. Paradoxical hypertension with cardiac tamponade. *Am J Cardiol*. 2012;110(7):1066–1069.

Argulian E, Messerli F. Misconceptions and facts about pericardial effusion and tamponade. *Am J Med*. 2013;126(10):858–861.

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Jacob S, Sebastian JC, Cherian PK, et al. Pericardial effusion impending tamponade: a look beyond Beck's triad. *Am J Emerg Med*. 2009;27(2):216–219.

Roy CL, Minor MA, Brookhart MA, et al. Does this patient with a pericardial effusion have cardiac tamponade? *JAMA*. 2007;297(16):1810–1818.

A.9. Define pulsus paradoxus and describe its

pathophysiology.

Pulsus paradoxus describes an abnormal, exaggerated fall in arterial pressure during inspiration, conventionally defined as a fall in systolic pressure greater than 10 mmHg. Pulsus paradoxus was first described in 1873 by Adolf Kussmaul, the German pathologist who saw a “paradox” in three patients with constrictive pericarditis; their palpated pulse would disappear during inspiration and reappear during expiration, despite the uninterrupted presence of a precordial cardiac impulse.

In healthy individuals, quiet negative pressure inspiration decreases intrathoracic pressure by approximately 5 to 10 mmHg, which is transmitted to the atria and ventricles. This augments venous return to the right heart, leading to maximal RV SV during inspiration. LV SV respiratory variation also occurs, influenced by both the lungs and the right ventricle. During inspiration, lung expansion exerts radial traction on the pulmonary vasculature and increases their capacitance. This decreases LV filling and SV, with the reverse occurring in expiration. Changes in RV SV affects LV filling with a delay of several seconds as it crosses the pulmonary circulation to the left heart. If both ventricles are “out of phase” with respect to pulmonary transit time, the effect of inspiration-augmented RV SV on LV filling is increased, increasing LV SV and systemic arterial pressure respirophasic variation. The opposite can occur if the two ventricles are “in phase.” This accounts for the respiratory variation in arterial pressure in healthy individuals with fluctuations in systolic arterial pressure ≤10 mmHg. This becomes increasingly notable when both ventricles are preload sensitive (i.e., on the steep part of the Starling curve when the left ventricle is constrained and made small by tamponade).

In tamponade, elevated pericardial pressure is transmitted to all cardiac chambers, increasing their filling pressures relative to extrapericardial structures including the majority of the venae

cava. Furthermore, increasing pericardial constraint on the cardiac chambers exaggerates parallel and series ventricular interdependence. Both factors lead to an augmentation of the respirophasic rise and fall in LV SV.

Pulsus paradoxus is not a particularly sensitive or specific sign of tamponade. It can also be seen in patients with respiratory distress due to increased negative intrathoracic pressures during inspiration, constrictive pericarditis, and RV failure. It may be absent, even in tamponade, in patients who cannot generate negative intrathoracic pressures (e.g., neuromuscular diseases, chest wall trauma) or in patients with aortic regurgitation or an atrial septal defect. Patients who are ventilated with positive pressure may display a "reversed" pulsus paradoxus, that is, an exaggerated increase in systolic arterial pressure with inspiration due to increased RV afterload causing a leftward septal shift during positive inspiratory pressure.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia: For Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:883–973.

Swami A, Spodick DH. Pulsus paradoxus in cardiac tamponade: a pathophysiologic continuum. *Clin Cardiol*. 2003;26(5):215–217.

Wong FW. Pulsus paradoxus in ventilated and non-ventilated patients. *Dynamics*. 2007;18(3):16–18.

A.10. What is Kussmaul sign? Is this finding consistent with tamponade physiology?

Kussmaul sign describes an abnormal rise or absence of fall in jugular venous pressure with negative pressure inspiration. It is typically quantified as a <5 mmHg fall in inspiratory right atrial pressure. It is classically associated with constrictive pericarditis, but it can be seen in conditions associated with restricted right-sided filling including tricuspid stenosis and RV dysfunction.

Some controversy exists as to whether Kussmaul sign can be present in tamponade. If defined solely as a pathologic *rise* in jugular venous pressure with negative pressure inspiration, it is said that Kussmaul sign cannot be present in tamponade unless there is concurrent constriction from abnormal pericardium, pericardial clot, or adhesions. The difference between tamponade, assuming free-flowing intrapericardial fluid, and constrictive physiology is the influence of intrathoracic pressure on the intracardiac filling pressures. In constrictive pericarditis, changes in intrathoracic pressure are not well transmitted through the abnormally thickened pericardium. This effectively disassociates the cardiac chamber pressures from intrathoracic pressure changes. The RA and RV, invested within a constrictive pericardium, have abnormally high filling pressures with little to no respirophasic variation. During the rapid filling phase of diastole, right atrial and RV pressures equalize rapidly as they encounter pericardial constraint, and venous return from the inferior vena cava (IVC) and superior vena cava (SVC) compete for entry into the high-pressure RA. Because IVC inflow is favored over that from the SVC due to augmentation by transdiaphragmatic pressure, jugular venous pressure rises due to constricted SVC inflow. This causes the characteristic, paradoxical rise in jugular venous pressure in Kussmaul sign.

In tamponade, respiratory changes in intrathoracic pressure are exerted on intrapericardial fluid. right atrial and RV pressures will fall together with intrathoracic pressure during spontaneous inspiration despite the presence of tamponade, augmenting the gradient for venous return in both the SVC and IVC. This would result in a fall in jugular venous pressure with inspiration.

Johnson SK, Naidu RK, Ostopowicz RC, et al. Adolf Kussmaul: distinguished clinician and medical pioneer. *Clin Med Res*. 2009;7(3):107–112.

Talreja DR, Nishimura RA, Oh JK, et al. Constrictive pericarditis in the modern era: novel criteria for diagnosis in the cardiac catheterization laboratory. *J Am Coll Cardiol*. 2008;51(3):315–319.

A.11. Which medical conditions mimic cardiac tamponade?

Cardiac tamponade is the pathologic increase in intrapericardial volume and pressure that impairs diastolic filling and CO. It is often classified as a form of "obstructive shock," which is clinically characterized by hemodynamic compromise with signs of elevated filling pressures and other evidence of great vessel obstruction or cardiac compression. Other causes of obstructive shock include pulmonary embolism, tension pneumothorax, dynamic ventricular inflow or outflow obstruction (e.g., from asymmetrical septal hypertrophy, hyperdynamic mid-cavitary ventricular obstruction, or cardiac myxoma), and effusive constrictive pericarditis. An unusual cause of tamponade is a large pleural effusion, which can cause clinical and echocardiographic findings of tamponade in the presence of a small "low-pressure" pericardial effusion. Experimental data in canines have demonstrated increasing intrapleural fluid and pleural pressure is transmitted to the pericardial sac, which then compresses the heart. In this situation, only thoracentesis will relieve tamponade.

Cardiogenic shock, and RV failure in particular, can also have similar signs and symptoms to tamponade, including jugular venous distension, pulsus paradoxus, dyspnea, and hypotension. The presence of a fever, especially in inflammatory pericarditis and tamponade, can confound the diagnosis. However, some forms of sepsis are hyperdynamic, vasodilatory shock, whereas tamponade is notable for low SV and vasoconstriction, which is an important discriminator.

Saito Y, Donohue A, Attai S, et al. The syndrome of cardiac tamponade with "small" pericardial effusion. *Echocardiography*. 2008;25:321–327.

Traylor JJ, Chan K, Wong I, et al. Large pleural effusions producing signs of cardiac tamponade resolved by thoracentesis. *Am J Cardiol*. 2002;89(1):106–108.

Vaska K, Wann LS, Sagar K, et al. Pleural effusion as a cause of right ventricular diastolic collapse. *Circulation*. 1992;86(2):609–617.

B. Preoperative Evaluation and Preparation

B.1. Interpret and explain the pathophysiologic basis for this patient's hemodynamic findings.

This patient is normotensive but tachycardic, which together with her physical findings suggests a compensated shocked state. This is confirmed by her low CO and high calculated systemic vascular resistance (SVR) (**Table 12.5**). The differential diagnoses for low SV are hypovolemia, impaired LV and/or RV contractility, and obstruction of the heart or great vessels by pericardial fluid or embolism. To some degree, PAC data can assist in narrowing the diagnosis.

TABLE 12.5 Measured and Calculated Hemodynamic Parameters

Measured Parameters	Patient Data	
Heart rate (HR, bpm)	120	
Systemic blood pressure (BP, mmHg)	115/66	
Pulmonary artery pressure (mmHg)	55/21	
Central venous pressure (CVP, mmHg)	23	
Pulmonary artery occlusion pressure (PAOP, mmHg)	14	
CO (L/min)	2.7	
Calculated Parameters	**Patient Data**	**Equation**
Stroke volume (SV, mL)	22.5	SV = CO / HR
Mean arterial pressure (MAP, mmHg)	82.3	MAP = dBP + 1/3 PP
Systemic vascular resistance (SVR, dynes/sec/cm^5)	1,758	SVR = [(MAP − CVP) / CO] × 80
Pulmonary vascular resistance (PVR, dynes/sec/cm^5)	543	PVR = [(mPAP − PAOP) / CO] × 80

CO, cardiac output; dBP, diastolic systemic blood pressure; mPAP, mean pulmonary arterial pressure;

PP, systemic pulse pressure.

The patient's CVP is markedly elevated, which can be a result of potential intracardiac or extracardiac pathology. In the absence of significant tricuspid valve stenosis or regurgitation, intracardiac causes include hypervolemia (unlikely, given this patient's clinical presentation) and RV dysfunction from ischemia or outflow obstruction. This dysfunction increases RV end-diastolic pressure (EDP) and leads to a correspond rise in the venous filling pressures. Extracardiac causes of an elevated CVP include extrinsic cardiac compression by pericardial or intrapleural conditions, including tamponade and tension pneumothorax. It is important to note that in cases of extrinsic compression, the CVP is measuring the intracardiac pressure *and* the pressure applied to the RA (e.g., a hypovolemic patient with a transmural right atrial pressure of 3 mmHg can have a measured CVP of 23 mmHg once 20 mmHg of pressure is applied to the RA, creating a false impression of the patient's true filling pressures).

The patient's PA pressure is elevated. With a PAOP <15 mmHg and elevated diastolic pulmonary gradient, this points to a precapillary cause and is confirmed by the elevated calculated pulmonary vascular resistance (PVR) (**Table 12.5**). In this patient, the most likely causes are long-standing pulmonary vascular remodeling from chronic mitral disease and more acutely from pulmonary atelectasis from this patient's dyspnea and altered respiratory mechanics.

The PAOP is a surrogate measure for left atrial pressure (LAP) and can inform about LV filling as well as LV and mitral valve function. This patient's PAOP is normal and makes prosthetic mitral valve dysfunction from obstruction or regurgitation unlikely. As with CVP, caveats apply in the interpretation of PAOP and LAP with regard to LV volume

status. Furthermore, any alteration in the thick-walled LV's compliance will affect the degree to which LAP represents LV preload, which is ultimately represented by LV end-diastolic volume (EDV). For example, acute ischemia will decrease LV compliance, which would result in a higher EDV for the same EDP.

Taken together, the patient's clinical and hemodynamic findings suggest a low CO state due to either tamponade and/or RV dysfunction from ischemia or from increased RV afterload due to embolism. Concurrent LV dysfunction cannot be excluded based on PAC data alone. Echocardiography can assist with further refinement of the differential diagnoses by defining RV and LV function, relative atrial pressures and the presence of pericardial fluid.

Note that the absence of "equalization of pressures" in this patient—that is, the fact that CVP, PA diastolic, and PAOP are not within 5 mmHg of each other—does not exclude the diagnosis of tamponade. Equalization of pressures presumes that intrapericardial pressure is equally distributed through the pericardial sac and is usually a late finding when compensatory mechanisms are almost exhausted.

Kern MJ, Lim MJ, Goldstein JA. *Hemodynamic Rounds: Interpretation of Cardiac Physiology From Pressure Waveform Analysis*. 3rd ed. Hoboken, NJ: Wiley-Blackwell; 2009:269.

Magder S. Invasive hemodynamic monitoring. *Crit Care Clin*. 2015;31(1):67–87.

Opitz CF, Hoeper MM, Gibbs SR, et al. Pre-capillary, combined, and post-capillary pulmonary hypertension: a pathophysiological continuum. *J Am Coll Cardiol*. 2016;68(4):368–378.

B.2. How would you optimize this patient's cardiovascular status prior to definitive diagnosis and treatment?

The key resuscitation goals prior to definitive management are

a. To optimize CO (which is determined by HR and SV), and
b. To maintain adequate perfusion pressure to critical organs (i.e., heart, brain, kidneys).

This patient requires SV correction to increase her CO; however, without a clear etiology for her low CO state, this should be approached cautiously. This patient's high CVP is due to either tamponade or RV dysfunction; the effect of aggressive volume administration can either improve SV or precipitate RV failure because both conditions exist on different points of the Frank-Starling curve (**Fig. 12.6**). In the absence of further diagnostic information, a prudent approach would be to administer a small fluid challenge and assess for volume responsiveness in the form of a blood pressure and/or CO increase.

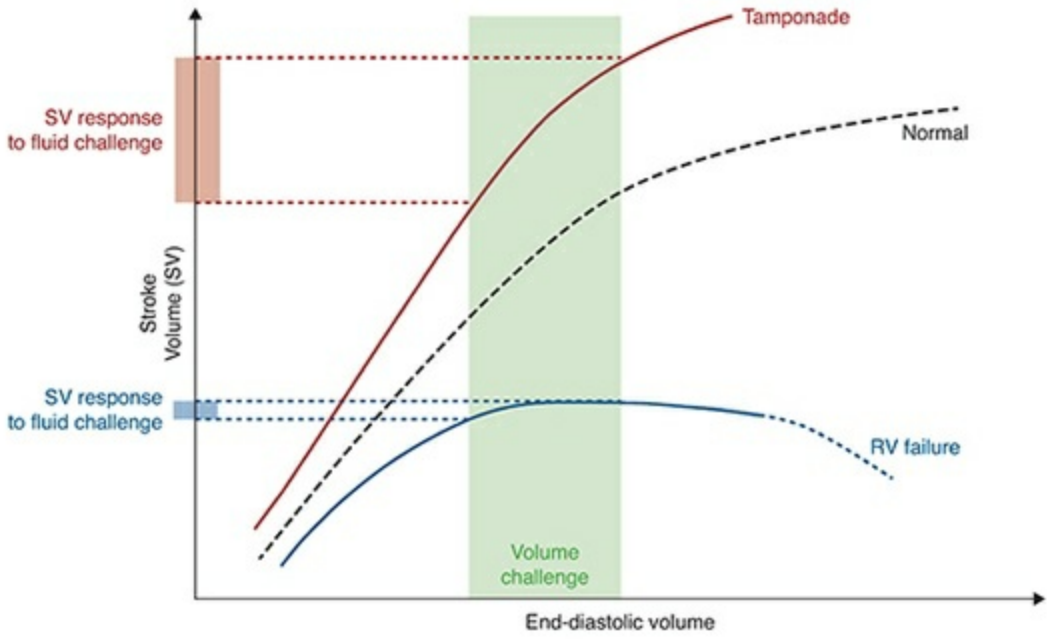

FIGURE 12.6. Predicted response to volume challenge in tamponade versus right ventricular (RV) dysfunction. This figure shows two different Frank-Starling curves referenced to a hypothetical normal curve. In tamponade, the right ventricle is underfilled and hyperdynamic. This is in contrast to the curve in RV dysfunction, where the decreased slope and early plateau reflects its depressed inotropic state. Applying the same volume to these two models leads to a large SV response in tamponade, but a minimal change in RV dysfunction, and, in this example, pushes the right ventricle into failure.

Because RV and possibly LV dysfunction are important differential diagnoses, a positive inotrope should be initiated to increase contractility and SV, especially if the patient does not exhibit a response to fluid challenge. This effectively increases the slope of the ventricle's functional Frank-Starling curve (**Fig. 12.6**). The choice of inotrope should take into account this patient's clinical trajectory as well as the pharmacologic profile for the inotropes being considered. Epinephrine, dopamine, and dobutamine are highly titratable with shorter half-lives than milrinone. Dopamine, however, is associated with severe arrhythmias and increased mortality when used in cardiogenic shock at higher doses. Dobutamine and milrinone, as inodilators, cause decreases in SVR and PVR that can improve myocardial performance in a failing ventricle but can also compromise organ perfusion pressures. In this patient, a low-dose infusion of epinephrine (0.02 to 0.05 μg/kg/min) may confer the greatest benefit in inotropy and titratability while minimizing unexpected afterload reduction and dose-related tachyarrhythmia from dobutamine. If severe RV dysfunction remains a concern, targeted pulmonary vasodilation with inhaled nitric oxide or iloprost can further optimize RV SV while limiting alterations in systemic blood pressure.

Together with SV optimization, a systemic mean arterial pressure (MAP) of at least 60 to 65 mmHg should be targeted to maintain adequate cerebral and renal perfusion. Myocardial perfusion in this patient is compromised due to depressed coronary blood flow, preexisting tachycardia, and potential tamponade. Any attempts, however, to lower HR in an effort to reduce myocardial oxygen demand without correcting SV will risk a further decline in CO that will correspondingly lower all organ blood flow, including the heart.

Carmona P, Mateo E, Casanovas I, et al. Management of cardiac tamponade

after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2012;26(2):302–311.

De Backer D, Biston P, Devriendt J, et al. Comparison of dopamine and norepinephrine in the treatment of shock. *New Engl J Med*. 2010;362(9):779–789.

Kline JA, Hall CL, Jones AE, et al. Randomized trial of inhaled nitric oxide to treat acute pulmonary embolism: the iNOPE trial. *Am Heart J*. 2017;186:100–110.

B.3. What are the radiographic findings in tamponade?

On standard posteroanterior chest radiography, cardiomegaly is a common finding in patients with pericardial effusions, especially those measuring 200 mL or more; the overall sensitivity is 89%. Evolving cardiomegaly in absence of pulmonary vascular congestion supports the diagnosis of effusion over cardiomyopathy and associated congestive heart failure. A pathognomic finding on an erect chest radiograph for massive effusions, often >1,000 mL, is the “water bottle” heart. This reflects the dependent distribution of fluid within the pericardial space when upright, tapering up toward the pericardial reflection at the level of the proximal great vessels. Another finding associated with pericardial effusions is the “Oreo cookie” or “fat pad” sign on lateral chest radiography. This describes a vertical radiopaque line sandwiched by two vertical radiolucent stripes located between the sternum and RV border. The opaque line represents pericardial fluid separating epicardial fat from pericardial fat within the pericardial space. In the case of tension pneumopericardium, the air surrounding the heart creates a sharply delineated air pericardiogram.

Cardiac computerized tomography can define not just the presence of a pericardial effusion but also cardiac anatomy and pericardial pathology. However, its utility in a patient with unstable hemodynamics is limited and unfeasible. Intravenous contrast enhances pericardial inflammation and hemopericardium including active extravasation. Attenuation

values of pericardial fluid can aid in characterizing the type of effusion. Transudates have lower radiodensity than exudates, which in turn are less dense than blood or clots. Other computerized tomography findings consistent with tamponade include compression of cardiac chambers, distension of the venae cavae, and reflux of contrast into the IVC or azygos vein suggesting impaired right-sided filling.

Two-dimensional and Doppler echocardiography are considered first-line imaging for tamponade. Advantages include a high sensitivity for detecting pericardial fluid and its effects on the cardiac structures, the ability to assess cardiac function and filling patterns, portability, and the lack of ionizing radiation. However, the utility of transthoracic echocardiography is limited in postcardiac surgery patients due to increased artifact from sternal wires, chest tubes, and surgical dressings.

Bogaert J, Francone M. Pericardial disease: value of CT and MR imaging. *Radiology*. 2013;267(2):340–356.

Kearns MJ, Walley KR. Tamponade: hemodynamic and echocardiographic diagnosis. *Chest*. 2018;153(5):1266–1275.

Restrepo CS, Lemos DF, Lemos JA, et al. Imaging findings in cardiac tamponade with emphasis on CT. *Radiographics*. 2007;27(6):1595–1610.

B.4. A limited bedside transthoracic echocardiogram is performed, demonstrating a layer of clotted blood anterior to the right atrium (RA) and ventricle. What echocardiographic findings support the diagnosis of tamponade?

A key concept when interpreting imaging in a patient with suspected tamponade is that the size of a pericardial effusion does not correspond to severity of clinical symptoms; a small acute pericardial effusion can cause life-threatening tamponade but remain occult on imaging. For example, the presence of mediastinal clot is an anatomical finding that may simply reflect

a postsurgical state. Echocardiographic findings that correspond to the pathophysiology of tamponade in this patient include the following:

a. *Increased intrapericardial pressures causing diastolic collapse of the atria and/or right ventricle*. The RA is most sensitive to compression just after the atrial kick (i.e., P wave on electrocardiogram [ECG]), when atrial pressure is lowest (**Fig. 12.7**). The period of collapse extends further through the cardiac cycle with increasing pericardial pressures, so that right atrial collapse exceeding one-third of the cardiac cycle is nearly 100% sensitive and specific for tamponade. The right ventricle, with a higher chamber pressure than the atria, is less susceptible to compression, but the finding of RV diastolic collapse remains a highly specific sign of tamponade. The right ventricle is most sensitive to compression in early diastole (i.e., after T wave on ECG), when its chamber pressure is lowest.

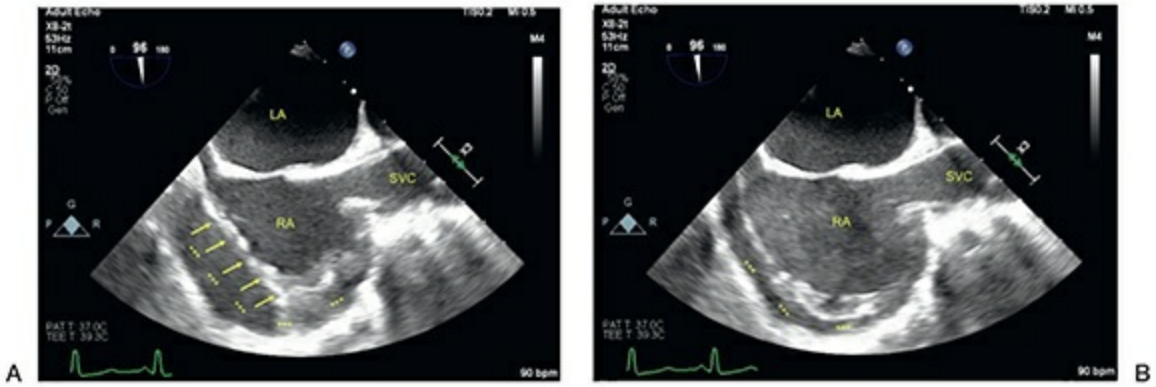

FIGURE 12.7. Right atrium (RA) collapse from early tamponade. The figures show the RA in the midesophageal bicaval view in the same patient with an acute pericardial effusion (labeled with *asterisks*). In **A**, the RA is compressed by the effusion (*arrows*) in early ventricular systole as denoted by the ECG, corresponding approximately to the x-descent on a CVP waveform when the RA is most susceptible to compression. **B** shows the RA in late ventricular systole, corresponding to a point just before the V-wave, when the atrium is at its fullest just before tricuspid valve opening. LA, left atrium; SVC, superior vena cava.

b. *Exaggerated ventricular interdependence*. Doppler

interrogation of mitral and tricuspid inflow velocities will demonstrate increased RV filling and decreased LV filling during spontaneous inspiration. This increased RV filling will cause a ventricular septal “bounce” toward the LV as RV free wall expansion meets pericardial constraint. Pulsed-wave Doppler of tricuspid inflow will show an increase in peak E-wave velocity by 40% compared with expiration, whereas mitral inflow will show a 25% inspiratory decrease in peak E-wave velocity (**Fig. 12.8**). Venous inflow to the RA can also be interrogated via pulsed-wave Doppler of the hepatic vein, which will initially show systolic blunting of systolic velocities, with increased respiratory variation in diastolic velocity. In critical tamponade, diastolic velocities may be near-absent except during spontaneous inspiration or mechanical expiration.

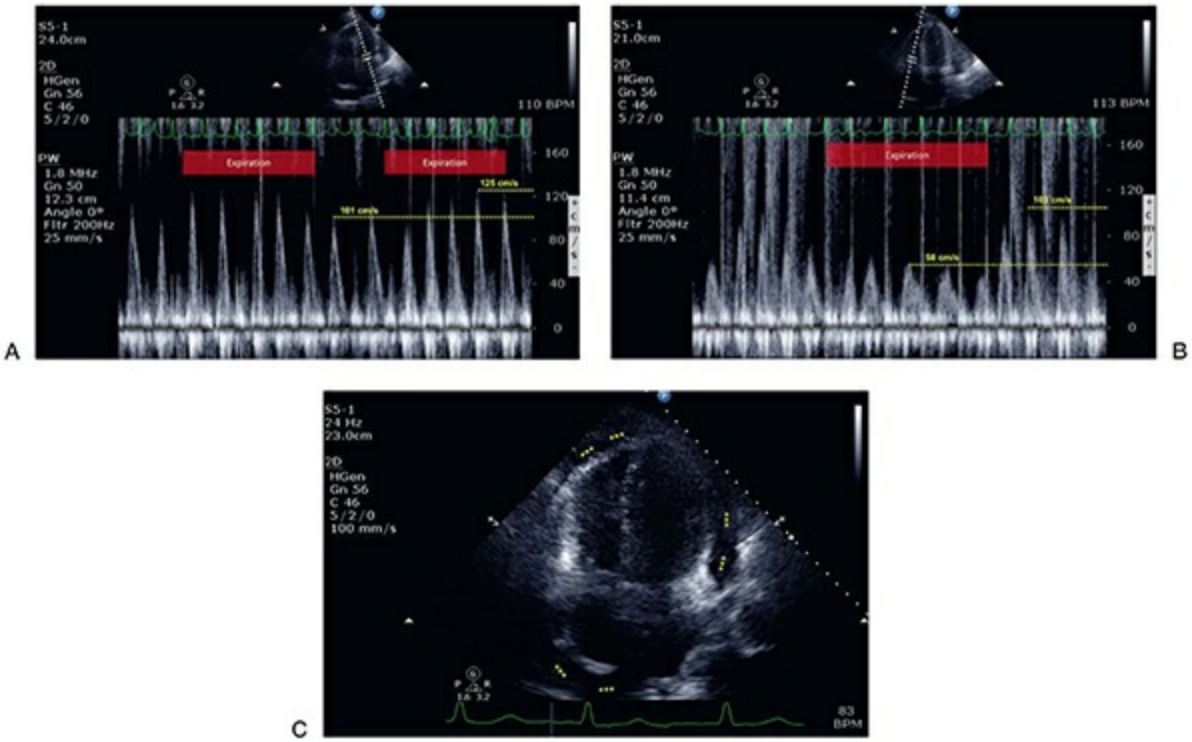

FIGURE 12.8. Exaggerated ventricular interdependence. A and **B** show pulsed-wave Doppler interrogation of transmitral and transtricuspid velocities obtained during a transthoracic echocardiographic study in a patient with suspected tamponade. The patient is breathing spontaneously;

although there is no respirogram on the original images, the patient's marked sinus arrhythmia clearly defines inspiratory and expiratory phases. During negative pressure inspiration, **A** demonstrates a 25% decrease in transmitral E-wave velocities, whereas **B** shows a >45% increase in transtricuspid E-wave velocities. This exaggerated, reciprocal change in ventricular filling is a hallmark of cardiac tamponade and constrictive physiology. **C** shows an apical four-chamber view of this patient's heart, demonstrating a large effusion outside the right and left ventricles as well as a deep pool surrounding the RA (*labeled by asterisks*). Although not evident on this still image, interventricular septal "bounce" was prominent.

c. *Decreased volume within cardiac chambers*. This is suggested by decreasedLV cavity size and exaggerated interatrial septal motion (in the presence of a high measured CVP) reflecting low transmural LA and RA pressures and the abnormal ventricular filling patterns due to increased interdependence. The IVC may be distended due to obstructed venous return.

Carmona P, Mateo E, Casanovas I, et al. Management of cardiac tamponade after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2012;26(2):302–311.

Gillam LD, Guyer DE, Gibson TC, et al. Hydrodynamic compression of the right atrium: a new echocardiographic sign of cardiac tamponade. *Circulation*. 1983;68:294–301.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia: For Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:505–634.

B.5. What additional information should be obtained from a limited echocardiographic study?

Once the diagnosis of tamponade is established, a focused assessment of concurrent conditions by an appropriately trained echocardiographer is prudent as long as it does not delay clinical stabilization and definitive management. The right and left ventricles should be grossly assessed for size and systolic function. A distended right ventricle with or without worsening tricuspid regurgitation raises concern for outflow obstruction or systolic dysfunction. Regional wall motion abnormalities may be apparent if there is active myocardial ischemia. The mitral

valve prosthesis should be evaluated for malfunction using color flow Doppler, which may reveal stenosis or intravalvular regurgitation from leaflet dysfunction or paravalvular leak from suture line dehiscence.

Carmona P, Mateo E, Casanovas I, et al. Management of cardiac tamponade after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2012;26(2):302–311.

Labovitz AJ, Noble VE, Bierig M, et al. Focused cardiac ultrasound in the emergent setting: a consensus statement of the American Society of Echocardiography and American College of Emergency Physicians. *J Am Soc Echocardiogr*. 2010;23(12):1225–1230.

B.6. Describe the procedures for treating cardiac tamponade. What are the clinical indications for each approach?

Pericardial decompression can be performed percutaneously or surgically. Percutaneous echocardiographically guided catheter decompression is the treatment of choice in patients with nonloculated, free-flowing pericardial fluid. Subxiphoid, parasternal, and apical approaches each have advantages and disadvantages (**Table 12.6**). Existing cardiology literature and guidelines advocate taking the approach with the maximal effusion depth on ultrasound to minimize the risk of cardiac puncture. Percutaneous options are unlikely to be appropriate for this patient because there is a high likelihood of compression from clotted blood on imaging.

TABLE 12.6 Approaches to Pericardiocentesis

Approach	Insertion Site	Approach-Specific Complications
Subxiphoid	Between xiphoid process and left costal margin	Peritoneal injury
Apical	Near apex beat, at fifth to seventh intercostal space in the anterior axillary line	Left pneumothorax
Parasternal	Fifth intercostal space, left sternal	Pneumothorax

margin	
	Internal mammary artery injury

Adapted from De Carlini CC, Maggiolini S. Pericardiocentesis in cardiac tamponade: indications and practical aspects. *e-J Cardiol Pract*. 2017;15(19). Available at https://www.escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-15/Pericardiocentesis-in-cardiac-tamponade-indications-and-practical-aspects.

In patients with an intact pericardium and free-flowing pericardial fluid, surgical decompression can be performed in conjunction with a limited pericardiectomy, opening a drainage "window" to the pleural space to prevent recurrence. Minor pericardial adhesions can be manually divided and loculated effusions drained. Subxiphoid, transthoracic via anterior mini-thoracotomy, and thoracoscopic approaches have all been described. It should be noted that the subxiphoid approach does not technically create a "pericardial window"; rather, it provokes inflammatory fusion of the pericardium to the epicardium, thereby obliterating the potential space for recurrence. In unstable patients, only subxiphoid and anterior thoracotomy approaches are suitable. An important advantage of the subxiphoid approach is that it can be performed under local anesthesia and conscious sedation in anatomically suitable patients (e.g., nonobese body habitus, absence of ascites) who are otherwise too unstable for induction of general anesthesia. Local anesthesia for the anterior thoracotomy approach has also been described but may be poorly tolerated because it requires dissection through the pectoralis muscles and intercostal spaces. In postcardiac surgery patients, a limited sternal reopening under local anesthesia and conscious sedation may be tolerated and can confer some physiologic benefit prior to definitive exploration. However, most patients within this population are typically not candidates for limited rescue techniques and will require full sternotomy to evacuate clotted blood, drain residual fluid, and identify the source of ongoing bleeding.

Adler Y, Charron P, Imazio M, et al. 2015 ESC guidelines for the diagnosis and management of pericardial diseases: the Task Force for the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology (ESC) endorsed by: the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J*. 2015;36(42):2921–2964.

De Carlini CC, Maggiolini S. Pericardiocentesis in cardiac tamponade: indications and practical aspects. *e-J Cardiol Pract*. 2017;15(19).

Langdon SE, Seery K, Kulik A. Contemporary outcomes after pericardial window surgery: impact of operative technique. *J Cardiothorac Surg*. 2016;11(1):73.

Sugimoto JT, Little AG, Ferguson MK, et al. Pericardial window: mechanisms of efficacy. *Ann Thorac Surg*. 1990;50(3):442–445.

B.7. Having made the diagnosis of tamponade, what additional investigations are required prior to surgery?

This patient has cardiac tamponade likely arising from postcardiac surgery bleeding. Although her vital signs are adequate, she is at risk for decompensation and should undergo a focused, expedited workup so that surgical treatment is not unnecessarily delayed. Point of care blood tests such as arterial blood gases (ABGs) and rotational thromboelastometry can provide rapid, relevant information to guide preoperative preparation. An ABG may reveal a low pH and/or elevated lactate from hypoperfusion, gas exchange abnormalities, electrolyte derangements, and anemia. Rotational thromboelastometry provides real-time information on coagulation factor activity and clot kinetics. Formal laboratory investigations should include a complete blood count, coagulation profile, and type and screen. The presence of anemia, thrombocytopenia, or coagulation abnormalities guides the type and amount of blood products required and should be immediately available in the operating room prior to surgery. A baseline ECG can provide additional information if the suspicion for ischemia is high and may provide supportive

information such as low voltage QRS complexes, electrical alternans, and RV strain. Although radiographic findings were discussed earlier, a chest x-ray or CT is unlikely to add diagnostic value in this patient and should not delay surgery unless there is a strong clinical indication.

Carmona P, Mateo E, Casanovas I, et al. Management of cardiac tamponade after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2012;26(2):302–311.

B.8. Explain the technical and physiologic principles behind rotational thromboelastometry.

Rotational thromboelastometry measures the viscoelastic properties of blood samples. Citrated blood is introduced into a cuvette together with an activator, which is heated to 30°C to 40°C. A pin with a rotating axis is suspended into the cuvette during the test, and as the blood becomes more viscous, pin rotation is impeded. This impedance is detected by an optical detector system. The time course of changing viscoelasticity is plotted graphically and numerically. The parameters defining a typical a rotational thromboelastometric assay correlate to the events of coagulation as described by the cell-based model of hemostasis and are summarized in **Table 12.7**.

TABLE 12.7 Rotational Thromboelastometry Numerical Parameters

Parameter	Definition	Physiologic Correlate
Clotting time (CT)	Time for trace to reach 2 mm amplitude	Clot initiation phase
Clot formation time (CFT)	Time for trace to increase from 2 to 20 mm	Clot amplification and propagation phase
Amplitude 10 min (A10)	Trace amplitude 10 min after CT	Fibrin-platelet interaction via glycoprotein IIb/IIIA receptors
Maximum clot firmness (MCF)	Maximum amplitude (MA) of the trace, when test is run for 20 min	
Lysis Index 30 (LI30)	Percentage reduction in amplitude 30 min after MA is reached	Plasmin, thrombin-activatable fibrinolysis inhibitor (TAFI) and plasminogen activator inhibitor (PAI) activity

ROTEM *delta* and ROTEM *sigma* (Instrumentation Laboratories, Bedford MA, USA) are two commercially-available devices that can perform up to four tests concurrently. ROTEM *delta* requires manual pipetting of the blood samples and test reagents, whereas ROTEM *sigma* is a fully-automated system that uses a cartridge with integrated freeze-dried reagents. Depending on the activator reagents used, assays targeting specific components of the coagulation cascade can be performed. The INTEM reagent contains ellagic acid and phospholipid, which produces contact activation of the intrinsic pathway. EXTEM contains tissue factor and preferentially actives the extrinsic pathway. FIBTEM also activates the extrinsic pathway but contains cytochalasin D, which blocks the platelet contribution to clot formation; this isolates the fibrinogen contribution to clot formation. APTEM contains aprotinin, an antifibrinolytic, and will "correct" an EXTEM assay in the presence of hyperfibrinolysis.

Dias JD, Haney EI, Mathew BA, et al. New-generation thromboelastography: comprehensive evaluation of citrated and heparinized blood sample storage effect on clot-forming variables. *Arch Pathol Lab Med*. 2017;141(4):569–577.

Whiting D, DiNardo JA. TEG and ROTEM: technology and clinical applications. *Am J Hematol*. 2014;89(2):228–232.

B.9. A rotational thromboelastometry was performed, and a 10-minute analysis reveals the following results (see Fig. 12.9 and Table 12.8). How do you interpret this information?

There are significant derangements across the EXTEM, INTEM, FIBTEM, and APTEM assays. The CT EXTEM and INTEM are prolonged, which occurs in the presence of low coagulation factors (i.e., usually below 30% of normal levels). The A10 EXTEM and INTEM are decreased, indicating inadequate clot

firmness. This can be due to a lack of platelets or fibrinogen, because the FIBTEM A10 is also decreased, fibrinogen deficiency is implicated. Because the EXTEM and INTEM A10 are so far below the lower reference range, and platelet function contributes approximately 80% of clot amplitude, platelet deficiency or dysfunction also may coexist. The APTEM does not significantly differ from EXTEM, which suggests that hyperfibrinolysis is unlikely. However, fibrinolysis may not be apparent at 10 minutes. The assays should continue running for at least 30 minutes to more fully assess hyperfibrinolysis.

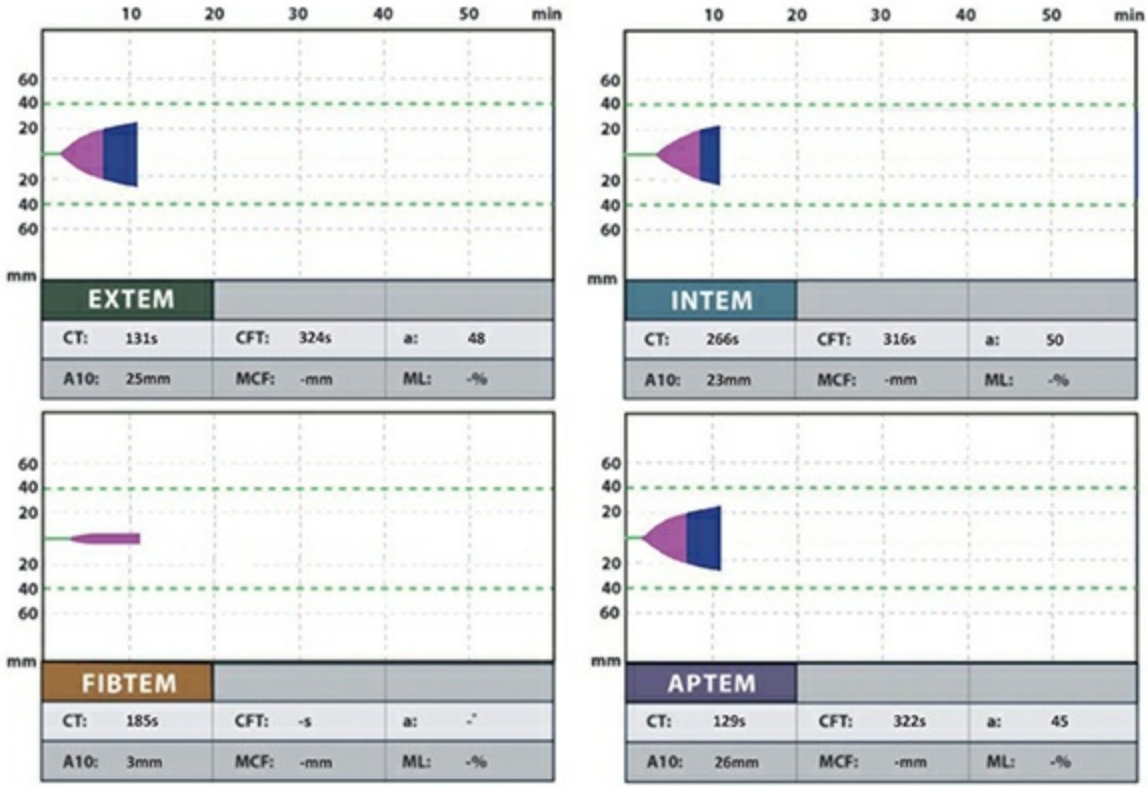

FIGURE 12.9. ROTEM® assay data. See section B.9.

TABLE 12.8 Rotational Thromboelastometry Data for Section B.9

Parameters	Patient Data	Reference Range	Parameters	Patient Data	Reference Range
EXTEM			**INTEM**		
CT (sec)	131	38–79	CT (sec)	266	100–240

CFT (sec)	324	34–159	CFT (sec)	316	30–110
α (degrees)	48	63–83	α (degrees)	50	70–83
A10 (mm)	25	43–65	A10 (mm)	23	44–66
FIBTEM			**APTEM**		
CT (sec)	185	N/A	CT (sec)	129	38–79
A10 (mm)	3	7–23	CFT (sec)	322	34–159
			α (degrees)	45	63–83
			A10 (mm)	26	43–65

References ranges are for ROTEM *delta* assays performed in European clinical reference laboratories in healthy adult population samples.
A10, amplitude 10 min; CFT, clot formation time; CT, clotting time; N/A, not available.

Whiting D, DiNardo JA. TEG and ROTEM: technology and clinical applications. *Am J Hematol*. 2014;89(2):228–232.

B.10. Given the ROTEM® findings and high clinical suspicion for occult postsurgical bleeding, what hemostatic products would you arrange to have in the operating room?

Clinical coagulopathy usually occurs when coagulation factor levels are <30% normal levels, fibrinogen levels are below approximately 70 mg per dL, and platelet count is ≤10,000 per mL. On ROTEM®, there is evidence of coagulation factor, fibrinogen, and possibly platelet deficiency. Therefore, sufficient plasma, cryoprecipitate, and platelets to normalize coagulation function should be arranged before the start of surgery.

Plasmas, be it fresh frozen (i.e., fresh frozen plasma, frozen within 8 hours of phlebotomy) or frozen within 24 hours of phlebotomy (FP24), differ slightly in their levels of the labile factors, factors VIII and V, but are dosed the same. A 15 mL per kg of plasma will increase most coagulation factors by 25%. Therefore, it is reasonable to have 15 mL per kg of plasma available. In this patient, using her ideal or adjusted body weight, which is approximately 60 to 70 kg, it corresponds to 4 units.

Cryoprecipitate is a concentrated blood component made from frozen plasma thawed to 1°C to 6°C. At this temperature, residues that constitute cryoprecipitate appear in plasma and are separated from the supernatant. One unit of cryoprecipitate is prepared from one unit of plasma, and contains approximately 10 to 15 mL plasma, 150 to 250 mg fibrinogen (i.e., 300 to 3,000 mg per dL, 32% of original plasma content), and factors VIII and XIII. This is often pooled into a single bag containing 5 to 10 units from multiple donors. One unit of cryoprecipitate increases plasma fibrinogen by 10 mg per dL; therefore, the equivalent of 5 to 10 units should be available.

Platelets are apheresed directly from the donor or separated from whole blood. The volume of one apheresed unit of platelets is approximately 200 to 400 mL, whereas 4 to 6 units of platelets spun from whole blood will need to be pooled to produce the equivalent volume. A dose of 10 mL per kg will raise platelet count by 30,000 to 50,000 per mL. For an ideal or adjusted body weight of between 60 and 70 kg, 1 to 2 units of apheresed or pooled platelets should be available.

Nagrebetsky A, Al-Samkari H, Davis NM, et al. Perioperative thrombocytopenia: evidence, evaluation, and emerging therapies. *Br J Anaesth*. 2019;122(1):19–31.

Nascimento B, Goodnough LT, Levy JH. Cryoprecipitate therapy. *Br J Anaesth*. 2014;113(6):922–934.

B.11. How would you organize and conduct the transport of this patient to the operating room?

Proper transport of this patient to the operating room requires specific attention to patient monitoring and safety, essential medications and equipment, and team coordination. Patient monitoring should consist of a continuous ECG trace for arrhythmia and HR, invasive arterial access for continuous blood pressure monitoring, and audible pulse oximetry. The

transport monitor should be confirmed to be functional, positioned so that the vitals are clearly displayed, and the battery fully charged. An adequate oxygen supply and an effective oxygen delivery device for the patient's respiratory requirements should be initiated before transport. Emergency airway equipment and a defibrillator should accompany the patient. Intravenous access should be functional and secured with clearly identified injection ports for medication administration. Vasoactive infusions initiated by the treatment team should be verified and infusions pump settings confirmed. Syringes of vasopressors and inotropes, including phenylephrine, epinephrine, norepinephrine, and calcium, and intravenous fluid for volume resuscitation, if required, should be available.

Given her respiratory distress, this patient should be transported in her position of comfort, likely sitting up. Transport to the operating room should not begin until there is sufficient transport personnel present to monitor, treat the patient, and safely operate the bed; the operating room should be ready to receive the patient with the scrub technicians and perfusionists prepared, surgeon immediately available, and blood products in the room.

Fanara B, Manzon C, Barbot O, et al. Recommendations for the intra-hospital transport of critically ill patients. *Crit Care*. 2010;14(3):R87.

C. Intraoperative Management

C.1. What are the cardiovascular effects of commonly used intravenous anesthetic and coinduction agents?

Propofol

Propofol is a potent sympatholytic and vascular smooth muscle dilator. This results in hypotension from vasodilation, preload reduction from venodilation, and myocardial depression. It

blunts the baroreceptor reflex while preserving vagal tone, and bradycardia has been reported with its use. The overall effect is a decrease in venous return, CO, and systemic blood pressure, which would hasten cardiovascular collapse in this patient if given in standard induction doses.

Etomidate

Etomidate is characterized by its stable hemodynamic profile when used for induction of anesthesia. Its imidazole-based structure bears structural similarities to α_2-agonists and is thought to be responsible for peripheral vasoconstriction and the occasional hypertensive response when injected rapidly as the sole agent. Minor decreases in SVR, to a much lesser degree than propofol or thiopental, have also been reported when used in conjunction with a volatile agent. Baroreceptor and sympathetic reflexes are preserved, and there is minimal effect on myocardial contractility. Because hemodynamic responses to laryngoscopy are not affected by etomidate, a significant increase in HR and BP should be expected when given as a sole induction agent. The primary disadvantage of etomidate is the established connection between adrenocortical suppression and its use, which can occur after a single dose. However, this has not translated into increased postoperative hypotension, morbidity, or mortality in cardiac surgery patients. Taken together, etomidate is the most cardiostable intravenous anesthetic and is the drug of choice in patients with impending hemodynamic collapse.

Ketamine

Ketamine is associated with an increase in norepinephrine release that increases sympathetic outflow and is largely responsible for its stable hemodynamic profile. The mechanism by which it causes this norepinephrine release is unclear, but a direct central effect and reuptake inhibition has been postulated.

An induction dose of ketamine increases blood pressure, HR, CO, and myocardial oxygen consumption. Ketamine should be used with caution in patients with depleted endogenous catecholamine levels, such as those who are critically ill because this can unmask the direct negative inotropic effects of ketamine. This patient's sympathetic outflow appears intact, as evidenced by her tachycardia and increased SVR. In the absence of myocardial ischemia, ketamine is a reasonable choice for induction.

Thiopental

Thiopental is included here for historical interest. It is a direct myocardial depressant and also has indirect negative inotropic effects through the suppression of sympathetic outflow. It also causes vascular dilation, but because the baroreceptor reflex is preserved, there is less hypotension when compared with an equivalent dose of propofol, and the subsequent tachycardia minimizes the decrease in CO from venodilation. In a patient with tamponade, however, the hypotensive effects are exaggerated, and its use is not recommended.

Fentanyl

The hallmark of fentanyl is that it causes minimal to no myocardial depression. However, its strong vagotonic effect leads to a decrease in HR, which may lead to a decrease in SV. It preserves coronary autoregulation and has no histaminergic effects. When given in combination with midazolam or other sedatives, however, fentanyl may produce more clinically significant hypotension.

Midazolam

Midazolam exerts a dose-related veno- and vasodilatory effect. When given in typical anxiolytic doses, it can decrease SV and SVR by 10%, but because the baroreceptor reflex is preserved,

CO is maintained. Hypotension can become marked if it is used in higher doses or in combination with fentanyl. It suppresses sympathetic outflow and decreases myocardial oxygen consumption. Because of its rapid onset and MAC-sparing, midazolam can be a useful coinduction agent in this patient. Some hypotension should be expected because of her dependence on sympathetic tone to compensate for her shocked state.

Carmona P, Mateo E, Casanovas I, et al. Management of cardiac tamponade after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2012;26(2):302–311.

Wagner CE, Bick JS, Johnson D, et al. Etomidate use and postoperative outcomes among cardiac surgery patients. *Anesthesiology*. 2014;120(3):579–589.

C.2. What is the effect of supine positioning and positive pressure ventilation on the hemodynamics of a patient with tamponade?

Instituting positive pressure ventilation in a patient with tamponade can result in cardiovascular collapse due to critical impedance of cardiac filling. The increase in intrathoracic pressure is added to intrapericardial pressure, which worsens the Starling resistor pathophysiology of tamponade. Supine positioning, with or without positive pressure, can also further impede filling. An anterior clot or effusion can, with gravity, worsen right atrial and RV compression when the patient is supine. Increased diaphragmatic splinting in a patient already in respiratory distress will limit the negative intrathoracic pressures generated in spontaneous ventilation; this further compromises the gradient for venous return to the RA.

Carmona P, Mateo E, Casanovas I, et al. Management of cardiac tamponade after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2012;26(2):302–311.

Faehnrich JA, Noone RB Jr, White WD, et al. Effects of positive-pressure ventilation, pericardial effusion, and cardiac tamponade on respiratory

variation in transmitral flow velocities. *J Cardiothorac Vasc Anesth*. 2003;17(1):45–50.

Möller CT, Schoonbee CG, Rosendorff C. Haemodynamics of cardiac tamponade during various modes of ventilation. *Br J Anaesth*. 1979;51(5):409–415.

C.3. Describe the induction process for cardiac tamponade.

Standard monitoring, secure intravenous access, functional equipment, and skilled assistance should be prepared per usual practice. As previously discussed, intravenous fluids, vasopressors, positive inotropes, and blood products should be immediately available. Preinduction invasive arterial pressure monitoring is required due to expected hemodynamic instability during the procedure. Although PAC data may be useful for intra- and postoperative optimization, it is not essential for safe induction. Transesophageal echocardiography (TEE) is a useful adjunct and should be utilized postinduction if a skilled operator is available. A rapid sequence induction with etomidate or ketamine as the induction agent; a rapid-acting muscle relaxant; and additional modifiers, such as midazolam, lidocaine and an opioid, to ensure amnesia and to blunt the hemodynamic responses to intubation, should be the primary induction plan. During the preoxygenation process, the patient should be positioned in a way that considers the patient's comfort (e.g., sitting upright) while allowing for quick conversion to a more favorable intubating stance with induction of anesthesia. Because of the potential for hemodynamic collapse with general anesthesia and positive pressure ventilation, it is imperative that induction only takes place once the patient is surgically draped and the surgeons are gowned and gloved ready for immediate chest decompression.

Carmona P, Mateo E, Casanovas I, et al. Management of cardiac tamponade after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2012;26(2):302–311.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia: For Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:883–973.

C.4. Following induction and intubation, the systemic blood pressure decreases to 55/30 mmHg. Describe your management.

This is likely a culmination of the anticipated effects of anesthetic agents, the supine position, and positive pressure ventilation. Pericardial decompression is the definitive treatment; the surgeons should be informed immediately to begin without delay while resuscitative efforts continue. Preload should be maximized with fluid challenges and minimization of positive pressure ventilation—a combination of hand ventilation with low tidal volumes and limited apnea with 100% inspired oxygen may be required. Contractility should be maintained with boluses of epinephrine and calcium if deficient, and anesthetic agents should be titrated to ensure amnesia without excessive negative inotropy. Afterload should be maintained by titrating in norepinephrine to achieve a MAP of 60 to 65 mmHg for preservation of critical organ perfusion. In the event of worsening CO, cardiac massage may be required. It should be noted that external cardiac massage has reduced efficacy in tamponade due to the elevated cardiac filling pressures, which continues to impede venous return during the relaxation phase of chest compressions. In a situation where chest compressions are being seriously considered, opening the pericardium should occur immediately instead.

Carmona P, Mateo E, Casanovas I, et al. Management of cardiac tamponade after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2012;26(2):302–311.

Kaplan JA, Augoustides JGT, Manecke GR, et al, eds. *Kaplan's Cardiac Anesthesia: For Cardiac and Noncardiac Surgery*. 7th ed. Philadelphia, PA: Elsevier; 2017:883–973.

C.5. What hemodynamic changes are frequently associated with opening the pericardial space?

When opened, the pericardial space is exposed to atmospheric pressure. For free-flowing pericardial effusions, this will immediately decompress the cardiac chambers leading to a rapid rise in preload, SV, and CO. This can often be seen on hemodynamic monitoring as a dramatic rise in systemic blood pressure, a reduction in pulmonary artery pressure (PAP) and CVP, and normalization of tachycardia (**Fig. 12.10**). In a patient who may have required high doses of vasopressors to maintain perfusion prior to pericardiotomy, this can result in severe hypertension. In patients who have had an overly aggressive fluid resuscitation, the sudden release of cardiac constraint can lead to acute pulmonary overcirculation and edema as well as RV dysfunction. For this reason, it is important to be aware of the surgical progression in order to properly anticipate the effects of pericardial opening. Should extremes of hypertension occur, it is effectively treated with rapid weaning of vasopressors, deepening the level of anesthesia, administering analgesia, and titrating short-acting vasodilators until the blood pressure is normalized.

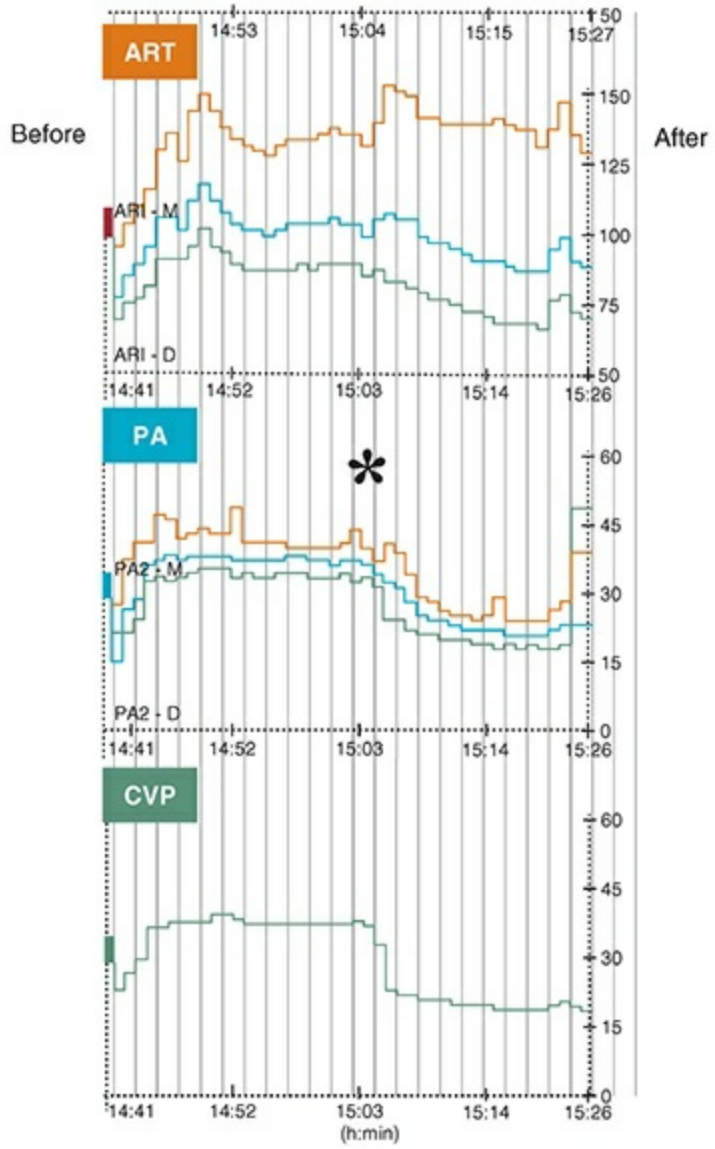

FIGURE 12.10. Intraoperative hemodynamics before and after pericardial decompression. Arterial blood pressure (ART), pulmonary artery pressure (PA), and central venous pressure (CVP) are shown during mediastinal exploration for cardiac tamponade. The moment of pericardial decompression is marked by the *asterisk*. Note the elevated CVP, PA diastolic pressure, as well as the narrow systemic pulse pressure prior to decompression, demonstrating extrinsic pericardial pressure on the RA and LA and its effect on decreasing LV SV. Shortly following pericardial decompression, CVP and PA pressures decrease almost immediately accompanied by an increase in systemic arterial pressure. Systemic pulse pressure continues to increase, reflecting the recovery of SV and presumably CO.

Carmona P, Mateo E, Casanovas I, et al. Management of cardiac tamponade after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2012;26(2):302–311.

C.6. Following the removal of approximately 500 mL of dark blood and clots from the mediastinum, the patient's CO remains low. What are your differential diagnoses?

Persistent hypotension following pericardial decompression can be a result of deficient preload, afterload, and/or contractility. If there is surgical evidence of ongoing hemorrhage, treating hypovolemia should be a priority. Because this patient has a PAC in situ, a review of CVP and diastolic PAP trends can be helpful in assessing ventricular filling pressures and optimizing fluid resuscitation. Residual clot and regional tamponade should be evaluated with TEE and careful surgical exploration; in particular, clot located posteriorly within the oblique sinus can continue to compress the LA (**Fig. 12.3**) and may not be immediately apparent on initial surgical survey.

TEE is also invaluable in evaluating myocardial contractility. Ventricular function may be impaired from coronary insufficiency and active ischemia or it may persist even after restoration of adequate coronary perfusion (i.e., "myocardial stunning"). Both conditions may present as cardiogenic shock and manifest wall motion abnormalities on TEE and should be managed by optimizing myocardial oxygen supply and demand while preserving critical organ perfusion with careful use of inotropic support if required.

A low SVR state may result from vasodilatory medications, including anesthetics and inotropes (e.g., milrinone, dobutamine, low-dose epinephrine). Isolated vasoplegia, although not typically associated with this procedure, can occur in the presence of an exuberant surgical inflammatory response, stress-related depletion of endogenous vasopressin, and acquired catecholamine resistance. Norepinephrine is recommended as a first-line agent for treating vasoplegia, although this is largely

extrapolated from septic shock study data. If high doses of norepinephrine are required to maintain adequate perfusion pressures, the addition of vasopressin may be useful to overcome catecholamine resistance, limit catecholamine doses, and possibly reduce the incidence of postoperative renal failure.

Geffroy A, Beloeil H, Bouvier E, et al. Prolonged right ventricular failure after relief of cardiac tamponade. *Can J Anaesth*. 2004;51(5):482–485.

Lambden S, Creagh-Brown BC, Hunt J, et al. Definitions and pathophysiology of vasoplegic shock. *Crit Care*. 2018;22(1):174.

Shaefi S, Mittel A, Klick J, et al. Vasoplegia after cardiovascular procedure—pathophysiology and targeted therapy. *J Cardiothorac Vasc Anesth*. 2018;32(2):1013–1022.

C.7. What is pericardial decompression syndrome (PDS)?

PDS describes paradoxical cardiogenic shock and pulmonary edema following drainage of pericardial effusions. It can present immediately following percutaneous or surgical drainage but can be delayed by up to 24 to 48 hours. The exact etiology of PDS is unclear but has been attributed to many causes including myocardial stunning from impaired epicardial perfusion, acute RV failure from volume overload with decompression, acute septal shift from RV filling causing LV dysfunction, stress cardiomyopathy from postdrainage neurohormonal alterations, acute severe postdrainage hypertension, and abrupt catecholamine withdrawal following restoration of normal cardiac filling dynamics. In a retrospective review of 35 cases, almost all of the patients presented with cardiac tamponade (94%) with normal predrainage ventricular function and large pericardial effusions, although PDS occurring after drainage of effusions as small 250 mL, has been described. The majority of patients presented with LV or biventricular failure (60%), followed by isolated cardiogenic pulmonary edema (29%) and RV failure (9%). There is a paucity of information regarding preventive measures apart from slow, rather than rapid,

pericardial decompression, and treatment is supportive. The timeline to myocardial recovery is variable.

Ayoub C, Chang M, Kritharides L. A case report of ventricular dysfunction post pericardiocentesis: stress cardiomyopathy or pericardial decompression syndrome? *Cardiovasc Ultrasound*. 2015;13:32.

Chung J, Ocken L, Wolo E, et al. Acute right ventricular failure after surgical drainage of pericardial tamponade: a case report of pericardial decompression syndrome and review of the literature. *J Cardiothorac Vasc Anesth*. 2019;33(3):768–771.

Geffroy A, Beloeil H, Bouvier E, et al. Prolonged right ventricular failure after relief of cardiac tamponade. *Can J Anaesth*. 2004;51(5):482–485.

Pradhan R, Okabe T, Yoshida K, et al. Patient characteristics and predictors of mortality associated with pericardial decompression syndrome: a comprehensive analysis of published cases. *Eur Heart J Acute Cardiovasc Care*. 2015;4(2):113–120.

D. Postoperative Management

D.1. A pericardial drain is placed following mediastinal decompression. How should this drainage tube be managed?

Following open surgical drainage, a pericardial drain is connected to a closed, underwater seal system to prevent air entry into the mediastinum during negative pressure inspiration. Low-pressure suction (in the range of −15 to −25 cm H_2O), is typically applied to facilitate clearance of effusions and air, but clots can still form within the tubing leading to a recurrence of tamponade if not cleared. Although a small respiratory "swing" may be present in drain tubing fluid or in the water seal, "bubbling" is not typical unless there is a concurrent pneumomediastinum or a pneumothorax in direct connection to the drain. For percutaneous drainage, a pigtail catheter is typically connected to a closed drainage system for gravity drainage with a stopcock for aspiration and flushing to maintain

catheter patency. Some percutaneous drain care protocols advocate regular aspiration every 4 to 6 hours with instillation of heparinized saline after each aspiration attempt. Regardless of the type of drainage tube, all patients should be monitored closely for reaccumulation of pericardial fluid from catheter malfunction. The dwell time for the catheter should be minimized to prevent infective complications. Drains are typically removed when there is <30 to 50 mL drainage over a 24-hour period or after 24 to 72 hours.

De Carlini CC, Maggiolini S. Pericardiocentesis in cardiac tamponade: indications and practical aspects. *e-J Cardiol Pract*. 2017;15(19).

Zisis C, Tsirgogianni T, Lazaridis G, et al. Chest drainage systems in use. *Ann Transl Med*. 2015;3(3):43.

D.2. How would you manage hypertension in the intensive care unit?

Hypertension following resolution of tamponade is common. The etiology can be directly related to the posttamponade state, a postprocedural complication, or from issues that are generally applicable to any postsurgical patient. In posttamponade patients, hypertension is typically due to ongoing sympathetic activation and relative baroreceptor insensitivity, although residual consequences of tamponade such as acidosis, hyper- or hypovolemia, and/or systemic inflammatory response can also be responsible. Serious complications that may present with hypertension such as heart failure with pulmonary edema, stroke, hemorrhage, and myocardial ischemia should be actively ruled out. More general causes of postoperative hypertension including pain, anxiety, cold, hypoxemia, hypercarbia, and delirium should be individually addressed with specific pharmacologic and nonpharmacologic therapies.

Controlling hypertension is important not only in order to prevent myocardial strain and end-organ damage but also to

limit direct complications including surgical bleeding and worsening reperfusion injury. Initiating antihypertensive therapy takes into account not only the likely mechanism of hypertension but also the patient's comorbidities and baseline systemic blood pressure. The evidentiary basis for maintaining MAP within 20% of baseline values comes from clinical data showing an increased risk of end-organ hyperperfusion and damage with sustained blood pressures (i.e., >10 minutes) beyond this range. By targeting the patient's baseline MAP, organ perfusion pressures are maintained within the individual's autoregulatory range.

Assuming reversible causes of hypertension are corrected, the ideal antihypertensive for acute control should be short acting and titratable. Maintenance antihypertensive therapy should also have an evidence base demonstrating benefit when contextualized to the patient's comorbidities. In acute perioperative hypertension with or without associated excess sympathetic discharge, intravenous dihydropyridine calcium channel blockers such as nicardipine and clevidipine are recommended. Clevidipine has a rapid onset–offset profile due to its metabolism by tissue and blood esterases, resulting in a half-life of approximately 1 minute and is an ideal agent for acutely controlling hypertension. Nicardipine, by contrast, has a rapid distributive α half-life of 2.7 minutes, which increases to 44.8 minutes and 14.4 hours for its intermediate β and γ half-lives, respectively. Outside of acute antihypertensive therapy, the dihydropyridine calcium channel blockers play an adjunctive role for maintenance therapy in patients with ischemic heart disease and are not recommended in patients with heart failure with reduced ejection fraction.

Labetalol is an alternate agent that is particularly useful in the presence of tachycardia. Given intravenously, it has an approximately 7:1 nonselective β- to α_1-antagonist effect with an

onset of effect in 2 to 5 minutes. Its peak hypotensive effect occurs within 10 minutes, and its elimination half-life is 3 to 5 hours. If warranted, maintenance β-blocker therapy, with carvedilol, the nonselective β- and α_1-blocker or cardioselective agents such as metoprolol, confers additional survival benefit in this patient with ischemic heart disease and is a first-line therapy for chronic treatment.

Aronson S, Dyke CM, Stierer KA, et al. The ECLIPSE trials: comparative studies of clevidipine to nitroglycerin, sodium nitroprusside, and nicardipine for acute hypertension treatment in cardiac surgery patients. *Anesth Analg*. 2008;107(4):1110–1121.

Cheung AT. Exploring an optimum intra/postoperative management strategy for acute hypertension in the cardiac surgery patient. *J Card Surg*. 2006;21(suppl 1):S8–S14.

Kotlyar E, Macdonald PS, Keogh AM, et al. Optimization of left ventricular function with carvedilol before high-risk cardiac surgery. *J Heart Lung Transplant*. 2001;20:1129–1131.

Varon J, Marik PE. Perioperative hypertension management. *Vasc Health Risk Manag*. 2008;4:615–627.

Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2018;71(19):e127–e248.

13 Heart Transplantation and Subsequent Noncardiac Surgery

Jeff T. Granton , Ranjana Bairagi, and Davy Cheng

A 41-year-old man with a history of idiopathic dilated cardiomyopathy (IDCM) is admitted to the cardiac care unit in a quaternary cardiac center for potential heart transplantation assessment. He has known systolic dysfunction, with an ejection fraction of <20% on transthoracic echocardiogram. Recurrent ventricular arrhythmias necessitated the insertion of an implantable cardioverter-defibrillator (ICD). Right heart catheterization revealed a pulmonary vascular resistance (PVR) of 4 Wood units. Recently, his symptoms have worsened and have progressed to New York Heart Association class IV. He is subsequently placed on the transplant list with high priority. However, due to further deterioration, consideration is being given to the insertion of a left ventricular assist device (LVAD) to maintain adequate end-organ perfusion while waiting for a donor heart to become available.

A. Medical Disease and Differential Diagnosis

1. What are the common diagnoses requiring adult heart transplantation?

2. What are the indications and relative contraindications for recipient selection?
3. What are the criteria for donor heart selection?
4. What is the role of donation after cardiac death (DCD) for heart transplantation?
5. What are the principles of perioperative donor management?
6. What are the risk factors associated with posttransplant mortality?
7. What is the difference between the biatrial and bicaval surgical techniques of heart transplant?
8. When is a combined heart-lung transplant indicated? What are the important differences?
9. What are the medical and surgical alternatives to cardiac transplantation?
10. What is the role of ventricular assist devices (VADs) in this type of patient?
11. What are the considerations in anesthetizing patients for LVAD insertion?

B. Preoperative Management

Three weeks after insertion of an LVAD, a donor heart becomes available.

1. How would you assess this patient preoperatively?
2. How would you premedicate this patient? Why?

C. Intraoperative Management

1. What anesthetic equipment and monitors would you set up? Why?
2. What is the role of transesophageal echocardiography (TEE)?
3. Describe the induction and maintenance of anesthesia.
4. How would you manage this patient during cardiopulmonary bypass (CPB)?

D. Postoperative Management

1. What are the early postoperative complications?
2. What are the mechanisms of early right ventricular (RV) failure?
3. How would you treat RV failure following heart transplantation?
4. How does inhaled nitric oxide (NO) work as a selective pulmonary vasodilator?
5. What is the pathophysiology of the denervated heart?
6. What are the common cardiac dysrhythmias following heart transplant?
7. What are the causes of posttransplant bleeding?
8. How would you treat posttransplant bleeding?
9. What are the causes of early graft failure?
10. How would you manage this patient in the intensive care unit?

E. Subsequent Noncardiac Surgery

The patient recovers successfully following heart transplant. However, 2 years postoperatively, he fractures his left radius after a fall. He then presents for open reduction and internal fixation of the fracture.

1. How would you monitor this patient?
2. What type of anesthetic is best for the heart-transplanted patient?
3. What anesthetic technique would you choose for this patient?
4. Do you need to use a muscarinic antagonist with cholinesterase inhibitors to reverse the muscle relaxant in heart-transplanted patients?
5. What are the anesthetic implications for heart-transplanted patients?
6. What is the significant implication of the denervated heart?
7. What is the significance of allograft rejection?
8. What is the significance of infection in these patients?
9. What are the significant implications of drug interactions?

10. What is cardiac allograft vasculopathy (CAV)? Why is this important?
11. What is the significant implication of posttransplant hypertension?
12. What is the significant implication of renal dysfunction?
13. What types of malignancy are found in recipients?
14. Is ambulatory surgery appropriate for heart transplant recipients?

A. Medical Disease and Differential Diagnosis

A.1. What are the common diagnoses requiring adult heart transplantation?

Heart transplantation is now considered to be a viable treatment option for selected patients with end-stage heart disease. At present, more than 5,800 heart transplants are done annually worldwide. The indications for adult heart transplantation, as reported to the Registry of the International Society for Heart and Lung Transplantation in 2018, are shown in **Figure 13.1**. Ischemic coronary artery disease (33.1%) and nonischemic cardiomyopathy (50.5%) represent the most frequent causes for transplantation.

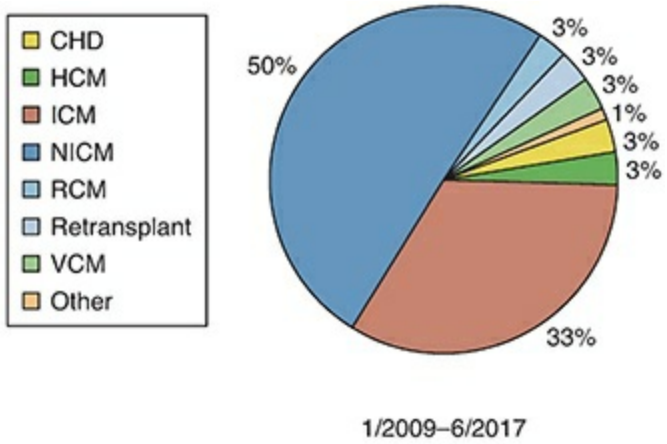

FIGURE 13.1. International Society for Heart and Lung Transplantation: Adult Heart Transplant Diagnosis for transplants performed between January 1, 2009, and June 30, 2017.

CHD, congenital heart disease; HCM, hypertrophic cardiomyopathy; ICM, ischemic cardiomyopathy; NICM, nonischemic cardiomyopathy; RCM, restrictive cardiomyopathy; VCM, valvular cardiomyopathy. (*Data from Lund LH, Khush KK, Cherikh WS, et al. The registry of the International Society for Heart and Lung Transplantation: thirty-fourth adult heart transplantation report—2017; focus theme: allograft ischemic time*. J Heart Lung Transplant. *2017;36[10]:1037–1046.*)

A.2. What are the indications and relative contraindications for recipient selection?

It should be noted that indications/contraindications can be flexible and can vary from center to center.

Criteria for selection can include the following:

- End-stage heart disease with poor quality of life or poor survivability
- Refractory arrhythmias or angina despite optimal medical and surgical care
- Physiologic age younger than 70 years. However, in 2016, greater than 13.2% of heart transplant recipients were 65 years of age or older. There are cases of patients older than 70 years receiving a heart transplant.
- Maximal oxygen uptake ($\dot{V}O_{2max}$) during cardiopulmonary exercise testing is considered. Although the cut-offs are highly variable and have many caveats, generally, patients with a peak $\dot{V}O_{2max}$ <10 mL/kg/min have an indication for transplantation.
- A heart failure prediction scoring system can also be used.

Contraindications (not necessarily absolute)

- Neoplasm with significant chance of recurrence
- Obesity (body mass index [BMI] >30 kg per m^2)
- Fixed (nonresponsive) pulmonary hypertension: PVR greater than 6 Wood units or pulmonary artery transpulmonary gradient greater than 15 mmHg
- Nonreversible renal dysfunction
- Age older than 70 years
- Peripheral vascular disease, carotid stenosis (depending on

severity)

- Diabetes with end-organ damage neuropathy, nephropathy, or retinopathy
- Psychosocial impairments
- Drug or alcohol addiction, smoking, mental defect that will limit compliance with postoperative care or history of noncompliance
- Other diseases that may limit survival (HIV, pulmonary disease, hepatitis, etc.)

Chan WX, Ross H. Who needs a transplant and when? *Curr Opin Organ Transplant*. 2012;17:531–539.

Haddad H, Isaac D, Legare JF, et al. Canadian Cardiovascular Society Consensus Conference update on cardiac transplantation 2008: executive summary. *Can J Cardiol*. 2009;25(4):197–205.

International Society for Heart and Lung Transplantation: Quarterly Data Report. Characteristics for Transplants performed between January 1, 2016 and December 31, 2016.

Merha MR, Kobashigawa J, Starling R, et al. Listing criteria for heart transplantation: International Society for Heart and Lung Transplantation guidelines for the care of cardiac transplant candidates—2006. *J Heart Lung Transplant*. 2006;25(9):1024–1042.

Steinman TI, Becker BN, Frost AE, et al. Guidelines for the referral and management of patients eligible for solid organ transplantation. *Transplantation*. 2001;71:1189–1204.

A.3. What are the criteria for donor heart selection?

The limiting factor in heart transplantation is the shortage of donor organs. In Canada, there were 202 heart transplants performed in 2016, with 189 people on the waiting list at the end of that year. In the United States, 2,655 heart transplants were performed in 2014, with over 4,000 patients on the waiting list. Following the diagnosis of brain death, organ procurement may be considered for the purpose of donation. Preferably, the donor should not have sustained prolonged cardiac arrest, severe chest trauma, intracardiac injections, septicemia, or excessive

inotropic support and should be younger than 55 years of age. In all cases, a careful clinical examination of the potential donor is undertaken to rule out coronary artery atherosclerosis and contractile dysfunction; investigations may include angiography and echocardiography. The use of coronary angiography would be dictated by patient age, sex, and risk factors. In general, a contrast left ventriculogram is avoided to reduce the risk of nephrotoxicity.

Poor ejection fraction, despite optimization of physiologic variables, would exclude a potential donation. Transplantation can proceed with mild left ventricular hypertrophy; however, wall thickness >13 mm or electrocardiogram (ECG) criteria for left ventricular hypertrophy would make transplantation unadvisable. In general, severe congenital or valvular abnormalities would preclude donation, with the exception of abnormalities in which “bench” repair can be undertaken before transplant.

Blood group ABO compatibility is important because mismatch may result in hyperacute rejection. The donor body weight should be within 20% of that of the recipient. However, in the case of a small donor matching, using BMI or height is more accurate than using weight. Preferably, donor heart ischemic time should be less than 4 hours. Prolonged ischemic time may contribute to early allograft failure; however, techniques to allow improved tolerance of ischemia may be on the horizon.

The concept of “extended-donor criteria” is becoming popular, and outcomes are favorable. At times, donor hearts are considered for transplant with one or more of the following: size mismatch, ischemic time longer than 4 hours, ventricular hypertrophy, donor age older than 55 years, malignant brain tumors, long-standing death by poisoning, and significant inotropic requirements. In fact, looking at a wide variety of

traditional reasons not to accept a donor heart, only diabetes mellitus was found to be predictive of 1-year mortality in a recipient, leading to concerns that many viable and "less than perfect" donor hearts are not being used for transplant.

Non–heart-beating (DCD) donors are now used in multiple jurisdictions for kidney, liver, and lung transplantation. There have been cases of heart transplantation from non–heart-beating donors. However, the ethical and legal issues surrounding the technique for this form of heart donation are controversial.

Canadian Institute for Health Information. *Canadian Organ Replacement Register Annual Report: Treatment of End-Stage Organ Failure in Canada, 2007 to 2016*. Ontario, Canada: Canadian Institute for Health Information; 2017.

Costanzo MR, Dipchand A, Starling R, et al. The International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients. *J Heart Lung Transplant*. 2010;29:914–956.

Eynon AC, Murphy PG, Smith M, et al. Heart transplantation after declaration of death by cardiorespiratory criteria. *J Heart Lung Transplant*. 2010;29:232–233.

Khush KK, Menza R, Nguyen J, et al. Donor predictors of allograft use and recipient outcomes after heart transplantation. *Circ Heart Fail*. 2013;6:300–309.

Mancini D, Lietz K. Selection of cardiac transplantation candidates in 2010. *Circulation*. 2010;122:173–183.

Morrissey PE, Monaco AP. Donation after circulatory death: current practices, ongoing challenges, and potential improvements. *Transplantation*. 2014;97:258–264.

United Network for Organ Sharing. Organ procurement and transplantation network, 2014 data. http://www.unos.org/donation. Accessed May 12, 2015.

A.4. What is the role of donation after cardiac death (DCD) for heart transplantation?

Cardiac transplantation is limited by a critical shortage of suitable organs from brain-dead donors. As a result, there has been renewed interest in DCD. Hearts from DCD donors suffer significant ischemic injury prior to organ procurement.

Therefore, the traditional approach to the transplantation of hearts from brain-dead donors is not applicable to the DCD context. Advances in the understanding of ischemic postconditioning have facilitated development of DCD heart resuscitation strategies that can be used to minimize ischemia-reperfusion injury at the time of organ procurement. Clinically approved ex-situ heart perfusion devices allow for DCD heart preservation in a normothermic beating state and minimize exposure to incremental cold ischemia. Organ viability can then be assessed prior to transplantation, thereby minimizing the risk of primary graft dysfunction. One study in which 28 DCD heart transplants were performed showed comparable short-term outcomes to traditional donation before cardiac death (DBD) heart transplants with respect to hospital length of stay, treated rejection episodes, allograft function, and 1-year survival (DCD 86%; DBD 88%; p = 0.98). Limited data currently available suggest that 29% of DCD heart transplant recipients will require temporary mechanical circulatory support. However, all patients were successfully weaned from support and the majority exhibited normal biventricular function on follow-up echocardiogram. Further investigation into optimizing resuscitation, preservation, evaluation, and long-term outcomes is vital to ensure a broader application of DCD heart transplantation in the future.

Dhital KK, Chew HC, Macdonald PS. Donation after circulatory death heart transplantation. *Curr Opin Organ Transplant*. 2017;22(3):189–197.

Messer S, Page A, Axell R, et al. Outcome after heart transplantation from donation after circulatory-determined death donors. *J Heart Lung Transplant*. 2017;36(12):1311–1318.

White CW, Messer SJ, Large SR, et al. Transplantation of hearts donated after circulatory death. *Front Cardiovasc Med*. 2018;5:8. doi:10.3389/fcvm.2018.00008.

A.5. What are the principles of perioperative donor

management?

The goals of management are to maintain euvolemic, achieve relatively normal afterload, and optimize cardiac output (CO) without excessive use of inotropic medications, in particular *β*-agonists. Unfortunately, the brain-dead patient often can become extraordinarily unstable and achieving hemodynamic stability can be a challenge. In addition, the treatment modalities to support certain end organs for donation are often at odds with each other. The onset of diabetes insipidus needs to be considered when excessive urine output (>300 mL per hour) is observed and must be treated promptly with desmopressin (1-deamino-8-D-arginine vasopressin [DDAVP]). As a result of dysfunction of the hypothalamic-pituitary system, it is suggested that hormonal replacement therapy be undertaken. This includes the use of intravenous (IV) exogenous thyroid therapy, arginine vasopressin, and methylprednisolone. In addition, adequate glycemic control should be achieved.

Haddad H, Isaac D, Legare JF, et al. Canadian Cardiovascular Society Consensus Conference update on cardiac transplantation 2008: executive summary. *Can J Cardiol*. 2009;25(4):197–205.

Shemie SD, Ross H, Pagliarello J, et al. Organ donor management in Canada: recommendations of the forum on medical management to optimize donor organ potential. *CMAJ*. 2006;174(6):S13–S32.

Van Bakel AB, Pitzer S, Drake P, et al. Early hormonal therapy stabilizes hemodynamics during donor procurement. *Transplant Proc*. 2004;36:2573–2578.

Zaroff JG, Rosengard BR, Armstrong WR, et al. Consensus conference report: maximizing use of organs recovered from the cadaver donor: cardiac recommendations, March 28–29, 2001, Crystal City, Va. *Circulation*. 2002;106:836–841.

A.6. What are the risk factors associated with posttransplant mortality?

Overall survival at 1 year was 85.3% for recipients between 50 and 64 years of age for transplants performed from January 1,

2013, to December 12, 2016. Having congenital heart disease as the indication for transplant is a powerful predictor of postoperative 1-year mortality. In addition, the requirement of extracorporeal circulatory support, dialysis, preoperative mechanical ventilation, female gender, nonidentical ABO matching, previous blood transfusions, coronary artery disease as the indication for transplant, and being hospitalized immediately before transplant all are risk factors for 1-year mortality. Mortality during the first year is greater than the next 4 years combined; so, risk factors associated with 1-year mortality are also powerful predictors of 5-year mortality. For those who have survived after 1 year, allograft vasculopathy during the first posttransplant year, diabetes mellitus, treatment for rejection during the first posttransplantation year, recipient age, donor age, recipient weight, and transplant center volume are risk factors for 5-year mortality. Older age is associated with lower survival. Older donor age is more strongly associated with recipient posttransplant mortality, especially in the early posttransplant period.

The most common causes of death are the following:

Within 30 days posttransplant

- Graft failure, multiorgan failure, non-cytomegalovirus (CMV) infection

From 31 to 365 days posttransplant

- Non-CMV infection, graft failure, acute rejection

After 5 years

- Allograft vasculopathy, late graft failures, malignancies, non-CMV infections

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International Society for Heart and Lung Transplantation: Quarterly Data Report. Survival Rates for Transplants performed between January 1, 2013 and December 31, 2016.

Lund LH, Khush KK, Cherikh WS, et al. The registry of the International Society for Heart and Lung Transplantation: thirty-fourth adult heart

transplantation report–2017; focus theme: allograft ischemic time. *J Heart Lung Transplant*. 2017;36(10): 1037–1046.

Taylor DO, Stehlik J, Edwards LB, et al. Registry of the International Society for Heart and Lung Transplantation: twenty-sixth official adult heart transplant report—2009. *J Heart Lung Transplant*. 2009;28(10):1007–1022.

A.7. What is the difference between the biatrial and bicaval surgical techniques of heart transplant?

The older biatrial technique involves anastomoses of the recipient and donor atrial cuffs. The bicaval technique maintains the aforementioned left atrial anastomoses and attempts to maintain cardiac anatomy with separate recipient's bicaval anastomoses to the donor's right atrium. There may be an advantage of decreased need for pacemakers and improved mortality with the bicaval technique.

Davies RR, Russo MJ, Morgan JA, et al. Standard versus bicaval techniques for orthotopic heart transplantation: an analysis of the United Network for Organ Sharing database. *J Thorac Cardiovasc Surg*. 2010;140:700–708.

Morgan JA, Edwards NM. Orthotopic cardiac transplantation: comparison of outcome using biatrial, bicaval, and total techniques. *J Card Surg*. 2005;20:102–106.

A.8. When is a combined heart/lung transplant indicated? What are the important differences?

Congenital cardiac disease and primary pulmonary hypertension are the most common indications for combined heart/lung transplant. Other indications include cystic fibrosis, α_1-antitrypsin deficiency, and other forms of lung disease, such as emphysema and idiopathic pulmonary fibrosis. The procedure is performed through a transverse thoracotomy incision, and the donor heart/lungs are transplanted en bloc. Important postoperative problems include bleeding and reperfusion lung injury, which may require inhaled NO or occasionally extracorporeal membrane oxygenation (ECMO). Survival following heart/lung transplant is 68% and 51% at 1 and 3 years,

respectively.

International Society for Heart and Lung Transplantation: Quarterly Data Report. Survival Rates for Transplants performed between April 1, 2010 and March 31, 2014.

A.9. What are the medical and surgical alternatives to cardiac transplantation?

An ongoing worldwide shortage of donor hearts has put ongoing pressure to medically manage patients with end-stage cardiac failure. Patients need to adhere to strict lifestyle modifications and diet; otherwise, any other therapy will have limited usefulness. As heart failure progresses, patients may respond to a variety of medications. Angiotensin-converting enzyme (ACE) inhibitors have been shown to improve symptoms and decrease mortality in patients with heart failure. Angiotensin II receptor blockers can be considered for patients who cannot tolerate ACE inhibitors. Patients with severe forms of heart failure also may benefit from a low-dose aldosterone antagonist (spironolactone), with attention paid to the potential for hyperkalemia. Tailored doses of diuretic therapy may offer some symptomatic relief. β-Blockade with carvedilol, sustained-release metoprolol or bisoprolol has been shown to reduce the risk of death. Therapy to maintain sinus rhythm is also recommended. In addition, the risk of sudden cardiac death in patients with advanced heart failure may be reduced by inserting an ICD. Furthermore, ICD implantation combined with cardiac resynchronization therapy (this can also be done alone) has been shown to improve functional class and survival in medically optimized advanced heart failure patients. Intra-aortic balloon pump (IABP) and increasingly, VAD implantation or semi-implantable paracorporeal devices also are finding a role in the management of patients as a bridge to transplant, particularly for those presenting in acute decompensated heart failure.

Hunt SA, Abraham WT, Chin MH, et al. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult-summary article. *Circulation*. 2005;112:1825–1852.

Ramani GV, Uber PA, Mehra MP. Chronic heart failure: contemporary diagnosis and management. *Mayo Clin Proc*. 2010;85:180–195.

Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure. *J Am Coll Cardiol*. 2013;62(16):e147–e239.

A.10. What is the role of ventricular assist devices (VADs) in this type of patient?

The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) database has tracked over 15,000 patients, with total implants approaching 2,500 per year. There were 2,380 LVAD placements in 2014. The indications for LVAD insertion seem to be changing since 2006, when 40.8% were due to life-threatening cardiogenic shock. In 2014, only 15.0% of the patients had cardiogenic shock, and progressive decline of cardiac function (37%) remains the largest single indication. Of those who received an LVAD, 53.5% were listed or were being considered for heart transplant in 2014. In general, three major categories of patients considered for VAD include (1) temporary insertion while cardiac function recovers from insult (bridge to recovery), (2) insertion while awaiting transplant or transplant assessment (bridge to transplant), and (3) patients who need long-term support but are not transplant candidates (destination therapy). Interestingly in 2014, the INTERMACS registry found that in 38.2% of patients, LVAD insertion was considered a destination therapy. The vast majority of VADs are continuous-flow pumps instead of pulsatile flow. A variety of composite risk scores have been developed to help guide patient selection for LVAD implantation. LVADs are inserted to improve end-organ function ahead of a heart transplant. Issues such as aortic valve incompetence and the presence of intracardiac shunts need to be

investigated because these may make LVAD insertion unadvisable without repair. RV function needs to be carefully assessed before and after LVAD insertion because it may preclude the insertion of an LVAD or require a biventricular device.

Kirklin JK, Naftel DC, Kormos RL, et al. The seventh INTERMACS annual report: 15,000 implants and counting. *J Heart Lung Transplant*. 2015;34:1495–1504.

Miller LW, Guglin M. Patient selection for ventricular assist devices: a moving target. *J Am Coll Cardiol*. 2013;61:1209–1221.

Wilson SR, Mudge GH Jr, Stewart GC, et al. Evaluation for a ventricular assist device: selecting the appropriate candidate. *Circulation*. 2009;119:2225–2232.

A.11. What are the considerations in anesthetizing patients for LVAD insertion?

Significant cardiac abnormalities (e.g., aortic insufficiency, patent foramen ovale) should be identified preoperatively and, if possible, addressed at the time of surgery. The choice and dose of agents for induction and maintenance of a general anesthetic should be done cautiously in the context of a patient with severe cardiac dysfunction. These patients may have an ICD in place, and if deactivated, placement of external defibrillator pads is advisable. LVADs can be inserted via a sternotomy or a left thoracotomy. Patients are at high risk for significant perioperative blood loss; large-bore IV access is essential, and antifibrinolytics are often administered. TEE is mandatory for LVAD insertion to assess the presence of a patent foramen ovale, ensure aortic valve competence, confirm proper position of device and cannulae, assess the amount of air in cardiac chambers, guide fluid management, and monitor the RV function. Inadequate right heart function is a potential complication after LVAD insertion and can be treated with phosphodiesterase inhibitors and inhaled NO. Vasopressin

and/or norepinephrine may be required to maintain adequate systemic vascular resistance post-CPB. However, caution needs to be exercised with vasoconstrictors because excessive afterload can impair the device function.

Broussard D, Donaldson E, Falterman J, et al. Anesthesia for left ventricular assist device insertion: a case series and review. *Ochsner J*. 2011;11(1):70–77.

Feussner M, Mukherjee C, Garbade J, et al. Anaesthesia for patients undergoing ventricular assist-device implantation. *Best Pract Res Clin Anaesthesiol*. 2012;26(2):167–177.

Tan LH, Cokis C. Anesthesia for implantation of the Jarvik 2000 Flowmaker LVAD. *Anaesth Intensive Care*. 2006;34:746–752.

B. Preoperative Management

Three weeks after insertion of an LVAD, a donor heart becomes available.

B.1. How would you assess this patient preoperatively?

Prospective transplant candidates usually have been fully preoperatively evaluated by a multidisciplinary team, including cardiologists, pulmonologists, surgeons, as well as anesthesiologists. The anesthesiologist should review the recipient's current cardiac status, including medications and level of mechanical support, with particular attention to hemodynamic parameters and reversibility of elevated PVR. Pertinent anesthetic history, concomitant diseases, and fasting status also must be ascertained. Baseline electrolytes, urea, creatinine, blood glucose, international normalized ratio (INR)/prothrombin time (PT), and complete blood count should be obtained. In addition, specific preoperative investigations need to be reviewed, such as echocardiogram, pulmonary function tests, ECG, and chest radiograph. A plan also needs to be devised regarding how to handle an ICD on induction of anesthesia, and preoperative consultation with a cardiologist or

electrophysiologist may be appropriate to achieve this.

There are typically two types of patients presenting for heart transplantation. The first type of patient is relatively compensated, possibly being ambulatory in the nonhospital setting or requiring IV inotropic support. The second type is moribund and decompensated, requiring mechanical ventilation and/or mechanical circulatory support. It should be noted, however, a third type of patient is emerging, the stable and ambulatory patient with an LVAD in place. Based on data from 2009 to 2017, at the time of transplant, 39.7% of patients were on IV inotropes, 41.7% had an LVAD, 7.0% had an IABP, and 1.9% were mechanically ventilated. As the use of VADs increases, one would expect more patients to be presenting for transplant with LVADs in place. Recipients who have undergone prior cardiac surgery need to be identified because this will increase the surgical time to establish CPB due to adhesions and bleeding. Large-bore IV access must be secured and crossmatched blood should be readily available in the operating room before surgery begins. The use of antifibrinolytics is routine for these cases.

Chambers DC, Cherikh WS, Goldfarb SB, et al. The international thoracic organ transplant registry of the International Society for Heart and Lung Transplantation: thirty-fifth adult lung and heart-lung transplantation report—2018; focus theme: multiorgan transplantation. *J Heart Lung Transplant*. 2018;37(10):1169–1183.

Goldfarb SB, Hayes D Jr, Levvey BJ, et al. The international thoracic organ transplant registry of the International Society for Heart and Lung Transplantation: twenty-first pediatric lung and heart-lung transplantation report—2018; focus theme: multiorgan transplantation. *J Heart Lung Transplant*. 2018;37(10):1196–1206.

Khush KK, Cherikh WS, Chambers DC, et al. The international thoracic organ transplant registry of the International Society for Heart and Lung Transplantation: thirty-fifth adult heart transplantation report—2018; focus theme: multiorgan transplantation. *J Heart Lung Transplant*. 2018;37(10):1155–1168.

Lund LH, Edwards LB, Kucheryavaya AY, et al. The registry of the International Society for Heart and Lung Transplantation: thirty-first official adult heart transplant report—2014. *J Heart Lung Transplant*. 2014;33(10):996–1008.

Rossano JW, Cherikh WS, Chambers DC, et al. The international thoracic organ transplant registry of the International Society for Heart and Lung Transplantation: twenty-first pediatric heart transplantation report—2018; focus theme: multiorgan transplantation. *J Heart Lung Transplant*. 2018;37(10):1184–1195.

B.2. How would you premedicate this patient? Why?

Patients should be transported to the operating room with oxygen supplementation. Caution should be exercised with sedative or narcotic premedication. Sedation may blunt the patient's respiratory and sympathetic drive and can lead to hypoxemia, hypercapnia, and even hypotension. Antibiotic prophylaxis often is achieved with 1 to 2 g of cephazolin or 1 g vancomycin.

Jhaveri R, Tardiff B, Stanley TE III. Anesthesia for heart and lung transplantation. *Anesthesiol Clin North Am*. 1994;12:729–747.

C. Intraoperative Management

C.1. What anesthetic equipment and monitors would you set up? Why?

Anesthetic equipment includes a ventilator/anesthesia machine, airway and intubation setup, fluid/blood warmer, forced air warming blanket, ultrasound for central line insertion, extracorporeal bypass machine (CPB machine), and inhaled NO delivery and monitoring system. Ultrasound may also be useful for arterial line insertion due to the nature of nonpulsatile flow with LVADs. All invasive lines are placed with meticulous attention to sterile technique and under titrated sedation with supplemental oxygen. Monitors include a five-lead ECG, pulse oximeter, noninvasive blood pressure cuff, capnography, urinary

catheter, temperature probe(s), and peripheral nerve stimulator. At least one large-bore peripheral IV may be very useful if bleeding becomes excessive during the case. Routinely, a pulmonary arterial (PA) catheter is inserted via the right internal jugular vein for pre-CPB, post-CPB, and postoperative measurement of PA pressure, PVR, and CO. The PA catheter is withdrawn back to about a 20-cm position before cardiectomy. TEE also is very useful in the intraoperative management of the pretransplant and posttransplant periods. Electroencephalogram (EEG) monitoring may be applied before induction to assess depth of anesthesia. In some centers, cerebral oximetry also would be used as a monitor of cerebral oxygen delivery.

C.2. What is the role of transesophageal echocardiography (TEE)?

The echocardiographer can provide feedback to the surgeon regarding overall function of the transplanted heart. In particular, wall motion abnormalities, end-diastolic volume, valvular function, and the presence of anomalies (such as a patent foramen ovale) not appreciated prior to transplant can be assessed. Of particular interest is RV function assessment. TEE also may be useful in the assessment of surgical anastomosis. Specifically, the main PA anastomosis should be evaluated for stenosis. The long-axis view of the left atrium is composed of recipient and donor tissue and may appear large. If excessive tissue is present, an acquired cor triatriatum may develop. In addition, the stored images of the baseline function of the transplanted heart may serve as a useful comparison after transplantation.

Bryan AJ, Barzilai B, Kouchoukos NT. Transesophageal echocardiography and adult cardiac operations. *Ann Thorac Surg*. 1995;59:773–779.

Denault AY, Couture P, Buithieu J, et al, eds. *Transesophageal Echocardiography: A Perioperative Transdisciplinary Approach*. New York:

Taylor & Francis Group; 2005:471–480.

Romano P, Mangion JM. The role of intraoperative transesophageal echocardiography in heart transplantation. *Echocardiography*. 2002;19(7, pt 1):599–604.

Suriani RJ. Transesophageal echocardiography during organ transplantation. *J Cardiothorac Vasc Anesth*. 1998;12:686–694.

C.3. Describe the induction and maintenance of anesthesia.

It is important to time the anesthesia induction and surgery carefully to achieve CPB at the time of donor heart arrival in order to minimize ischemia time, particularly for a resternotomy patient. Prompt securing of the airway may be required because the recipient is not always properly fasted for transplantation surgery; however, a rapid sequence induction needs to be balanced against the risk of hemodynamic compromise. The patient can be anesthetized with a variety of agents in combination, such as midazolam and fentanyl or sufentanil, which are titrated based on hemodynamic status and level of consciousness. Muscle relaxation may be achieved with pancuronium, rocuronium, or other nondepolarizing agents. In particular, when an LVAD is not in place, succinylcholine is usually not used because of the concern about bradycardia during induction because blood pressure in pre–heart transplant recipients often is heart rate dependent. The maintenance phase uses a balanced anesthetic technique. Volatile agents (sevoflurane or isoflurane) are combined with fentanyl or sufentanil, midazolam, and muscle relaxation as needed. Nitrous oxide is avoided due to its effect on PVR.

Previously, transplant centers used aprotinin as an antifibrinolytic therapy. However, Bayer, the manufacturer of aprotinin, removed it from the market after concerns of increased mortality surfaced in clinical trials. Tranexamic acid is now used in many cardiac transplant centers.

At times, a great deal of bleeding can occur during the reopening the sternum after a previous LVAD insertion. Blood should be readily available to deal with what at times is the most challenging part of the case for anesthetic management.

Fergusson DA, Hébert PC, Mazer CD, et al. A comparison of aprotinin and lysine analogues in high-risk cardiac surgery. *N Engl J Med*. 2008;358:2319–2331.

Karkouti K, Beattie SW, Dattilo KM, et al. A propensity score case-control comparison of aprotinin and tranexamic acid in high-transfusion-risk cardiac surgery. *Transfusion*. 2006;46:327–338.

Mangano DT, Tudor IC, Dietzel C. The risk associated with aprotinin in cardiac surgery. *N Engl J Med*. 2006;354:353–365.

C.4. How would you manage this patient during cardiopulmonary bypass (CPB)?

The anesthetic management of CPB in these patients is often not different from that in nontransplant cardiac surgery patients except that rewarming usually is prolonged because of the profound cooling of the donor heart and the prolonged ischemic time. Early in the perfusion, mixed venous oxygen desaturation and metabolic acidosis must be corrected. The fluid balance, hematocrit, electrolyte composition, and serum glucose must be monitored closely. During CPB, anesthesia maintenance includes narcotic supplementation, an inhalational agent, and/or a benzodiazepine. Once a cardiac rhythm has been established and the anastomosis of the pulmonary artery is completed, the patient is placed in the head-down position for air evacuation from the left side of the heart. An isoproterenol infusion (1 to 5 μg per minute) may be considered to improve contractility and to increase heart rate to about 90 to 110 beats per minute. The heart may be externally paced via epicardial leads. Milrinone and NO are also often started as the patient is weaned from CPB to augment the RV function. The anesthesia team should be prepared for significant bleeding after separation from CPB,

especially in cases where VADs have been in place.

D. Postoperative Management

D.1. What are the early postoperative complications?

The early postoperative complications include the following:

- RV failure/pulmonary hypertension
- Denervated heart
- Bleeding
- Early graft failure

D.2. What are the mechanisms of early right ventricular (RV) failure?

Right-sided heart failure is an important cause of posttransplant morbidity and mortality. It has a diverse number of causes related to both increases in flow and resistance across the pulmonary vascular bed. One prime cause is long-standing elevation in left ventricular pressure, leading to an increase in pulmonary pressure and vasoconstriction. This pulmonary vasoconstriction may become fixed over time, compromising RV function after transplant. However, a normal preoperative PVR does not rule out the potential for RV failure posttransplant. Poor organ preservation and CPB also can have deleterious effects on graft ventricular function.

Iyer A, Kumarasinghe G, Hicks M, et al. Primary graft failure after heart transplantation. *J Transplant*. 2011;2011:175768.

Stobierska-Dzierzek B, Awad H, Michler RE. The evolving management of acute right-sided heart failure in cardiac transplant recipients. *J Am Coll Cardiol*. 2001;38:923–931.

Wagner F. Monitoring and management of right ventricular function following cardiac transplantation. *Appl Cardiopulm Pathophysiol*. 2011;15:220–229.

D.3. How would you treat RV failure following heart transplantation?

RV failure is associated with dilation, ischemia, and poor contractility. This can result in a shift of the ventricular septum to the left, with a reduction in left ventricular filling and reduced CO. Basic therapeutic goals are to maintain adequate coronary perfusion, optimize oxygen delivery, prevent further distention of the right ventricle by judicious use of fluids, minimize myocardial oxygen consumption, and reduce PVR to decrease RV afterload.

Phosphodiesterase inhibitors, such as milrinone, which have systemic and pulmonary vasodilatory effects in addition to positive inotropy, are particularly useful. Prostacyclin (PGI_2), isoproterenol (1 to 5 μg per minute), dobutamine, and nitrates also have been used with success to treat RV failure. However, vasodilator use can often be accompanied by arterial hypotension, requiring the administration of vasopressors to maintain adequate coronary perfusion. Inhaled NO also is widely used as a selective pulmonary vasodilator in severe pulmonary hypertension and RV failure. Sildenafil also can be considered when trying to reduce PVR. It should be remembered that the simple management of avoiding hypoxia and hypercarbia will help avoid elevated PVR.

In severe cases of refractory RV failure, posttransplant mechanical support should be considered, including IABP, right VAD (RVAD), or ECMO.

Costanzo MR, Dipchand A, Starling R, et al. The International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients. *J Heart Lung Transplant*. 2010;29:914–956.

Granton J, Moric J. Pulmonary vasodilators—treating the right ventricle. *Anesthesiol Clin*. 2008;26:337–353.

Stobierska-Dzierzek B, Awad H, Michler RE. The evolving management of acute right-sided heart failure in cardiac transplant recipients. *J Am Coll Cardiol*. 2001;38:923–931.

Wagner F. Monitoring and management of right ventricular function following cardiac transplantation. *Appl Cardiopulm Pathophysiol*. 2011;15:220–229.

D.4. How does inhaled nitric oxide (NO) work as a selective pulmonary vasodilator?

The advantage of inhaled NO as a pulmonary vasodilator lies mainly in the fact that its smooth muscle relaxant effect is limited to the pulmonary vasculature—the in vivo half-life of inhaled NO is only a few seconds. Therefore, it has little effect on the systemic circulation, unlike IV vasodilators, such as nitroprusside, nitroglycerin, prostaglandins, and calcium channel blockers. Furthermore, inhaled NO selectively causes vasodilation in ventilated lung units, thus decreasing ventilation/perfusion ($\dot{V}/\dot{Q}$) mismatch and shunt. Inhaled NO (1 to 20 ppm) can result in significant decreases in PA pressure, PVR, and central venous pressure (CVP) while increasing mean arterial pressure, CO, and arterial oxygenation. In addition, a TEE-documented alteration of the ventricular septal shift with a significant reduction in RV chamber and tricuspid valvular annulus size can be seen.

Girard C, Durand PG, Vedrinne C, et al. Inhaled nitric oxide for right ventricular failure after heart transplantation. *J Cardiothorac Vasc Anesth*. 1993;7:481–485.

Haddad H, Isaac D, Legare JF, et al. Canadian Cardiovascular Society Consensus Conference update on cardiac transplantation 2008: executive summary. *Can J Cardiol*. 2009;25(4):197–205.

Konstadt S. Nitric oxide: has it progressed from molecule of the year to wonder drug of the decade? *J Cardiothorac Vasc Anesth*. 1995;9:625–626.

D.5. What is the pathophysiology of the denervated heart?

Following cardiac transplantation, the cardiac plexus is interrupted, and the heart is denervated. The recipient atrium remains innervated but hemodynamically unimportant, whereas the donor atrium is denervated and is responsible for the electrophysiologic responses of the transplanted heart. The ECG often contains two P waves. The denervated heart retains its

intrinsic control mechanisms, which include the Frank-Starling mechanism and intact α- and β-adrenoreceptor responses to circulating catecholamines. This denervated heart lacks the ability to respond acutely to hypovolemia or hypotension with reflex tachycardia but responds to stress primarily by an increase in stroke volume. This reflects dependence of the donor heart sinus node on direct stimulation by endogenously released catecholamines and the absence of control via neural mechanisms. Interestingly, however, some studies have demonstrated reinnervation within a year after transplantation. This has led to symptoms of angina pectoris when ischemia develops in the transplanted heart.

Cheng DC, Ong DD. Anaesthesia for non-cardiac surgery in heart-transplanted patients. *Can J Anaesth*. 1993;40:981–986.

Kobashigawa JA. Postoperative management following heart transplantation. *Transplant Proc*. 1999;31:2038–2046.

D.6. What are the common cardiac dysrhythmias following heart transplant?

A wide variety of arrhythmias can occur in the heart transplant recipient. Early on in the course of recovery from heart transplant, bradyarrhythmia is common and often self-limited. However, this underscores the utility of epicardial pacemaker placement at the time of surgery. The spectrum of other arrhythmias includes premature ventricular complexes, atrioventricular (AV) blockade, and supraventricular tachycardia. In fact, 5% to 24% of heart transplant recipients suffer from atrial fibrillation. The causes of arrhythmia include surgical disruption of normal conduction pathways and the sinus node, denervation, rejection, and coronary allograft vasculopathy. The presence of persistent arrhythmia, in particular ventricular in origin, is associated with increased long-term morbidity and mortality.

Chang HY, Lo LW, Feng AN, et al. Long-term follow-up of arrhythmia characteristics and clinical outcomes in heart transplant patients. *Transplant Proc*. 2013;45(1):369–375.

Stecker EC, Sterlich KR, Chugh SS, et al. Arrhythmias after orthotopic heart transplantation. *J Card Fail*. 2005;11(6):464–472.

D.7. What are the causes of posttransplant bleeding?

Perioperative bleeding is a significant contributor to mortality following heart transplantation. The causes of posttransplant bleeding are anastomosis leaks and coagulopathy. Immediately before weaning from CPB with the heart filled, the posterior anastomosis is carefully checked again by the surgeon for "water-tightness" because leaks in this area are more difficult and riskier to repair later. A coagulopathy, or what some term "medical bleeding," often results from a combination of mechanisms, including inadequate heparin reversal, dilution of platelets and coagulation factors, hypothermia, and CPB effects on fibrinolysis, platelet function, and factor activation. In addition, those patients with a VAD in place before transplant are at particular risk for perioperative hemorrhage, possibly exacerbated by the development of a von Willebrand syndrome.

Bourge RC, Naftel DC, Costanzo-Nordin MR, et al. Pretransplantation risk factors for death after heart transplantation: a multi-institutional study. *J Heart Lung Transplant*. 1993;12:549–562.

Diaz-Martin A, Escoresca-Ortega AM, Hernandez-Caballero C, et al. Considerations regarding major bleeding after cardiac transplantation. *Transplant Proc*. 2010;42:3204–3205.

Uriel N, Pak SW, Jorde UP, et al. Acquired von Willebrand syndrome after continuous-flow mechanical device support contributes to a high prevalence of bleeding during long-term support and at the time of transplantation. *J Am Coll Cardiol*. 2010;56(15):1207–1213.

Wegner JA, DiNardo JA, Arabia FA, et al. Blood loss and transfusion requirements in patients implanted with a mechanical circulatory support device undergoing cardiac transplantation. *J Heart Lung Transplant*. 2000;19:504–506.

D.8. How would you treat posttransplant bleeding?

Prevention of potential causes of bleeding is key. The use of antifibrinolytics is a strategy, especially if re-do sternotomy is to be undertaken. Avoidance of excessive crystalloid in the prebypass period may reduce the dilutional component of coagulopathy. Maintaining normothermia with forced air warming devices and fluid warmers also is imperative. When bleeding is evident in the postoperative period, the judicious use of packed red blood cells, fresh frozen plasma, and platelets is a starting point. If hemorrhage is not responsive to conservative measures, disseminated intravascular coagulopathy must be ruled out. If serum fibrinogen is low (less than 1.5 g per L), then the use of cryoprecipitate should be considered. Although not routine, desmopressin (0.3 μg per kg) also may have a role in refractory cases. Finally, recombinant factor VIIa has been used successfully to treat hemorrhaging in cardiac transplant patients. However, the risk of thrombosis needs to be weighed against the risk of ongoing bleeding, and consultation with a hematologist is advisable before administration. It always should be remembered that bleeding that is excessive and not clearly secondary to coagulopathy warrants surgical reexploration.

Costanzo MR, Dipchand A, Starling R, et al. The International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients. *J Heart Lung Transplant*. 2010;29:914–956.

Kogan A, Berman M, Kassif Y, et al. Use of recombinant factor VII to control bleeding in a patient supported by right ventricular assist device after heart transplantation. *J Heart Lung Transplant*. 2005;24:347–349.

D.9. What are the causes of early graft failure?

Graft failure, primary and nonspecific, is the most common cause of death in the first 30 days after heart transplant. Etiologies include biventricular failure, RV failure often due to high PVR, flow-limiting coronary stenosis, and hyperacute rejection.

Luckraz H, Goddard M, Charman SC, et al. Early mortality after cardiac transplantation: should we do better? *J Heart Lung Transplant*. 2005;24:401–405.

Lund LH, Edwards LB, Kucheryavaya AY, et al. The registry of the International Society for Heart and Lung Transplantation: thirty-first official adult heart transplant report—2014. *J Heart Lung Transplant*. 2014;33(10):996–1008.

D.10. How would you manage this patient in the intensive care unit?

Within the first 30 days, posttransplant graft failure (primary and nonspecific), multiorgan failure, and non-CMV infection are the most common causes of death at 39%, 18%, and 12.7%, respectively. Early management goals include prevention of infection and rejection, treatment of bleeding and dysrhythmias, cardiovascular support, and avoidance of elevated PA pressures. If possible, one should aim to wean the patient from the ventilator and extubate within 24 hours. In order to facilitate oxygenation and weaning, strict supervision of fluid balance and body weight is required. Immunosuppression often is achieved with a cocktail of medications, including steroids (methylprednisolone followed by prednisone), a calcineurin inhibitor (e.g., tacrolimus), and an antiproliferative agent (e.g., mycophenolate mofetil). Some patients may benefit from induction therapy using interleukin-2 (IL-2) antagonists and/or polyclonal antibodies, for example, highly sensitized patients, those with reactive donor-specific antigens, or those with renal dysfunction on tacrolimus-delaying immunosuppression strategies. It should be noted that a significant number of centers no longer routinely administer induction immunosuppression with good results. Secondary to immunosuppression, patients sometimes are covered with ganciclovir for CMV prophylaxis.

Blasco LM, Parameshwar J, Vuylsteke A. Anaesthesia for noncardiac surgery in the heart transplant recipient. *Curr Opin Anaesthesiol*. 2009;22:109–113.

Costanzo MR, Dipchand A, Starling R, et al. The International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients. *J Heart Lung Transplant*. 2010;29:914–956.

Lund LH, Edwards LB, Kucheryavaya AY, et al. The registry of the International Society for Heart and Lung Transplantation: thirty-first official adult heart transplant report—2014. *J Heart Lung Transplant*. 2014;33(10):996–1008.

Taylor DO. Cardiac transplantation: drug regimens for the 21st century. *Ann Thorac Surg*. 2003;75:S72–S78.

E. Subsequent Noncardiac Surgery

The patient recovers successfully following heart transplant. However, 2 years postoperatively, he fractures his left radius after a fall. He then presents for open reduction and internal fixation of the fracture.

E.1. How would you monitor this patient?

This patient should be monitored like for nontransplant patients undergoing similar procedures. Smooth and safe anesthesia is contingent upon careful preoperative assessment, which may reduce the need for invasive monitoring with all its attendant risks. Adequate preload must be attained preoperatively and intravascular volume status maintained intraoperatively because these patients are often “preload dependent.” Monitors in the given case should include an ECG, noninvasive blood pressure cuff, capnometer, and peripheral oxygen saturation probe, and if a general anesthetic is delivered, a temperature probe, agent-specific gas monitor, and a neuromuscular stimulator should be used. For cases with potential for blood loss and fluid shifts, however, additional intraoperative monitors, including an arterial line, central venous line, pulmonary artery catheter, and TEE, should be considered. Postoperatively, increased attention should be paid to preload status, renal function, and prevention of infection. Immunosuppressants should be continued postoperatively and their blood levels should be monitored.

Cheng DC, Ong DD. Anaesthesia for non-cardiac surgery in heart-transplanted patients. *Can J Anaesth*. 1993;40:981–986.

Choudury M. Post-cardiac transplant recipient: Implications for anaesthesia. *Indian J Anaesth*. 2017;61(9):768–774.

E.2. What type of anesthetic is best for the heart-transplanted patient?

In a series of 86 heart-transplanted recipients, 18 returned for 32 noncardiac surgical procedures. The anesthetic breakdown included 18 neurolept-anesthesia cases, 12 general anesthesia cases with a combination of N_2O/O_2/narcotic/relaxant and low doses of volatile agents, and 2 spinal cases. The patients had normal requirements of IV and inhalational agents, muscle relaxants, and local anesthetics. There was no prolonged action of any anesthetic agents. Generally, the choice of general or regional anesthesia does not affect postoperative outcome in heart-transplanted recipients undergoing subsequent noncardiac surgery.

Blasco LM, Parameshwar J, Vuylsteke A. Anaesthesia for noncardiac surgery in the heart transplant recipient. *Curr Opin Anaesthesiol*. 2009;22:109–113.

Cheng DC, Ong DD. Anaesthesia for non-cardiac surgery in heart-transplanted patients. *Can J Anaesth*. 1993;40:981–986.

E.3. What anesthetic technique would you choose for this patient?

This patient could safely receive a general anesthetic or a regional blockade of his brachial plexus for the upcoming surgery. No anesthetic technique has been shown to be superior as long as preload is maintained.

Cheng DC, Ong DD. Anaesthesia for non-cardiac surgery in heart-transplanted patients. *Can J Anaesth*. 1993;40:981–986.

E.4. Do you need to use a muscarinic antagonist with cholinesterase inhibitors to reverse the muscle

relaxant in heart-transplanted patients?

Although it does not compromise other hemodynamic parameters, neostigmine has been shown to produce a dose-dependent decrease in heart rate in heart-transplanted patients. A muscarinic antagonist should be administered simultaneously with cholinesterase inhibitors to block the cardiac and muscarinic side effects because slow development of cardiac reinnervation may be possible.

Ashary N, Kaye AD, Hegazi AR, et al. Anesthetic considerations in the patient with a heart transplant. *Heart Dis*. 2002;4:191–198.

Backman SB, Fox GS, Stein RD, et al. Neostigmine decreases heart rate in heart transplant patients. *Can J Anaesth*. 1996;43:373–378.

Bjerke RJ, Mangione MP. Asystole after intravenous neostigmine in a heart transplant recipient. *Can J Anaesth*. 2001;48(3):305–307.

Wilson RF, Christensen BV, Olivari MT, et al. Evidence for structural sympathetic reinnervation after orthotopic cardiac transplantation in humans. *Circulation*. 1991;83:1210–1221.

E.5. What are the anesthetic implications for heart-transplanted patients?

The anesthetic implications for heart-transplanted patients include the following:

- Denervated heart
- Allograft rejection
- Infection due to immunosuppression
- Drug interaction
- Allograft coronary artery disease
- Hypertension
- Renal dysfunction
- Immunosuppression-related malignancy

Ashary N, Kaye AD, Hegazi AR, et al. Anesthetic considerations in the patient with a heart transplant. *Heart Dis*. 2002;4:191–198.

Cheng DC, Ong DD. Anaesthesia for non-cardiac surgery in heart-transplanted patients. *Can J Anaesth*. 1993;40:981–986.

Ejtehadi F, Carter S, Evans L, et al. General anaesthesia and emergency surgery in heart transplant recipient. *Case Rep Surg*. 2015;2015:256465.

E.6. What is the significant implication of the denervated heart?

The denervated heart retains its intrinsic control mechanisms, which include the Frank-Starling mechanism, impulse formation and conductivity, and responsiveness to circulating catecholamines in the form of increased heart rate and contractility. However, the normal respiratory variations or response to carotid sinus massage and Valsalva maneuvers are absent. At rest, the heart rate reflects the intrinsic rate of depolarization of the donor sinoatrial node and, in the absence of any vagal tone, is faster than normal at about 90 to 100 beats per minute. The heart rate shows minimal response to drugs, such as muscle relaxants (pancuronium), anticholinergics (atropine, glycopyrrolate, and scopolamine), cholinesterase inhibitors (neostigmine, edrophonium, pyridostigmine, physostigmine), digoxin, nifedipine, phenylephrine, or nitroprusside, but will respond to isoproterenol, ephedrine, dopamine, and epinephrine.

Cardiac dysrhythmias may occur in heart-transplanted patients. Atrial, and less frequently ventricular, tachyarrhythmias are common. Bradyarrhythmia therapy in these patients should be a direct β-adrenergic stimulating agent (epinephrine, isoproterenol). Medications used to treat tachyarrhythmias (calcium channel blockers, β-blockers) need to be used with caution due to their negative inotropic effects.

Ashary N, Kaye AD, Hegazi AR, et al. Anesthetic considerations in the patient with a heart transplant. *Heart Dis*. 2002;4:191–198.

Blasco LM, Parameshwar J, Vuylsteke A. Anaesthesia for noncardiac surgery in the heart transplant recipient. *Curr Opin Anaesthesiol*. 2009;22:109–113.

Chang HY, Lo LW, Feng AN, et al. Long-term follow-up of arrhythmia characteristics and clinical outcomes in heart transplant patients. *Transplant Proc*. 2013;45(1):369–375.

Jurgens PT, Aquilante CL, Page RL II, et al. Perioperative management of cardiac transplant recipients undergoing noncardiac surgery: unique challenges created by advancements in care. *Semin in Cardiothorac Vasc Anesth*. 2017;21(3):235–244.

Stein KL, Darby JM, Grenvik A. Intensive care of the cardiac transplant recipient. *J Cardiothorac Anesth*. 1988;2:543–553.

E.7. What is the significance of allograft rejection?

Most rejection episodes occur in the first 6 months posttransplant. These patients can present with fever, malaise, arrhythmias, and shortness of breath. Hemodynamic compromise is considered a late sign of rejection. The gold standard for diagnosis is endomyocardial biopsy. Rejection episodes are treated primarily with steroids; however, more severe forms may require more aggressive immunosuppression with antithymocyte antibodies or plasmapheresis. The type of therapy is guided by symptom severity and the type of rejection (cellular mediated vs. antibody mediated).

Costanzo MR, Dipchand A, Starling R, et al. The International Society of Heart and Lung Transplantation guidelines for the care of heart transplant recipients. *J Heart Lung Transplant*. 2010;29:914–956.

Kobashigawa JA. Postoperative management following heart transplantation. *Transplant Proc*. 1999;31:2038–2046.

E.8. What is the significance of infection in these patients?

Immunosuppressive drugs are continued indefinitely in heart-transplanted patients, and infection remains a major cause of death, with 10% of mortality 5 years posttransplant secondary to non-CMV infections. Early postoperative bacterial infections (e.g., mediastinitis) and opportunistic infections (e.g., CMV, *Pneumocystis jirovecii*, *Toxoplasma*) are of great concern. Invasive monitoring techniques and all forms of instrumentation should be kept to the minimum consistent with safe anesthesia. Attention to sterile technique should be paramount. Intubation via the orotracheal route is preferable to the nasotracheal route

because the latter is associated with infection by diphtheroids and staphylococcal organisms from the nasopharynx and skin.

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Shaw IH, Kirk AJB, Conacher ID. Anaesthesia for patients with transplanted hearts and lungs undergoing non-cardiac surgery. *Br J Anaesth*. 1991;67:772–778.

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E.9. What are the significant implications of drug interactions?

Chronic steroid treatment may result in an abnormal stress response; so, patients should receive perioperative steroid coverage. Azathioprine has been reported to antagonize the competitive neuromuscular blocking drugs due to its phosphodiesterase-inhibiting properties; therefore, larger doses of relaxants may be required. In experimental animals, cyclosporine infusions have been shown to potentiate the neuromuscular blocking effects of atracurium and vecuronium. A single dose of cyclosporine may also result in a prolonged duration of action of both barbiturates and narcotics.

Ashary N, Kaye AD, Hegazi AR, et al. Anesthetic considerations in the patient with a heart transplant. *Heart Dis*. 2002;4:191–198.

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Rančić NK, Vavić NN, Kovačević AM, et al. Drug-drug interactions of tacrolimus. *Hosp Pharmacol*. 2015;2(3):291–296.

E.10. What is cardiac allograft vasculopathy (CAV)? Why

is this important?

The transplanted heart is vulnerable to an accelerated process of coronary atherosclerosis called CAV. Between the 1st and 10th year posttransplant, over 40% of patients develop CAV. It is characterized by concentric intimal proliferation and diffuse narrowing along the coronary vessel. The etiology is likely multifactorial with both immunologic and nonimmunologic factors. Traditional risk factors, such as pretransplant coronary artery disease, diabetes, and hyperlipidemia, put a recipient at risk for CAV. Donor characteristics, such as advanced donor age and mechanism of donor death, are also risk factors. The type of immunosuppression regime, CMV infections, and episodes of rejection also impact CAV development.

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Kobashigawa JA. Postoperative management following heart transplantation. *Transplant Proc*. 1999;31:2038–2046.

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E.11. What is the significant implication of posttransplant hypertension?

After 5 years, 91% of surviving patients have developed hypertension. Calcineurin inhibitors often are cited as a causative factor. Current therapy may consist of a calcium channel blocker such as diltiazem. However, care must be taken because diltiazem may increase cyclosporine serum levels. Nifedipine has a tendency to cause significant vasodilatation and may be tolerated poorly in these patients. When necessary, an ACE inhibitor may be added. Because cardiac responsiveness during exercise is dependent on circulating catecholamines, β-blockers often are avoided after heart transplantation.

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Valerio R Jr, Durra O, Gold ME. Anesthetic considerations for an adult heart transplant recipient undergoing noncardiac surgery: a case report. *AANA Journal*. 2014:82(4):293–299.

E.12. What is the significant implication of renal dysfunction?

Renal dysfunction is found in 51.1% of recipients at 5 years. Due to the nephrotoxic effects of calcineurin inhibitors, serum creatinine concentrations often gradually increase after cardiac transplantation, with 6.7% of recipients requiring dialysis after 10 years. Anesthetic drugs that are excreted mainly by renal clearance should be avoided if renal function is compromised. Also, one needs to be mindful of medications that may further compromise renal function, such as nonsteroidal anti-inflammatory drugs (NSAIDs).

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Lindenfeld JA, Page RL II, Zolty R, et al. Drug therapy in the heart transplant recipient: part III: common medical problems. *Circulation*. 2005;111:113–117.

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Miller LW. Long-term complications of cardiac transplantation. *Prog Cardiovasc Dis*. 1991;33:229–282.

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E.13. What types of malignancy are found in recipients?

Chronic immunosuppression puts patients at risk for the development of cancer. After 10 years, 27.7% of survivors have some form of malignancy. The vast majority are skin cancers, whereas a much smaller percentage suffers from posttransplant lymphoproliferative disorder. Malignancies account for 23% of the deaths 5 years after transplant.

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E.14. Is ambulatory surgery appropriate for heart transplant recipients?

Unfortunately, there is a paucity of information about ambulatory surgery in heart transplant recipients. In addition, the choice of anesthetic technique seems to have no influence on outcome. Regardless, these patients should be seen in preadmission clinics before the day of surgery and have appropriate screening tests done preoperatively, including but not limited to, an assessment of complete blood count, electrolytes, renal function, ECG, and an accurate blood pressure measurement. They also should be evaluated by the cardiology transplant service, and if any concern is raised, further testing, such as echocardiography, coronary angiography, or endomyocardial biopsy, may be suggested. Recommendations also should be obtained from the cardiac transplant service regarding perioperative antibiotic prophylaxis and immunosuppression.

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in the heart transplant recipient. *Curr Opin Anaesthesiol*. 2009;22:109–113.

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14 Ischemic Heart Disease and Noncardiac Surgery

Christopher Szabo and
Manuel Fontes

A 72-year-old man is scheduled for right hemicolectomy for colon cancer. Past history reveals a myocardial infarction (MI) 5 months ago and placement of a right coronary second-generation drug-eluting stent (DES). He also has type 2 diabetes mellitus. He is currently treated with dual antiplatelet therapy (DAPT) (aspirin and clopidogrel), atenolol, diltiazem, metformin, losartan, and an occasional sublingual nitroglycerin (NTG).

A. Medical Disease and Differential Diagnosis

1. What are the preoperative predictors for major adverse cardiac events (MACE) perioperatively?
2. What are the determinants of myocardial oxygen demand? How are they measured clinically?
3. What factors determine myocardial oxygen supply?
4. What is the mechanism of perioperative myocardial ischemia and MI?
5. What is the incidence of perioperative reinfarction for noncardiac surgery?

6. State the perioperative medical therapy you would employ to reduce the incidence of myocardial ischemia.
7. Based on his MI, would you recommend that the surgery be postponed for a certain period of time? If so, why?
8. you recommend that this elective colectomy be postponed if the patient underwent placement of a right coronary artery, second-generation DES, and is taking aspirin and clopidogrel (Plavix)?

B. Preoperative Evaluation and Preparation

1. How would you evaluate the patient's cardiac condition? What laboratory tests would you like to order?
2. Would you recommend further cardiac testing or coronary revascularization before surgery?
3. How would you classify the cardiac risk according to the type of surgery?
4. What is the role of exercise or pharmacologic stress test for this patient?
5. Would you discontinue any medication before surgery?
6. How would you premedicate this patient?
7. Is there a role for α_2-agonist in premedication?

C. Intraoperative Management

1. What are the intraoperative predictors for perioperative MACE?
2. How would you monitor the patient in the operating room?
3. What electrocardiogram (ECG) leads would you monitor? Why lead V_5?
4. Would you use a pulmonary artery catheter (PAC)?
5. Would you use transesophageal echocardiography (TEE) as a monitor?
6. Is regional anesthesia better than general anesthesia for patients with cardiac disease?

7. How will you induce general anesthesia?
8. Would you induce anesthesia with etomidate? Why?
9. What is the best choice of anesthetic agents for maintenance of anesthesia? Why?
10. You notice a new 3-mm ST-segment depression in lead V_5. How would you treat it?
11. Would you give prophylactic intravenous NTG to prevent myocardial ischemia?
12. What is the significance of tight control of the heart rate intraoperatively?
13. When would you extubate the trachea in this patient? What could you do to prevent hypertension and tachycardia during extubation and emergence?

D. Postoperative Management

1. What are the postoperative predictors of perioperative MACE?
2. How would you control postoperative pain?
3. Is postoperative anemia associated with adverse cardiac outcome?
4. Is postoperative hypothermia associated with postoperative myocardial ischemia?
5. How would you make a diagnosis of perioperative MI (PMI)?
6. How would you manage the patient with a suspected PMI?

A. Medical Disease and Differential Diagnosis

A.1. What are the preoperative predictors for major adverse cardiac events (MACE) perioperatively?

PMI is one of the most important predictors of short- and long-term mortality and morbidity associated with noncardiac surgery. Therefore, the prevention of PMI can improve postoperative outcomes. Numerous risk indices and predictors for perioperative cardiac morbidity (PCM) have been published

over the last 40 years.

In 1999, Lee et al. revised the Goldman Cardiac Risk Index, now called the Revised Cardiac Risk Index (RCRI), utilizing six independent predictors of cardiac risk, which are as follows:

- High-risk type of surgery
- History of ischemic heart disease (IHD)
- History of congestive heart failure (CHF)
- History of cerebrovascular disease
- Preoperative treatment of diabetes mellitus with insulin
- Preoperative serum creatinine greater than 2.0 mg per dL

They concluded that the rate of major cardiac complications (MI, pulmonary edema, ventricular fibrillation, and primary cardiac arrest) with 0, 1, 2, and more than or equal to 3 predictors were 0.5%, 1.3%, 4%, and 9%, respectively.

The 2014 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines categorize the patients into two groups: *low risk* and *elevated risk* based on the presence of clinical risk factors and risk of surgical procedures. Patients with less than 1% chance of MACE are categorized as low risk, whereas patients with cumulative risk of MACE more than 1% are categorized as elevated risk. Patients who have two or more RCRIs are considered at elevated risk. The other two indices are the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) Myocardial Infarction and Cardiac Arrest (MICA), and American College of Surgeons NSQIP Surgical Risk Calculator (http://riskcalculator.facs.org). Both are readily available on the web to evaluate patient risk. The European Society of Cardiology (ESC) guidelines define surgical risk procedures as low- (<1%), intermediate- (1% to 5%), and high-risk procedures (>5%). By ACC guideline criteria, this patient will be considered elevated risk, scheduled to undergo an intermediate-risk procedure (by ESC guidelines).

Although the new guidelines do not categorize the clinical

predictors of MACE into major, intermediate, and minor factors, in addition to the RCRI mentioned earlier, the following clinical factors significantly increase the risk of perioperative MACE.

- Unstable coronary syndromes: Acute (MI ≤7 days before examination) or recent MI (>7 days but ≤1 month) with evidence of important ischemic risk by clinical symptoms or noninvasive study. A study using discharge summaries demonstrated that the postoperative MI rate decreased substantially as the length of time from MI to operation increased (0 to 30 days = 32.8%; 31 to 60 days = 18.7%; 61 to 90 days = 8.4%; and 91 to 180 days = 5.9%), as did the 30-day mortality rate. However, risk was modified by coronary intervention. It is suggested that more than 60 days should elapse after MI before noncardiac surgery is undertaken in the *absence* of coronary intervention.
- Unstable or severe angina (Canadian class III): marked limitation of ordinary physical activity; walking one to two blocks on the level and climbing one flight of stairs in normal conditions at normal pace; and Canadian class IV: inability to carry on any physical activity without discomfort—anginal syndrome may be present at rest
- Decompensated heart failure (HF): Patients with active HF have significantly higher risk of postoperative death than do patients with coronary artery disease (CAD). Survival after surgery for those with a left ventricular ejection fraction (LVEF) less than 30% is significantly worse than for those with an LVEF ≥30%.
- Severe valvular disease (severe aortic stenosis [AS] with valve area less than 1 cm^2 or symptomatic) have a 2 to 3 times higher risk of 30-day mortality than patients without AS. Similar observations have been noted for severe mitral stenosis. Left-sided regurgitant lesions convey increased cardiac risk during noncardiac surgery but are better tolerated

than stenotic valvular disease.

- Significant arrhythmias, such as high-grade atrioventricular block, Mobitz type II atrioventricular block, third-degree heart block, or unanticipated symptomatic supraventricular and ventricular arrhythmias, increase operative risk. Risk of other supraventricular and ventricular arrhythmias seems to be lower than reported before.
- Age is considered a risk factor especially when it is associated with frailty. However, its exact role still needs to be defined further.
- Pulmonary hypertension: Patients with pulmonary artery hypertension are at an increased risk of cardiopulmonary complications after noncardiac surgery. Mortality rates of 4% to 26% and cardiorespiratory morbidity rates of 6% to 42% have been reported.

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Fleisher LA. The value of preoperative assessment before noncardiac surgery in the era of value-based care. *Circulation*. 2017;136:1769–1771.

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Kristensen SD, Knuuti J, Saraste A, et al. 2014 ESC/ESA guidelines on non-cardiac surgery: cardiovascular assessment and management: the Joint Task Force on Non-Cardiac Surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). *Eur Heart J*. 2014;35:2383–2431.

Lee TH, Marcantonio ER, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation*. 1999;100:1043–1049.

A.2. What are the determinants of myocardial oxygen demand? How are they measured clinically?

The three major determinants of myocardial oxygen demand are (1) myocardial left ventricular (LV) wall tension (LV preload and afterload), (2) cardiac contractility, and (3) heart rate.

A.3. What factors determine myocardial oxygen supply?

The factors determining myocardial oxygen supply include cardiac output, arterial oxygen content, heart rate, aortic diastolic pressure, LV end-diastolic pressure, patency of coronary arteries, and coronary vascular tone.

A.4. What is the mechanism of perioperative myocardial ischemia and MI?

Myocardial ischemia occurs whenever myocardial oxygen supply does not match myocardial oxygen demand. Intraoperative ischemia can be precipitated by increases in myocardial oxygen demand caused by tachycardia, hypertension, anemia, surgical stress, sympathomimetic drugs, or discontinuation of β-blockers. Potential etiologies for decreased supply include hypotension, tachycardia, increased cardiac filling pressures, anemia, hypoxemia, and decreased cardiac output. In one study, ischemia occurred (67%) at the end of anesthesia or immediately after surgery, during a period characterized by high sympathetic output, hypercoagulability, hypertension, and tachycardia. Ischemia in this period is usually silent, with only ST-segment depression as a marker. And in at least one-third of the patients, this ST-segment depression goes unnoticed. Hypotension is strongly correlated with PMI. In addition, internal factors such as acute coronary artery thrombosis and spasm may also play a role.

PMI is one of the most important predictors of short- and long-term morbidity and mortality associated with noncardiac surgery. Unfortunately, the exact nature of PMI remains uncertain and a subject of debate and controversy. The interaction between morphologic and functional factors is

unpredictable. Some older pathologic and angiographic studies suggested that the etiology of PMI resembles that in the nonsurgical setting, that is, plaque rupture was the cause of PMI in 50% of the cases. However, newer analysis suggests that myocardial oxygen supply/demand imbalance predominates in the first 3 to 4 postoperative days and patients suffer PMI from demand ischemia. In PMI, the severity of underlying coronary artery stenosis does not necessarily predict the infarct territory. The high incidence of histologically confirmed transmural infarctions seems to be contradictory to the ECG finding of almost exclusively non–Q-wave PMIs. On the other hand, the presence of subendocardial PMIs is consistent with a myocardial oxygen supply/demand mismatch being the main trigger of myocardial injury. However, myocardial oxygen supply/demand mismatch and plaque rupture are not mutually exclusive mechanisms, and PMIs may be developed by different mechanisms at different locations in the same patient.

Most PMIs occur early after surgery (0 to 4 days) and 90% occur within 7 days, are asymptomatic, of the non–Q-wave type (60% to 100%), and are commonly preceded by ST-segment depression rather than ST-segment elevation. Long duration (single duration >20 to 30 minutes or cumulative duration >1 to 2 hours intraoperatively or postoperatively) rather than just the presence of postoperative ST-segment depression seems to be the important factor associated with adverse cardiac outcome.

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Cheung C, Martyn A, Campbell N, et al. Predictors of intraoperative hypotension and bradycardia. *Am J Med*. 2015;128:532–538.

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Subramaniam B, Subramaniam K. Not all perioperative myocardial infarctions can be prevented with preoperative revascularization. *Anesthesiology*. 2010;112:524–526.

A.5. What is the incidence of perioperative reinfarction for noncardiac surgery?

The risk assessment for noncardiac surgery of patients with CAD is based on the time interval between the MI and surgery. Using a discharge database of more than half million patients, it was shown that postoperative MI rate for the recent MI cohort decreased substantially as the length of time from MI to operation increased (0 to 30 days = 32.8%; 31 to 60 days = 18.7%; 61 to 90 days = 8.4%; and 91 to 180 days = 5.9%), as did 30-day mortality (0 to 30 days = 14.2%; 31 to 60 days = 11.5%; 61 to 90 days = 10.5%; and 91 to 180 days = 9.9%). MI within 30 days of an operation was associated with a highest risk of postoperative MI. However, with improvements in perioperative care, this difference has become blurred. The importance of the timing of the MI in relation to the proposed surgical procedure may no longer be valid in the era of thrombolytics, angioplasty, and risk stratification. Although many patients with a history of an MI may continue to have myocardium at risk, others may not. If a stress test does not indicate residual myocardium at risk, the likelihood of reinfarction is low. The current AHA/ACC guidelines for

perioperative cardiovascular evaluation suggests that more than 60 days should elapse after MI, before noncardiac surgery is undertaken in the *absence* of coronary intervention. Landesberg et al. reported that early mortality after PMI ranges from 3.5% to 25% and is higher among patients with marked troponin elevation compared with patients with minor troponin elevation (0% to 7%). This is in contrast to older data that reported a very high incidence of mortality.

A 2016 study, using information in a large administrative database of United States hospital admissions (2004 to 2013), found a 3% incidence of major adverse cardiovascular and cerebrovascular events (in-hospital, all-cause death, acute MI, or acute ischemic stroke). These events were most common after vascular, thoracic, and transplant surgery.

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A.6. State the perioperative medical therapy you would employ to reduce the incidence of myocardial ischemia.

β-Adrenergic Antagonists (Esmolol, Atenolol,

Metoprolol, Bisoprolol)

β-Blockers reduce myocardial oxygen consumption, improve coronary blood flow by prolonging diastolic perfusion period, improve supply/demand ratio, stabilize cellular membranes, improve oxygen dissociation from hemoglobin (Hgb), and inhibit platelet aggregation. *β*-Blockers suppress perioperative tachycardia and appear most efficacious in preventing perioperative myocardial ischemia. In view of their beneficial effects, prophylactic use of *β*-blocker to decrease PMI has been explored in many trials. Mangano et al. reported a beneficial effect of atenolol in a randomized double-blind, placebo-controlled trial on overall survival and cardiovascular morbidity in noncardiac surgery patients with or at risk for CAD. Poldermans et al. reported that the *β*-blocker, bisoprolol, reduced the perioperative incidence of death from cardiac causes and nonfatal MI in vascular surgical patients with known CAD. Bisoprolol, started before noncardiac surgery (30 days), can substantially reduce perioperative cardiac complications in all but the highest risk patients. However, results of subsequent large trials have not shown efficacy of high-dose, acutely administered, perioperative *β*-blockers to reduce overall mortality in patients undergoing noncardiac surgery. The largest of these trials, the PeriOperative ISchemic Evaluation (POISE) study, did show better perioperative *cardiac* outcomes with *β*-blocker use; however, *increased mortality* and stroke rate also was noted in the *β*-blocker group. ACC/AHA has conducted a systematic review on the topic, and the main findings are (1) preoperative use of *β*-blockers was associated with a reduction in cardiac events in the studies examined, but few data support the effectiveness of preoperative administration of *β*-blockers to reduce the risk of surgical death; and (2) a clear association exists between *β*-blocker administration and adverse outcomes, such as bradycardia and stroke. Currently, the only class I

recommendation for perioperative β-blockers use is to continue their use in the patients who are already on β-blockers (class I, level of evidence B). β-Blockers can be used in patients with elevated risk, such as ischemia during preoperative stress testing or in patients with three or more RCRI risk factors (class IIb, level of evidence B). Although there are some differences between the ESC and the AHA guidelines, both recommend that if β-blockers are used for prophylactic purposes, they should be slowly titrated (2 to 7 days prior to elective surgery) and acute administration of high-dose β-blockers in high-risk patients undergoing low-risk surgery is not recommended (class III, level of evidence B).

α_2-Adrenergic Agonist (Clonidine)

α_2-Agonist (clonidine) decrease sympathetic outflow, blood pressure, and heart rate. Although older studies suggested possible beneficial effect of α_2-agonists, the most recent POISE-2 trial that enrolled 10,010 patients did not show any statistically beneficial effect of clonidine. Clonidine did not reduce the rate of 30-day risk of all-cause death or nonfatal MI in patients with or at risk of atherosclerotic disease who were undergoing noncardiac surgery. Clonidine did increase the rate of nonfatal cardiac arrest and clinically important hypotension. Based on the ACC/AHA guidelines, α_2-agonists for prevention of cardiac events are not recommended in patients who are undergoing noncardiac surgery (class III, level of evidence B).

Nitrovasodilators (Nitroglycerin, Isosorbide Dinitrate)

Nitrates are associated with the following:

- Decreased LV preload (low dose)
  - Systemic venous dilation
  - Pulmonary arterial bed dilation

  - Pulmonary vein dilation
  - Decreased LV filling pressure
  - Decrease in LV diastolic compressive forces
  - Decreased LV diastolic chamber size
- Decreased LV afterload (high dose)
  - Decreased systolic pressure
  - Decreased systemic vascular resistance
  - Decreased aortic impedance
- Coronary circulation
  - Coronary artery and arteriolar dilation (high dose)
  - Spasm reversal or prevention
  - Stenosis dilation
  - Increased collateral flow
  - Improvement of regional subendocardial ischemia

NTG, one of the oldest antianginal therapies, has had very few trials in noncardiac surgery to evaluate its role in perioperative ischemia reduction. However, there are no significant studies within the past 10 years examining the effect of prophylactic NTG on perioperative myocardial ischemia. Prior studies yielded conflicting results, were small (<50 patients), and not blinded. A recent meta-analysis by Zhao et al. further strengthened the position of not using prophylactic nitrates for noncardiac surgery.

The current guidelines do not recommend the use of prophylactic intravenous NTG to reduce myocardial ischemia undergoing noncardiac surgery.

Calcium Channel Blockers (Verapamil, Diltiazem, Nifedipine, Nicardipine)

Calcium channel blockers reduce myocardial oxygen demand by depression of myocardial contractility and dilation of coronary and collateral vessels, which improves blood flow. However, the most important effect may be the prevention of sympathetically

mediated coronary vasoconstriction.

A meta-analysis of perioperative calcium channel blockers in noncardiac surgery (11 studies involving 1,007 patients) showed significantly reduced ischemia and postoperative supraventricular tachycardia. The beneficial effects were mostly due to the use of diltiazem, whereas the use of a 1,4-dihydropyridine (DHP) derivative nifedipine was associated with ischemia. Another study in 1,000 patients having acute or elective aortic aneurysm surgery showed that DHP calcium channel blocker use was independently associated with an increased incidence of perioperative mortality. The use of short-acting DHP, in particular nifedipine capsules, should be avoided. The AHA makes no specific recommendations for the prophylactic use of calcium channels blockers. Routine use of calcium channel blockers to reduce the risk of perioperative cardiovascular complications is not recommended (class III).

Aspirin

Aspirin (acetylsalicylic acid) inhibits platelet aggregation by blocking the production of thromboxane A_2. Observational data suggest that preoperative withdrawal of aspirin increases thrombotic complications. However, the value of aspirin in nonstented patients in preventing ischemic complications is uncertain. The Pulmonary Embolism Prevention (PEP) trial, which randomized 13,356 patients undergoing hip surgery to 160 mg aspirin or placebo, did not show benefit of aspirin. The POISE-2 trial randomized 10,010 patients who were undergoing noncardiac surgery to aspirin 200 mg or placebo. Aspirin did not have a protective effect for MACE or death in patients either continuing aspirin or starting aspirin. However, aspirin increased the chance of major bleeding especially in the first 5 days after surgery. This is supported by a previous large meta-analysis, including 41 studies in 49,590 patients, which compared

periprocedural withdrawal versus bleeding risks of aspirin, concluded that the risk of bleeding complications was increased by 1.5 but that aspirin did not lead to higher severity levels of bleeding complications. Initiation of aspirin is not beneficial in patients undergoing elective noncardiac, noncarotid surgery who have not had previous coronary stenting, unless the risk of ischemic events outweighs the risk of surgical bleeding.

Statins

Statins are primarily used for their lipid-lowering effects and are widely prescribed in patients with or at risk for IHD. Statins also induce coronary plaque stabilization by decreasing lipid oxidation, inflammation, matrix metalloproteinase, and cell death. These so-called non-lipid or pleiotropic effects may prevent plaque rupture and subsequent MI in the perioperative period. A meta-analysis of 223,010 patients from 12 retrospective and 3 prospective trials showed that statins reduced mortality significantly by 44% in noncardiac surgery and by 59% in vascular surgery. The accumulated evidence to date suggests a protective effect of perioperative statin use on cardiac complications during noncardiac surgery. Most of the data come from observational studies. The time of initiation of statin therapy and the duration of therapy are often unclear in the observational trials. Randomized clinical trials are limited in patient numbers and types of noncardiac surgery. Both the AHA and ESC guidelines recommend continuing statin therapy for patients currently taking statins and scheduled for noncardiac surgery (class I). ESC recommends that preoperative statin therapy should be considered in patients undergoing vascular surgery and initiated at least 2 weeks before surgery.

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Devereaux PJ, Sessler DI, Leslie K, et al. Clonidine in patients undergoing

noncardiac surgery. *N Engl J Med*. 2014;370(16):1504–1513.

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Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;64:e77–e137.

Kristensen SD, Knuuti J, Saraste A, et al. 2014 ESC/ESA guidelines on non-cardiac surgery: cardiovascular assessment and management: the Joint Task Force on Non-Cardiac Surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). *Eur Heart J*. 2014;35:2383–2431.

Mangano DT, Layug EL, Wallace A, et al. Effect of atenolol on mortality and cardiovascular morbidity after noncardiac surgery. *N Engl J Med*. 1996;335:1713–1720.

Poldermans D, Boersma E, Bax JJ, et al; for Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group. The effect of bisoprolol on perioperative mortality and myocardial infarction in high-risk patients undergoing vascular surgery. *N Engl J Med*. 1999;341:1789–1794.

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Schouten O, Boersma E, Hoeks SE, et al. Fluvastatin and perioperative events in patients undergoing vascular surgery. *N Engl J Med*. 2009;361:980–989.

Wallace AW, Galindez D, Salahieh A, et al. Effect of clonidine on cardiovascular morbidity and mortality after non-cardiac surgery. *Anesthesiology*. 2004;101:284–293.

Zhao N, Xu J, Singh B, et al. Nitrates for the prevention of cardiac morbidity and mortality in patients undergoing non-cardiac surgery. *Cochrane Database Syst Rev*. 2016;(8):CD010726.

A.7. Based on his MI, would you recommend that the surgery be postponed for a certain period of time? If so, why?

The arbitrary delaying of a surgical procedure is not supported by the ACC/AHA guidelines. According to these guidelines, an acute MI (≤7 days) or recent MI (>7 days but ≤1 month) with

evidence of important ischemic risk by clinical symptoms or noninvasive study is a major predictor of PMI. A discharge database analysis showed that patients with a recent MI who were revascularized before surgery had an approximately 50% decreased rate of reinfarction (5.1% vs. 10.0%). Thirty-day (5.2% vs. 11.3%) and 1-year mortality (18.3% vs. 35.8%) was also decreased in the revascularized patients. Current management of MI provides for risk stratification during the convalescence period. If a recent stress test does not indicate residual myocardium at risk, the likelihood of reinfarction after noncardiac surgery is low. Although there are no adequate clinical trials on which to base firm recommendations, it appears reasonable to wait 60 days after MI in a nonrevascularized patient to perform elective surgery due to the decrease in incidence of fatal arrhythmias and ventricular rupture after this period of time. However, the guidelines do not recommend that routine coronary revascularization be performed before noncardiac surgery exclusively to reduce perioperative cardiac events (class III, level of evidence B).

Devereaux PJ, Chan MT, Alonso-Coello P, et al. Association between postoperative troponin levels and 30-day mortality among patients undergoing noncardiac surgery. *JAMA*. 2012;307:2295–2304.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130:e278–e333.

A.8. Would you recommend that this elective colectomy be postponed if the patient underwent placement of a right coronary artery, second-generation DES, and is taking aspirin and clopidogrel (Plavix)?

Coronary stents are particularly predisposed to stent thrombosis. Typically, stent thrombosis is defined according to the time of

occurrence: (1) acute, within 24 hours; (2) early, 2 to 30 days; (3) late, >1 month to <1 year; and (4) very late, >1 year. Both bare metal stents (BMS) and DES are predisposed to stent thrombosis and require prolonged DAPT after stent placement: BMS, 4 to 6 weeks; DES, 12 months; and stents placed after acute coronary syndrome (ACS), 12 months. Second-generation DESs may require a minimum of 6 months DAPT after stent placement; however, data in this area is still evolving.

The cumulative incidence of noncardiac surgery after coronary stenting is more than 10% at 1 year and more than 20% at 2 years. Patients with a coronary stent pose a special challenge in the perioperative period. Bleeding is the major risk of continuing DAPT during the perioperative period. Surgical blood loss is increased 2.5% to 20% by aspirin alone and 30% to 50% by aspirin and clopidogrel—but with no increased risk of bleeding-related mortality, except during intracranial surgery. When surgery was performed within 180 days, discontinuation of DAPT was associated with an increased risk of stent thrombosis. Extremely high mortality rates (up to 20%) have been reported secondary to acute stent thrombosis if surgery is performed within weeks after coronary stenting with discontinuation of DAPT. Thus, the risks of stent thrombosis and bleeding should be balanced. Antiplatelet therapy should generally be continued throughout the perioperative period, except in cases where the risk of morbidity or mortality from bleeding significantly outweighs the risk of acute stent thrombosis, as in procedures likely to be associated with "major" blood loss or performed in a closed space.

Current recommendations for DAPT after percutaneous coronary intervention (PCI) with stenting (BMS) is that patients should take aspirin and other $P2Y_{12}$ platelet inhibitor (clopidogrel, prasugrel, ticagrelor) for at least 30 to 45 days to prevent restenosis and allow reendothelialization of the stent to

be completed. Therefore, it is prudent to postpone the elective surgery for a minimum of 30 days and ideally for up to 3 months after BMS implantation (ESC guidelines). Importantly, whenever possible, aspirin should be continued throughout surgery. A large meta-analysis, including 41 studies in 49,590 patients, which compared periprocedural withdrawal versus bleeding risks of aspirin, concluded that the risk of bleeding complications with aspirin therapy was increased by 50% but that aspirin did not lead to greater severity of bleeding complications. In subjects at risk of—or with proven—IHD, nonadherence/withdrawal of aspirin tripled the risk of MACE.

Although DES delays in-stent thrombosis, their major drawback is the need for prolonged DAPT by aspirin and $P2Y_{12}$ platelet inhibitors for at least 12 months. It is generally recommended that after DES implantation, elective surgery should not take place until after at least 6 months of continuous DAPT. Even after 6 months, patients should be sent for noncardiac surgery with continuation of at least aspirin therapy. If the risk of surgical delay is greater than risk of thrombosis, with the newer generation stents, the guidelines suggest to consider surgery between 3 and 6 months of DAPT. The patient should continue on aspirin (unless patient is scheduled for surgery associated with high risk of bleeding or consequence of bleeding) (**Fig. 14.1**). Typically, $P2Y_{12}$ platelet inhibitors should be stopped 5 days (clopidogrel, ticagrelor) or 7 days (prasugrel) before scheduled surgery and restarted as soon as possible.

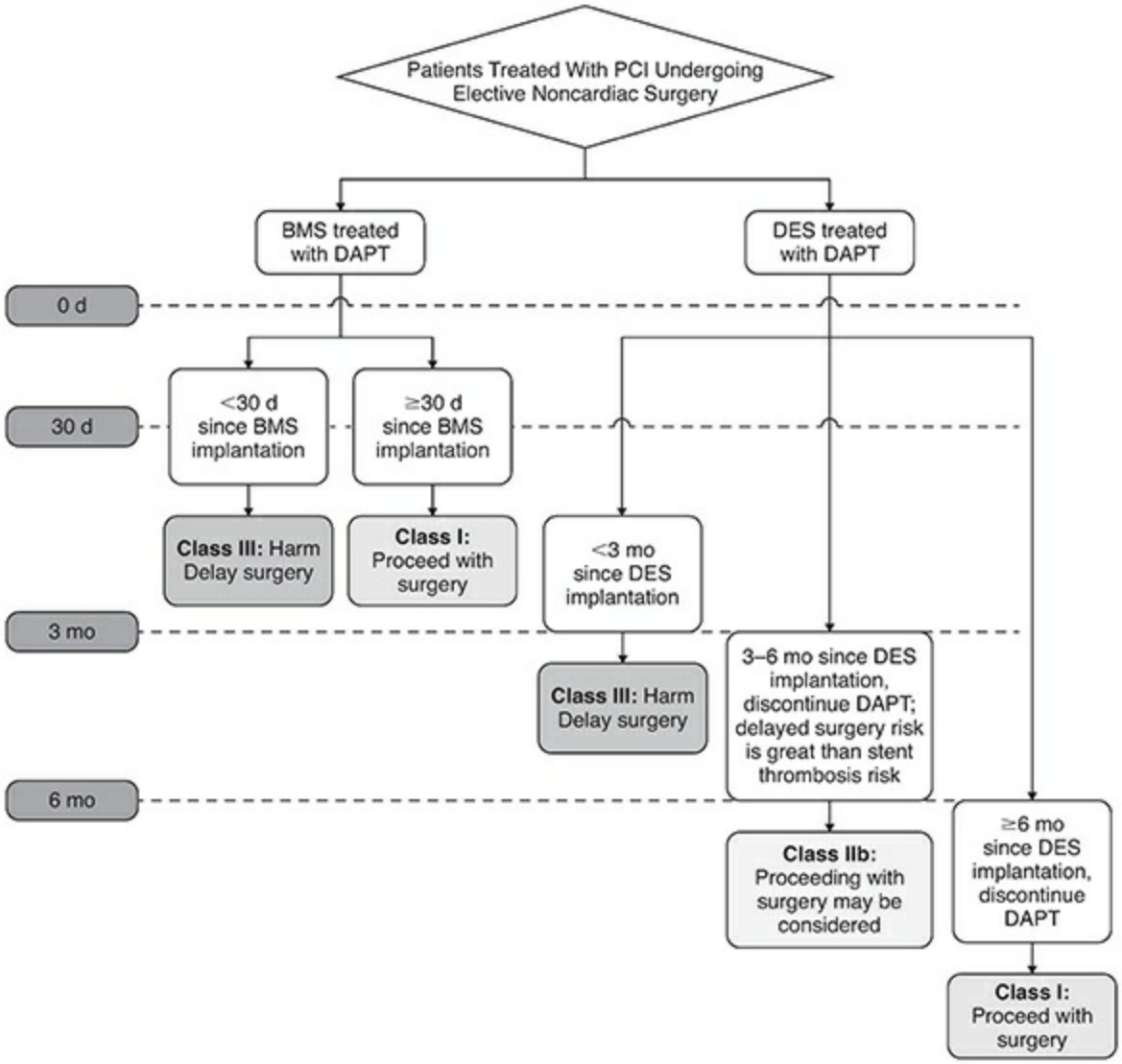


FIGURE 14.1. Treatment algorithm for timing of elective noncardiac surgery in patients with coronary stents. BMS, bare metal stents; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; PCI, percutaneous coronary intervention. (*Reprinted with permission from Levin GN, Bates ER, Bittle JA, et al. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines.* Circulation. *2016;134[10]:e123–e155.*)

In this patient, with a DES placed 5 months before surgery in the setting of ACS, the discontinuation of DAPT increases the risk of stent thrombosis. Furthermore, this is not high-risk surgery (laparoscopic colectomy), although risk of bleeding will be appreciably increased if patient is maintained on DAPT. This is a clinical situation where careful "case-by-case" consideration

is advisable and discussion between the anesthesiologist, the surgeon, and the treating cardiologist is recommended.

Barash P, Akhtar S. Coronary stents: factors contributing to perioperative major adverse cardiovascular events. *Br J Anaesth*. 2010;105(suppl 1):i3–i15.

Culkin DJ, Exaire EJ, Green D, et al. Anticoagulation and antiplatelet therapy in urological practice: ICUD/AUA review paper. *J Urol*. 2014;192:1026–1034.

Darvish-Kazem S, Gandhi M, Marcucci M, et al. Perioperative management of antiplatelet therapy in patients with a coronary stent who need noncardiac surgery: a systematic review of clinical practice guidelines. *Chest*. 2013;144(6):1848–1856.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;64:e77–e137.

Hawn MT, Graham LA, Richman JS, et al. Risk of major adverse cardiac events following noncardiac surgery in patients with coronary stents. *JAMA*. 2013;310(14):1462–1472.

Kristensen SD, Knuuti J, Saraste A, et al. 2014 ESC/ESA guidelines on non-cardiac surgery: cardiovascular assessment and management: the Joint Task Force on Non-Cardiac Surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). *Eur Heart J*. 2014;35:2383–2431.

Levin GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association task Force on Clinical Practice Guidelines: an update of the 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention, 2011 ACCF/AHA guideline for coronary artery bypass graft surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease, 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction, 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes, and 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery. *Circulation*. 2016;134:e123–e155.

Oprea AD, Popescu WM. Perioperative management of antiplatelet therapy. *Br J Anaesth*. 2013;111(suppl 1):i3–i17.

Stefanini GG, Holmes DR Jr. Drug-eluting coronary-artery stents. *N Engl J*

Med. 2013;368(3):254–265.

Vetter TR, Hunter JM Jr, Boudreaux AM. Preoperative management of antiplatelet drugs for a coronary artery stent: how can we hit a moving target? *BMC Anesthesiol*. 2014;14:73.

Vetter TR, Short RT III, Hawn MT, et al. Perioperative management of the patient with a coronary artery stent. *Anesthesiology*. 2014;121(5):1093–1098.

Wolf AM, Pucci MJ, Gabale SD, et al. Safety of perioperative aspirin therapy in pancreatic operations. *Surgery*. 2014;155(1):39–46.

B. Preoperative Evaluation and Preparation

B.1. How would you evaluate the patient's cardiac condition? What laboratory tests would you like to order?

The initial history, physical examination, and electrocardiographic assessment should focus on the identification of potentially serious cardiac disorders such as CAD (e.g., prior MI, angina pectoris), CHF, and symptomatic arrhythmias and valvular heart disease. In addition to identifying the presence of preexisting heart disease, it is essential to define disease severity, stability, and prior treatment. For patients who have been revascularized, it is also important to determine the presence or absence of any coronary syndrome/symptoms after coronary revascularization and any results of stress test results post-MI/revascularization. The initial history should also elicit presence of other components of RCRI; that is, history of cerebrovascular accident (stroke or transient ischemic attack), presence of diabetes, or renal insufficiency.

This patient is an insulin-dependent diabetic. Diabetes is associated with a two- to fourfold increase in the risk of developing CAD. The risk of an MI in patients with diabetes and no evidence of CAD match that of patients without diabetes who have had a previous MI. In patients with CAD and diabetes, the mortality rate can be up to 70% in 10 years. In addition, patients

will have a worse outcome for any CAD manifestation.

Other factors that help determine cardiac risk include functional capacity, age, comorbid conditions (peripheral vascular disease, chronic pulmonary disease, and pulmonary hypertension), and type of surgery (vascular procedures and prolonged, complicated thoracic, abdominal, and head and neck procedures are considered elevated risk procedures) (see section B.3). Poor exercise tolerance has been associated by some with twofold higher odds for postoperative complications. It is a good indicator of global cardiopulmonary functional status of the patient, which can have direct impact on perioperative outcomes.

For this patient, the preoperative laboratory workup should include an Hgb/hematocrit (Hct), prothrombin time, partial thromboplastin time, electrolytes, creatinine, blood urea nitrogen, and an ECG. The preoperative ECG may provide a useful baseline standard against which to measure changes in the postoperative period. The value of the preoperative 12-lead ECG is likely to increase with the risk of the surgical procedure, particularly for patients with known coronary heart disease, arrhythmias, peripheral arterial disease, cerebrovascular disease, or other significant structural heart disease.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;64:e77–e137.

B.2. Would you recommend further cardiac testing or coronary revascularization before surgery?

Successful perioperative evaluation and treatment of cardiac patients undergoing noncardiac surgery requires careful teamwork and communication between patient, primary care physician, cardiologist, anesthesiologist, and surgeon. In

general, indications for further cardiac testing and treatment are the same as those in the nonoperative setting, but their timing is dependent on factors such as the urgency of noncardiac surgery, the patient's risk factors, and specific surgical considerations. Preoperative testing should be limited to circumstances in which the results will affect patient treatment and outcomes. A conservative approach to the use of expensive tests and treatments is recommended. Coronary revascularization before noncardiac surgery to enable the patient to "get through" the noncardiac procedure is inappropriate. However, in a high-risk subset of patients, such as those with left main or severe multivessel disease, severe AS, and ejection fraction less than 20%, revascularization or valve replacement may be indicated. Currently, there is overwhelming agreement that aggressive medical management to provide myocardial protection during the perioperative period is a very important element in the reduction of perioperative cardiovascular complications.

Several studies have suggested that a stepwise approach to the assessment of CAD is both efficacious and cost-effective. The patient sustained MI 5 months ago and was managed with a DES and is scheduled for hemicolectomy, which is considered an intermediate-risk procedure. If the patient has more than 4 metabolic equivalents (METs) of physical activity (e.g., washing dishes, climbing one flight of stairs with a bag of groceries, walking on level ground at 4 miles per hour) without chest pain or shortness of breath, if no new cardiac symptoms are present since the revascularization, and if the resting ECG showed no new changes compared to 5 months ago, the patient can undergo anesthesia and surgery without further testing. If any of these factors are positive, then stress test is recommended. If the ischemic area is small, surgery is permissible with recommended aggressive medical therapy management. If the ischemic area is moderate to large, with a suspicion of new or

severe coronary stenosis, cardiac catheterization is recommended before the planned surgery. Also see Chapter 10, section B.2, **Figure 10.2**.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;64:e77–e137.

McFalls EO, Ward HB, Moritz TE, et al. Coronary-artery revascularization before elective major vascular surgery. *N Engl J Med*. 2004;351:2795–2804.

B.3. How would you classify the cardiac risk according to the type of surgery?

Surgery-specific cardiac risk of noncardiac surgery is related to two important factors: the type of surgery and the degree of hemodynamic stress associated with the procedure(s). The duration and intensity of coronary and myocardial stressors can be helpful in estimating the likelihood of perioperative cardiac events, particularly for emergency surgery. Surgery-specific risk for noncardiac surgery can be stratified as high, intermediate, and low.

- *High-risk* surgery (cardiac risk >5%) includes major emergency surgery, particularly in the elderly; aortic and other major vascular surgery; peripheral vascular surgery; and anticipated prolonged procedures associated with large fluid shifts and/or blood loss.
- *Intermediate-risk* procedures (cardiac risk <5%) include carotid endarterectomy, head and neck surgery, intraperitoneal and intrathoracic, orthopedic, and prostate surgery. Endovascular aortic stent procedures also are included in this category.
- *Low-risk* procedures (cardiac risk <1%) include endoscopic and superficial procedures, cataract surgery, and breast surgery.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;64:e77–e137.

B.4. What is the role of exercise or pharmacologic stress test for this patient?

The aim of functional cardiovascular testing is to elicit evidence and severity of CAD by subjecting the heart to physiologic stress. Noninvasive diagnostic testing must be used judiciously. Ideally, testing should be accurate, add useful information to the overall risk assessment, and avoid unnecessary delays in surgery. Noninvasive tests of myocardial perfusion are classified by the type of stress applied to elicit transient and reversible ischemia or by the mode of detecting the ischemic area. Myocardial stress can be induced by exercise (e.g., treadmill), by a pharmacologic agent that increases heart rate and myocardial contraction (e.g., dobutamine, atropine), or by a pharmacologic agent that can cause redistribution of coronary blood flow (e.g., dipyridamole). Physiologic exercise provides an estimate of functional capacity, provides blood pressure and heart rate response, and detects myocardial ischemia through ECG ST-segment or other imaging technique changes. The accuracy of exercise ECG varies significantly among studies. Preexisting ST-segment abnormalities at rest, especially in precordial leads V_5 and V_6, hamper reliable ST-segment analysis. However, most of these studies are dated and do not reflect the current protocols and contemporary practice. Meta-analysis of studies using treadmill testing in vascular surgery patients showed a rather low sensitivity (74%) and specificity (69%) to detect myocardium at risk, comparable with daily clinical practice.

A significant fraction of the high-risk population cannot

exercise to an adequate level and will require pharmacologic stress testing. Pharmacologic stress testing with dobutamine stress echocardiography (DSE), dipyridamole/adenosine/regadenoson myocardial perfusion imaging with thallium-201, and/or technetium-99m and rubidium-82 can be used in patients undergoing noncardiac surgery who cannot perform exercise to detect stress-induced myocardial ischemia and CAD. Reversible wall motion abnormalities on echocardiography or reversible perfusion defects on radionuclide imaging suggest reversible ischemia.

The myocardial perfusion imaging and DSE before vascular surgery predict PMI or death, with a positive predictive value of only 12% to 14% and a negative predictive value of 88% and 94%, respectively. However, the large majority of the cited thallium studies involved older planar imaging technology that is no longer used. The newer nuclear imaging studies have higher sensitivity for detecting IHD, and patients with normal scans have excellent prognosis. Cardiovascular magnetic resonance (CMR) imaging can also be used for detection of myocardial ischemia. Although its accuracy in assessment of myocardial ischemia is high, there is practically no data in the setting of preoperative risk stratification. Computed tomography can be used to detect coronary calcium, which reflects coronary atherosclerosis; however, currently, there is no data available in the setting of preoperative risk stratification.

Selection of the noninvasive stress test should be based primarily on patient characteristics, local availability, and expertise in interpretation. DSE is the preferred test if there is an additional question regarding valvular function or LV dysfunction.

Akhtar S. Ischemic heart disease. In: Hines RL, Marschall K, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:79–106.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;64:e77–e137.

B.5. Would you discontinue any medication before surgery?

Patients with CAD are usually on a variety of medications. All antianginal drugs, especially β-blockers and statins, should be continued up to the time of surgery. Sudden withdrawal of antianginal drugs may produce rebound tachycardia and hypertension that may precipitate acute myocardial ischemia or infarction.

Current management of hypertensive patients suggests the continuation of antihypertensive therapy up to the day of surgery. In particular, β-blockers, calcium channel blocker, and nitrates should be continued. There is continued controversy about withholding angiotensin-converting enzyme (ACE) inhibitors and angiotensin-2 receptor blockers (ARBs) 24 hours prior to surgery. Prolonged hypotension has been observed in patients who are undergoing general anesthesia and who have chronically been treated with ACE inhibitors. A meta-analysis demonstrated hypotension in 50% of patients taking ACE inhibitors or ARBs on the day of surgery but no change in cardiovascular outcomes such as death, MI, stroke, and renal failure. It is prudent to withhold ACE inhibitors and ARBs for 24 hours prior to surgical procedures involving major body fluid shifts on significant blood loss. If ACE inhibitors are withheld, it is important to restart them as soon as possible. Hypotension attributed to ACE inhibitors is frequently responsive to fluid and/or administration of sympathomimetic drugs, such as phenylephrine and ephedrine. If hypotension is refractory to these measures, treatment with vasopressin or its long-acting

analogue, terlipressin, may be effective.

Bertrand M, Godet G, Meersschaert K, et al. Should the angiotensin II antagonists be discontinued before surgery? *Anesth Analg*. 2001;92:26–30.

Rosenman DJ, McDonald FS, Ebbert JO, et al. Clinical consequences of withholding versus administering renin-angiotensin-aldosterone system antagonists in the preoperative period. *J Hosp Med*. 2008;3:319–325.

Turan A, You J, Shiba A, et al. Angiotensin converting enzyme inhibitors are not associated with respiratory complications or mortality after noncardiac surgery. *Anesth Analg*. 2012;114:552–560.

B.6. How would you premedicate this patient?

The classical teaching has been to adequately sedate the patient prior to bringing to the operating room to avoid anxiety-induced tachycardia and hypertension. Benzodiazepines are typically used for this purpose. However, benzodiazepines have been associated with delirium, especially in elderly patients. Indiscriminate use of benzodiazepines is discouraged and should only be used in selected patients.

Barr J, Fraser GL, Puntillo K, et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med*. 2013;41(1):263–306.

Maurice-Szamburski A, Auquier P, Viarre-Oreal V, et al. Effect of sedative premedication on patient experience after general anesthesia: a randomized clinical trial. *JAMA*. 2015;313(9):916–925.

B.7. Is there a role for α_2-agonist in premedication?

The α_2-agonists stimulate prejunctional α receptors and decrease norepinephrine release from prejunctional terminals, thereby decreasing noradrenergic central nervous system transmission, producing sedation, anxiolysis, and analgesia. Studies have shown that clonidine as a premedication reduces hypertension, tachycardia, and norepinephrine levels in patients undergoing aortic reconstruction. Clonidine also suppresses the normal postoperative increase in fibrinogen levels and antagonizes epinephrine-induced platelet aggregation. It has also been shown

to decrease intraoperative myocardial ischemia. A small study evaluating the prophylactic use of clonidine showed a significant reduction in intra- and postoperative myocardial ischemia when compared to placebo. However, a much larger POISE-2 trial did not show any difference in rate of death or nonfatal MI. The rate of nonfatal cardiac arrest and significant hypotension was increased in the clonidine group. Both ACC and ESC guidelines do not advocate prophylactic use of clonidine to decrease MACE, in patients scheduled for noncardiac surgery.

Devereaux PJ, Sessler DI, Leslie K, et al. Clonidine in patients undergoing noncardiac surgery. *N Engl J Med*. 2014;370(16):1504–1513.

Kristensen SD, Knuuti J, Saraste A, et al. 2014 ESC/ESA guidelines on non-cardiac surgery: cardiovascular assessment and management: the Joint Task Force on Non-Cardiac Surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). *Eur Heart J*. 2014;35:2383–2431.

Wallace AW, Galindez D, Salahieh A, et al. Effect of clonidine on cardiovascular morbidity and mortality after non-cardiac surgery. *Anesthesiology*. 2004;101:284–293.

C. Intraoperative Management

C.1. What are the intraoperative predictors for perioperative MACE?

Intraoperative Predictors

Classic intraoperative predictors for perioperative MACE include emergency surgery, major vascular surgery, and prolonged (>3 hours) thoracic or upper abdominal surgery. Among the dynamic predictors, both hypotension and tachycardia predict PCM. In a recent systematic review, the intraoperative predictors include a fall in mean arterial blood pressure >20 mmHg for >60 minutes, an increase in baseline systolic pressure >30%, or tachycardia in the recovery room

(>30 beats per minute from baseline) for >5 minutes. However, the most consistent factor that independently predicted greater risk of perioperative event was intraoperative blood transfusion. Most MIs occur early after surgery and are commonly associated with ST-segment depression. Prolonged duration of myocardial ischemia (>20 to 30 minutes or cumulative duration of >1 to 2 hours) seems to be the important factor associated with adverse cardiac outcome.

Biccard BM, Rodseth RN. What evidence is there for intraoperative predictors of perioperative cardiac outcomes? A systematic review. *Perioper Med (Lond)*. 2013;2:14.

Grocott MP, Dushianthan A, Hamilton MA, et al. Perioperative increase in global blood flow to explicit defined goals and outcomes following surgery. *Cochrane Database Syst Rev*. 2012;(11):CD004082.

Kheterpal S, O'Reilly M, Englesbe MJ, et al. Preoperative and intraoperative predictors of cardiac adverse events after general, vascular, and urological surgery. *Anesthesiology*. 2009;110(1):58–66.

Priebe HJ. Perioperative myocardial infarction—aetiology and prevention. *Br J Anaesth*. 2005;95:3–19.

Sprung J, Abdelmalak B, Gottlieb A, et al. Analysis of risk factors for myocardial infarction and cardiac mortality after major vascular surgery. *Anesthesiology*. 2000;93(1):129–140.

C.2. How would you monitor the patient in the operating room?

The patient should be monitored using the following American Society of Anesthesiologists standard guidelines:

- *ECG*—simultaneous leads V_5 and II
- *Blood pressure*—noninvasive automatic Doppler sphygmomanometer and an invasive arterial catheter
- *End-tidal carbon dioxide*—to determine continuous end-tidal CO_2 analysis
- *Oxygen saturation of arterial blood*—to assess arterial oxygenation
- *Fractional inspired oxygen concentration*—to determine

inspired fraction of oxygen

- *Respiratory rate*—which determined by multiple monitors
- *Availability of esophageal/bladder temperature probe*—to determine temperature changes

In addition to these monitors, this patient will also require the monitoring of urine output with a Foley catheter.

American Society of Anesthesiologists. *Standards for Basic Anesthetic Monitoring*. Schaumburg, IL: American Society of Anesthesiologists; 2005.

C.3. What electrocardiogram (ECG) leads would you monitor? Why lead V_5?

ECG ST-segment changes are most commonly used for detection of intraoperative myocardial ischemia. Multiple-lead ECG monitoring provides the best clinically available method of detecting perioperative ischemia, primarily by combining leads II, V_3, V_4, and V_5 (detection of ischemia is 80% with leads II/V_5 and 96% with leads II/V_4 and V_5).

Landesberg et al. were able to correlate the duration of ischemia observed in the ST-segment analysis of a continuously monitoring 12-lead ECG throughout the perioperative period with the incidence of postoperative MI. They also found that ischemia is transient even in patients who will develop an infarct.

Certain prerequisites must be met to use the ECG effectively:

- The diagnostic mode allows detection of ST-segment changes that are filtered out by the monitoring mode.
- The number of ECG leads and their location affects detection of ischemic events.
- Immediate availability of a hard copy of the ECG leads for more detailed analysis.
- Studies have reported that even trained observers recognize only 15% to 40% of electrocardiographic ischemic events

displayed on the monitor.

- The introduction of ST-segment trending helps as an early warning detection system but should not replace examination of the ECG printout.

Landesberg G, Beattie WS, Mosseri M, et al. Perioperative myocardial infarction. *Circulation*. 2009;119:2936–2944.

Landesberg G, Mosseri M, Wolf Y, et al. Perioperative myocardial ischemia and infarction: identification by continuous 12-lead electrocardiogram with online ST-segment monitoring. *Anesthesiology*. 2002;96:264–270.

London MJ, Hollenberg M, Wong MG, et al. Intraoperative myocardial ischemia: localization by continuous 12-lead electrocardiography. *Anesthesiology*. 1988;69:232–241.

C.4. Would you use a pulmonary artery catheter (PAC)?

Right heart catheterization is not recommended for monitoring patients for intraoperative ischemia. Large observational study and a randomized multicenter trial did not show benefit associated with the use of pulmonary artery catheterization after major noncardiac surgery. A meta-analysis of randomized controlled trials showed that the use of PAC neither increased mortality nor conferred any benefits to critically ill patients. A recent Cochrane review that included 13 studies (5,686 patients) concluded that use of a PAC did not alter the mortality and general intensive care unit (ICU) or hospital length of stay. PAC is a diagnostic and hemodynamic monitoring tool but not a therapeutic intervention. A number of studies report that PAC is an insensitive monitor for myocardial ischemia and should not be inserted with this as a primary indication.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;64:e77–e137.

Rajaram SS, Desai NK, Kalra A, et al. Pulmonary artery catheters for adult patients in intensive care. *Cochrane Database Syst Rev*. 2013;(2):CD003408.

C.5. Would you use transesophageal echocardiography (TEE) as a monitor?

TEE is a sensitive diagnostic method to detect new onset myocardial ischemia. The echocardiographic diagnosis of myocardial ischemia is based on the development of new regional wall motion abnormalities, decreased systolic wall thickening, and ventricular dilation. Usually, a cross-sectional view (transgastric mid-short axis) of the LV is imaged because this view displays the myocardial perfusion territories of the three major coronary arteries. TEE was found to be twice as predictive as ECG in identifying coronary artery bypass graft (CABG) patients who have an MI. In CABG patients, postbypass regional wall motion abnormalities were related to adverse clinical outcome.

However, practitioners should realize certain limitations of TEE. One, preintubation events are missed, as are the ischemic events that can occur frequently at the end of the surgery, when tachycardia and hypertension appear as part of the emergence from general anesthesia.

Notwithstanding TEE's limitations, ESC and the AHA guidelines recommend the use of TEE intraoperatively or perioperatively to determine the cause of an acute, persistent, and life-threatening hemodynamic abnormality (class IIa recommendation). However, its use as an ischemia monitor in noncardiac surgery is less validated and may only be considered in patients at high risk for developing myocardial ischemia who undergo major noncardiac surgery (class IIb recommendation by ESC). The routine use of intraoperative TEE during noncardiac surgery to screen for cardiac abnormalities or to monitor for myocardial ischemia is *not* recommended in patients without risk factors, or procedural risks for significant hemodynamic, pulmonary, or neurologic compromise.

American Society of Anesthesiologists and Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. Practice guidelines for perioperative transesophageal echocardiography. An updated report by the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. *Anesthesiology*. 2010;112(5):1084–1096.

Porter TR, Shillcutt SK, Adams MS, et al. Guidelines for the use of echocardiography as a monitor for therapeutic intervention in adults: a report from the American Society of Echocardiography. *J Am Soc Echocardiogr*. 2015;28(1):40–56.

C.6. Is regional anesthesia better than general anesthesia for patients with cardiac disease?

A number of studies in patients with cardiac disease have compared the effects of regional versus general anesthetics on the incidence of perioperative infarction, dysrhythmias, and CHF. No distinct advantage is apparent between them when considering PCM and mortality in patients undergoing peripheral vascular surgery. There is some evidence to support regional anesthesia over general anesthesia in an effort to optimize graft patency if the regional technique is extended into the postoperative period to provide neuraxial analgesia. The Multicenter Australian Study of Epidural Anesthesia (MASTER) trial randomized 915 patients undergoing major abdominal surgery to receive either combined general and epidural anesthesia/epidural analgesia or general anesthesia with opioid analgesia. Epidural anesthesia/analgesia did not decrease death or cardiovascular outcomes but modestly improved pulmonary outcomes compared with the general anesthesia group. A retrospective analysis, published in 2013, of nearly 400,000 patients undergoing total hip or knee arthroplasty, observed a significantly lower incidence of major morbidity and mortality in patients receiving neuraxial anesthesia. The most recent meta-analysis stated that, when epidurals or spinals were used to replace general anesthesia, there was a significant 29%

decrease in the risk of dying during surgery. In both situations, there was a significant decrease in the risk of pneumonia. However, neuraxial anesthesia failed to decrease the risk of MI. A 2011 Cochrane review meta-analysis of four studies examining neuraxial anesthesia versus general anesthesia for lower limb revascularization found an overall 4% MI rate in both groups. Thus, the current guidelines recommend that the choice of anesthesia is best left to the discretion of the anesthesia care team, which will consider the need for postoperative ventilation; pulmonary/neuromuscular comorbidities; cardiovascular effects, including myocardial depression; sympathetic blockade consequences; and dermatomal level of the procedure.

Barbosa FT, Jucá MJ, Castro AA, et al. Neuraxial anaesthesia for lower-limb revascularization. *Cochrane Database Syst Rev*. 2013;(7):CD007083.

Gogarten W, Vandermeulen E, Van Aken H, et al. Regional anaesthesia and antithrombotic agents: recommendations of the European Society of Anaesthesiology. *Eur J Anaesthesiol*. 2010;27:999–1015.

Leslie K, Myles P, Devereaux P, et al. Neuraxial block, death and serious cardiovascular morbidity in the POISE trial. *Br J Anaesth*. 2013;111:382–390.

Mauermann WJ, Shilling AM, Zuo Z. A comparison of neuraxial block versus general anesthesia for elective total hip replacement: a meta-analysis. *Anesth Analg*. 2006;103:1018–1025.

Memtsoudis SG, Sun X, Chiu YL, et al. Perioperative comparative effectiveness of anesthetic technique in orthopedic patients. *Anesthesiology*. 2013;118:1046–1058.

Norris EJ, Beattie C, Perler BA, et al. Double-masked randomized trial comparing alternate combinations of intraoperative anesthesia and postoperative analgesia in abdominal aortic surgery. *Anesthesiology*. 2001;95:1054–1067.

C.7. How will you induce general anesthesia?

It is essential to prevent hypotension, hypertension, and tachycardia, which can precipitate myocardial ischemia. Different induction techniques may be employed to achieve this goal. For example, while the patient is being preoxygenated,

fentanyl (up to 5 μg per kg) is given slowly to achieve drowsiness and to attenuate the sympathetic response to direct laryngoscopy and intubation of the trachea. Then, using lower doses of thiopental, propofol, or etomidate, unconsciousness is achieved. Succinylcholine or an intermediate duration nondepolarizing relaxant is administered to facilitate tracheal intubation. A few minutes before intubation, the use of a short-acting β-blocker (esmolol) could help to further attenuate the sympathetic response to intubation if necessary. Various techniques to induce general anesthesia have been used and tested in the past. High-dose opioid-based anesthesia was previously popularized because of cardiovascular stability; however, because of the need for prolonged postoperative mechanical ventilation and ICU stay, this technique is no longer considered the technique of choice. On the other hand, in patients undergoing cardiac surgery, volatile anesthetics have been shown to decrease troponin release, maintain LV function compared with propofol, midazolam, or balanced anesthesia technique with opioids. However, no real difference between volatile inhalational anesthesia versus intravenous anesthesia has been shown in randomized controlled trials or meta-analyses. A meta-analysis of more than 6,000 patients undergoing noncardiac surgery failed to demonstrate a difference in MI rates between patients who received volatile anesthesia and patients who received total intravenous anesthesia. The current AHA guidelines state that "use of either a volatile anesthetic agent or total intravenous anesthesia is reasonable for patients undergoing noncardiac surgery, and the choice is determined by factors other than the prevention of myocardial ischemia and MI."

Bignami E, Greco T, Barile L, et al. The effect of isoflurane on survival and myocardial infarction: a meta-analysis of randomized controlled studies. *J Cardiothorac Vasc Anesth*. 2013;27:50–58.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;64:e77–e137.

Martin DE, Rosenberg H, Aukburg SJ, et al. Low-dose fentanyl blunts circulatory responses to tracheal intubation. *Anesth Analg*. 1982;61:680–684.

C.8. Would you induce anesthesia with etomidate? Why?

Although etomidate has a negative inotropic effect on failing and nonfailing human heart muscle in doses that exceed the clinical dose, it appears to have a better hemodynamic profile than other commonly used induction agents, especially in the setting of coronary heart disease. With an induction dose of 0.2 to 0.3 mg per kg, there are minimal changes in heart rate, stroke volume, or cardiac output, and the blood pressure may decrease up to 15% because of decrease of systemic vascular resistance. Etomidate does suppress adrenocortical function, cause myoclonus, and prolong duration of seizure when used for electroconvulsive therapy.

Flood P, Rathmell JP, Shafer S. *Stoelting's Pharmacology and Physiology in Anesthetic Practice*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2015.

Haessler R, Madler C, Klasing S, et al. Propofol/fentanyl versus etomidate/fentanyl for the induction of anesthesia in patients with aortic insufficiency and coronary artery disease. *J Cardiothorac Vasc Anesth*. 1992;6:173–180.

Sprung J, Ogletree-Hughes ML, Moravec CS, et al. The effects of etomidate on the contractility of failing and nonfailing human heart muscle. *Anesth Analg*. 2000;91:68–75.

C.9. What is the best choice of anesthetic agents for maintenance of anesthesia? Why?

There appears to be no one best myocardial protective agent or technique. The knowledge of physiologic and pharmacologic effects of anesthetic agents in patients with cardiac disease will

allow flexibility in their selection. The use of inhalation versus opioid anesthesia in patients with cardiac disease is still debated, although the cardiovascular effects of both techniques and the physiologic differences between them are well documented. However, most outcome studies have not demonstrated a difference between the techniques. Studies of more than 3,000 noncardiac surgical patients with CAD have concluded that anesthetic type does not affect outcome.

Inhalation anesthetics are thought to possess ischemic preconditioning properties. Most investigations of anesthetic ischemic preconditioning have been done in patients undergoing cardiac surgery, but maybe there are potential beneficial effects in the high-risk cardiac patients undergoing noncardiac surgery as well. However, none of the trials to date were powered to evaluate MI or death as an outcome. The current consensus is that use of either a volatile anesthetic agent or total intravenous anesthesia is reasonable for patients undergoing noncardiac surgery.

The use of nitrous oxide in patients with history of CAD has been questioned since the early 1990s, when animal and human studies showed the increase in peripheral vascular resistance, diastolic dysfunction, and subsequently myocardial ischemia. Badner et al. demonstrated the increase on homocysteine plasma levels of patients during carotid endarterectomy when nitrous oxide was administered and the correlation of those levels with increased incidence of myocardial ischemia. However, the Evaluation of Nitrous Oxide in the Gas Mixture for Anaesthesia (ENIGMA-II) trial, which enrolled 7,110 patients, showed that nitrous oxide did not increase the risk of death and cardiovascular complications or surgical site infection.

The objectives during maintenance are not dissimilar to any other patient: amnesia, unconsciousness, and analgesia. These goals are constrained by the hemodynamic effect of each agent

in order to provide heart rate control, coronary pressure perfusion, and effects on LV function. The preferred anesthetic technique will be a balanced anesthetic approach: opioids, with low/moderate doses of volatile anesthetics and benzodiazepines.

Badner NH, Beattie WS, Freeman D, et al. Nitrous oxide-induced increased homocysteine concentrations are associated with increased postoperative myocardial ischemia in patients undergoing carotid endarterectomy. *Anesth Analg*. 2000;91(5):1073–1079.

Imberger G, Orr A, Thorlund K, et al. Does anaesthesia with nitrous oxide affect mortality or cardiovascular morbidity? A systematic review with meta-analysis and trial sequential analysis. *Br J Anaesth*. 2014;112(3):410–426.

Ko H, Kaye AD, Urman RD. Nitrous oxide and perioperative outcomes. *J Anesth*. 2014;28(3):420–428.

Leslie K, Myles P, Devereaux PJ, et al. Nitrous oxide and serious morbidity and mortality in the POISE trial. *Anesth Analg*. 2013;116(5):1034–1040.

Myles PS, Leslie K, Chan MT, et al. The safety of addition of nitrous oxide to general anaesthesia in at-risk patients having major non-cardiac surgery (ENIGMA-II): a randomised, single-blind trial. *Lancet*. 2014;384(9952):1446–1454.

Nigro Neto C, Landoni G, Cassarà L, et al. Use of volatile anesthetics during cardiopulmonary bypass: a systematic review of adverse events. *J Cardiothorac Vasc Anesth*. 2014;28:84–89.

Sanders RD, Graham C, Lewis SC, et al. Nitrous oxide exposure does not seem to be associated with increased mortality, stroke, and myocardial infarction: a non-randomized subgroup analysis of the General Anaesthesia compared with Local Anaesthesia for carotid surgery (GALA) trial. *Br J Anaesth*. 2012;109(3):361–367.

C.10. You notice a new 3-mm ST-segment depression in lead V_5. How would you treat it?

ST-segment depression can be an indicator of myocardial ischemia. Initial efforts should be focused on determining its etiology. Management of ischemia should include pharmacologic manipulation of the determinants of myocardial oxygen supply and demand.

The crucial aspect of such management includes the following:

- Heart rate control and adequate coronary perfusion pressure. If ST-segment depression is associated with tachycardia and hypertension, the most common cause during surgery is inadequate anesthesia. Therefore, adequate levels of anesthesia should be achieved first. Heart rate control can also be achieved by the use of β-blockers. Caution should be exerted in patients with known contraindications and hemodynamic instability. The calcium channel blockers are considered the drug of choice if coronary spasm is suspected.
- Avoidance of hypotension and use of vasopressors to sustain coronary perfusion pressure
- The use of nitrates is advocated as long as it does not compromise coronary perfusion pressure. Nitrates decrease myocardial oxygen demand by decreasing preload, intracavitary pressure, and myocardial wall tension. In addition, NTG increases the ratio of endocardial to epicardial blood flow.
- Oxygen delivery should be increased by correcting significant anemia (<7 g per dL) and increasing the fraction of inspired oxygen.
- Oxygen demand also could be reduced by correction of hypothermia and/or shivering, if present.
- Secondary therapies should consider the use, if feasible, of antiplatelet therapy such as aspirin.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;64:e77–e137.

C.11. Would you give prophylactic intravenous NTG to prevent myocardial ischemia?

There are no randomized data that support the use of prophylactic intraoperative intravenous NTG in patients at high

risk. NTG should be used only when ischemia is detected and the hemodynamic effects of other agents in use are considered.

Beattie WS. Evidence-based perioperative risk reduction. *Can J Anaesth*. 2005;52(suppl 1):R3.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;64:e77–e137.

C.12. What is the significance of tight control of the heart rate intraoperatively?

Numerous studies have shown that intraoperative tachycardia and the duration of tachycardia could cause myocardial ischemia. Therefore, control of heart rate intraoperatively could significantly reduce the risk of perioperative myocardial events. It is clear that heart rate should be maintained to less than 100 beats per minute; however, the optimal heart rate for all patients has not been determined. Some recommend maintaining the heart rate between 60 and 70 beats per minute in high-risk patients. Slogoff et al. in the 1980s were able to correlate tachycardia with the occurrence of intraoperative myocardial ischemia. Raby et al. demonstrated that by identifying the high-risk patients, whose preoperative Holter tracing showed signs of ischemia, and controlling the heart rate 20% below the ischemia threshold or approximately 60 beats per minute with esmolol, during vascular surgeries could reduce the risk of perioperative myocardial ischemia. Feringa et al. demonstrated that tight heart rate control instead of just the use of β-blockers reduced perioperative myocardial ischemia and improved long-term outcome in vascular surgery patients.

Biccard BM, Sear JW, Foëx P. Meta-analysis of the effect of heart rate achieved by perioperative beta-adrenergic blockade on cardiovascular outcomes. *Br J Anaesth*. 2008;100:23–28.

Feringa H, Bax J, Boersma E, et al. High-dose beta-blockers and tight heart rate control reduce myocardial ischemia and troponin T release in vascular surgery patients. *Circulation*. 2006;114:I-344–I-349.

Landesberg G, Beattie WS, Mosseri M, et al. Perioperative myocardial infarction. *Circulation*. 2009;119:2936–2944.

Raby KE, Brull SJ, Timimi F, et al. The effect of heart rate control on myocardial ischemia among high-risk patients after vascular surgery. *Anesth Analg*. 1999;88:477–482.

Slogoff S, Keats AS. Myocardial ischemia revisited. *Anesthesiology*. 2006;105:214–216.

C.13. When would you extubate the trachea in this patient? What could you do to prevent hypertension and tachycardia during extubation and emergence?

At the end of surgery, assuming no intraoperative complications, the trachea would be extubated when the patient is fully awake, breathing adequately, and neuromuscular blockade is fully reversed. To prevent tachycardia and hypertension associated with extubation and emergence, low doses of medications such as 1 mg per kg of lidocaine or esmolol, or 0.015 to 0.03 mg per kg of nicardipine, or 0.1 mg per kg of labetalol or diltiazem, before emergence in order to reduce sympathetic response of emergence and extubation can be administered.

Atlee JL, Dhamee MS, Olund TL, et al. The use of esmolol, nicardipine, or their combination to blunt hemodynamic changes after laryngoscopy and tracheal intubation. *Anesth Analg*. 2000;90:280–285.

Kristensen SD, Knuuti J, Saraste A, et al. 2014 ESC/ESA guidelines on non-cardiac surgery: cardiovascular assessment and management: the Joint Task Force on Non-Cardiac Surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). *Eur Heart J*. 2014;35:2383–2431.

Mikawa K, Nishina K, Maekawa N, et al. Attenuation of cardiovascular responses to tracheal extubation: verapamil versus diltiazem. *Anesth Analg*. 1996;82:1205–1210.

D. Postoperative Management

D.1. What are the postoperative predictors of perioperative MACE?

In noncardiac surgical patient, the highest risk of cardiac morbidity is in the postoperative period. It is during this period where up to 67% of the ischemic events occur. This period is characterized by increase in heart rate, blood pressure, sympathetic discharge, and hypercoagulability. Heart rate commonly increases postoperatively by 25% to 50% over intraoperative values, and tachycardia occurs in 10% to 25% of patients. Postoperative myocardial ischemia occurs in 27% to 41% of high-risk patients. Most of these events (50% or higher) are silent (without angina). Postoperative MI is usually preceded by prolonged ST-segment depression. This change on ECG is easily missed if ECG is not continuously monitored because most of the changes will revert completely to baseline. However, routine continuous postoperative ECG monitoring is not recommended, and even routine daily ECG for 3 days is no longer advocated. In a study involving 337 vascular surgery patients in whom troponin I levels were collected within 48 hours of surgery and 12-lead ECGs were performed daily for 3 postoperative days, although 40% of the subjects had elevated troponin levels, only 6% of the patients had ischemic changes on the ECG. Postoperative MI may be associated with tachycardia and pain. Studies involving large numbers of patients suggest that postoperative ischemia is the most important marker of immediate and long-term adverse cardiovascular events. It is associated with a 2.8-fold increase in the odds of all adverse cardiac outcomes.

The highest incidence of troponin elevation, a biochemical marker of ischemia, frequently occurs 8 to 24 hours after the surgical procedure; even mild elevations are associated with postoperative cardiac ischemia and they could help to categorize the short- and long-term risk of the surgical patient as they are

independent predictors of mortality. Postoperative MI has also been associated with other clinical conditions as postoperative hypothermia, hypercoagulability, postoperative pain, and anemia.

Garcia S, Marston N, Sandoval Y, et al. Prognostic value of 12-lead electrocardiogram and peak troponin I level after vascular surgery. *J Vasc Surg*. 2013;57:166–172.

Hines RL, Marschall K, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:79–106.

Le Manach Y, Perel A, Coriat P, et al. Early and delayed myocardial infarction after abdominal aortic surgery. *Anesthesiology*. 2005;102:885–891.

Nagele P, Brown F, Gage BF, et al. High-sensitivity cardiac troponin T in prediction and diagnosis of myocardial infarction and long-term mortality after noncardiac surgery. *Am Heart J*. 2013;166(2):325–332.

D.2. How would you control postoperative pain?

The postoperative period can be stressful due to the onset of pain during emergence from anesthesia, fluid shifts, temperature changes, and alteration of respiratory function. Marked changes occur in plasma catecholamine concentration, hemodynamics, ventricular function, and coagulation following noncardiac surgery, particularly in patients with preexisting cardiac disease. These stressors place the patient at increased risk for development of adverse cardiac outcome. Severe postoperative pain reported in 5% to 10% of patients. Effective pain management is essential to prevent adverse outcome and promote early recovery. Intravenous patient-controlled analgesia and/or patient-controlled epidural analgesia are popular methods for reducing postoperative pain. Several studies suggest that effective pain management leads to a reduction in postoperative catecholamine surges and hypercoagulability. A meta-analysis published in 2013, which analyzed the impact of epidural analgesia versus systemic analgesia, concluded that epidural analgesia was associated with a 40% decrease in mortality and a

significant decrease in the risk of atrial fibrillation, supraventricular tachycardia, deep vein thrombosis, respiratory depression, atelectasis, pneumonia, ileus, and postoperative nausea and vomiting, and also improved recovery of bowel function. However, epidural analgesia also significantly increased the risk of arterial hypotension, pruritus, urinary retention, and motor blockade.

Norris EJ, Beattie C, Perler BA, et al. Double-masked randomized trial comparing alternate combinations of intraoperative anesthesia and postoperative analgesia in abdominal aortic surgery. *Anesthesiology*. 2001;95:1054–1067.

Pöpping DM, Elia N, Van Aken HK, et al. Impact of epidural analgesia on mortality and morbidity after surgery: systematic review and meta-analysis of randomized controlled trials. *Ann Surg*. 2014;259(6):1056–1067.

D.3. Is postoperative anemia associated with adverse cardiac outcome?

Patients with IHD may be adversely affected by anemia. Based on existing literature, the evidence is sufficient to state that transfusions are rarely beneficial if the Hgb level exceeds 10 g per dL (Hct >30%) in the absence of acute blood loss. It is also reasonable to state that the patient may benefit from a transfusion if the Hgb level falls below 7 g per dL. The controversy remains between Hgb concentrations of 8.0 to 10.0 g per dL. The 2016 American Association of Blood Banks Guideline, which is based on expert opinion and studies, recommends a restricted transfusion strategy (Hgb <7 to 8 g per dL) in asymptomatic, hemodynamically stable patients without CAD. The guideline also recommends adherence to a restrictive transfusion strategy in hospitalized patients with cardiovascular disease and consideration of transfusion for patients with symptoms (e.g., chest pain, orthostasis, CHF) or Hgb less than 8 g per dL. In postoperative patients, the recommended maintenance Hgb concentration is 8 g per dL or more, unless the

patient exhibits symptoms. There were no specific recommendations for hemodynamically stable patients with ACS because of the lack of high-quality evidence for either a liberal or a restrictive transfusion strategy in these patients. The consensus of those experts recommended a symptom-guided approach to evaluating an Hgb level to determine whether to transfuse a patient with anemia.

Beattie WS, Karkouti K, Wijeysundera DN, et al. Risk associated with preoperative anemia in noncardiac surgery: a single-center cohort study. *Anesthesiology*. 2009;110:574–581.

Carson JL, Guyatt G, Heddle NM, et al. Clinical practice guidelines from the AABB: red blood cell transfusion thresholds and storage. *JAMA*. 2016;316(19):2025–2035.

Qaseem A, Humphrey LL, Fitterman N, et al. Treatment of anemia in patients with heart disease: a clinical practice guideline from the American College of Physicians. *Ann Intern Med*. 2013;159(11):770–779.

Simmons JW, Pittet JF. Revealing the real risks of perioperative transfusion: rise of the machines! *Anesthesiology*. 2015;122(1):1–2.

D.4. Is postoperative hypothermia associated with postoperative myocardial ischemia?

Hypothermia is common during anesthesia and surgery owing to anesthetic-induced inhibition of thermoregulatory control. The principal initial cause of hypothermia is core-to-peripheral redistribution of body heat.

Perioperative hypothermia is associated with numerous complications; it triples the incidence of adverse myocardial outcomes in high-risk patients, increases blood loss. Even mild hypothermia has been associated with an increased incidence of wound infection following colon resection. Also, it adversely affects oxygen availability in tissues, changes the kinetics and action of some anesthetic agents and muscle relaxants, and is associated with delayed postanesthetic recovery. It causes immune dysfunction and increased transfusion requirements.

Core hypothermia may increase circulating catecholamines levels, leading to tachycardia, hypertension, systemic vasoconstriction, and an imbalance between oxygen demand and supply. Frank et al. studied 100 patients undergoing lower extremity vascular surgery. They found that unintentional hypothermia (sublingual temperature less than 35°C [95°F]) on arrival to postoperative ICU is associated with a significantly higher incidence of myocardial ischemia (36% vs. 13%), angina (18% vs. 15%), and Pa_{O_2} less than 80 mmHg (52% vs. 30%) during the early postoperative period. However, a subsequent trial involving 1,000 patients with subarachnoid hemorrhage, which were randomized to perioperative hypothermia or normothermia, did not show a difference in perioperative cardiac events. Maintenance of normothermia may be reasonable to reduce perioperative cardiac events in patients undergoing noncardiac surgery.

Frank SM, Beattie C, Christopherson R, et al. Unintentional hypothermia is associated with postoperative myocardial ischemia. *Anesthesiology*. 1993;78:468–476.

Todd MM, Hindman BJ, Clarke WR, et al. Mild intraoperative hypothermia during surgery for intracranial aneurysm. *N Engl J Med*. 2005;352(2):135–145.

D.5. How would you make a diagnosis of perioperative MI (PMI)?

The definition of MI, according to the third universal definition of MI, is based on elevation of biomarkers, in conjunction with cardiac symptoms, ECG changes, new echocardiographic changes, or angiographic findings of intracoronary thrombus.

Most ischemic episodes occur after and not during the operation. This is probably because of the high postoperative stresses related to anesthesia and surgery. Several studies have examined the optimal method for diagnosing a PMI. Most

patients suffering from PMI do not complain of chest pain and the value of routine serial postoperative ECG is limited. Cardiac-specific enzyme elevations such as troponin I (cTnI) and troponin T (cTnT) are currently the standard of care for biochemical diagnosis of a PMI because they demonstrate sensitivity and tissue specificity superior to other available biomarkers.

In the purest physiologic sense, any detectable necrosis is an acute MI; however, troponin elevation can be observed in many other conditions in which the heart is stressed. Even small elevations of specific markers of myocardial damage, such as cardiac troponins, should be acknowledged as indicative of myocardial injury. This has been categorized as myocardial injury in the third universal definition of MI and includes myocardial injury related to demand (type II) and related to plaque rupture (type I). From a clinical perspective, there is clear evidence that any amount of detectable cardiac troponin release is associated with an increased risk of new adverse cardiac events. Many investigators agree that the increase in cardiac troponins postoperatively, even if no cardiovascular signs and symptoms are present, carries poor long-term outcome.

Clinicians need to be sensitive to redundancy in testing. Some authors have demonstrated that routine cardiac troponin monitoring is an easy, effective, and inexpensive way to detect postoperative myocardial injury. However, the ACC/AHA guidelines reserve the use of this biomarkers for patients at high risk and those with clinical, ECG, or hemodynamic evidence of cardiovascular dysfunction. Routine measurement of postoperative troponins in asymptomatic or low-risk patients undergoing low-risk procedure is not warranted.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of

Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;64:e77–e137.

Landesberg G, Shatz V, Akopnik I, et al. Association of cardiac troponin, CK-MB, and postoperative myocardial ischemia with long-term survival after major vascular surgery. *J Am Coll Cardiol*. 2003;42:1547–1554.

Lopez-Jimenez F, Goldman L, Sacks DB, et al. Prognostic value of cardiac troponin T after noncardiac surgery: 6-month follow-up data. *J Am Coll Cardiol*. 1997;29:1241–1245.

White HD, Thygesen K, Alpert JS, et al. Clinical implications of the third universal definition of myocardial infarction. *Heart*. 2014;100(5):424–432.

D.6. How would you manage the patient with a suspected PMI?

There is lack of control evidence regarding management of PMI in the postsurgical patient. PMI could include three different clinical scenarios/diagnosis: unstable angina (UA), non–ST-elevation MI (NSTEMI), and ST-elevation MI (STEMI).

The initial management should focus on the following diagnosis:

- Evaluation of chest pain if present
- 12-Lead ECG and determination of changes, if present
- Measurement of biomarkers of cardiac injury. A cardiac-specific troponin is the preferred marker.
- Immediate consultation of a cardiologist and risk stratification to determine high-risk patients

It is important to consider the recent surgical procedure and consultation with the surgical team regarding impact of aspirin and anticoagulant therapy.

Unless a contraindication exists, patients with an ACS of the type UA or NSTEMI should be treated with oxygen, aspirin (acetylene salicylic acid), sublingual/intravenous NTG for chest pain relief, as long as blood pressure is adequate, a β-blocker, unfractionated heparin or low molecular weight heparin, and/or a glycoprotein (GP) IIb/IIIa inhibitor.

The cardiology consultant should guide further management:

- Option 1 is a routine angiographic approach, in which coronary angiography and revascularization are performed unless a contraindication exists. Within this approach, the most common strategy advocates for a period of medical stabilization. A more aggressive approach calls for coronary angiography and revascularization performed within 24 hours of the onset of symptoms or diagnosis; the rationale for the more aggressive approach is the protective effect of carefully administered anticoagulant and antiplatelet therapy on reperfusion procedures outcome.
- The alternative approach, commonly referred to as the initially conservative strategy, is guided by ischemia, with angiography reserved for patients with recurrent ischemia despite medical therapy.

Regardless of the angiographic strategy, an assessment of LV function (echocardiography, ventriculogram, or nuclear ventriculography) should be strongly considered because of the importance of treating patients who have impaired LV function with ACE inhibitors, β-blockers, and surgical revascularization (CABG) when appropriate (e.g., three-vessel disease).

If the patient presents with a STEMI, recognized on the basis of the 12-lead ECG, the management will be initially similar to UA/NSTEMI (oxygen, acetylene salicylic acid, NTG, β-blockers), then one should attempt to complete restoration of flow in the infarct artery by PCI (balloon angioplasty with or without deployment of an intracoronary stent under the support of pharmacologic measures to prevent thrombosis), or surgical measures (CABG).

Evidence supports expeditious restoration of flow in the obstructed infarct artery after the onset of symptoms in patients with STEMI as a key determinant of short- and long-term outcomes. Early reperfusion of ischemic myocardium within the risk region of an occluded infarct-related artery interrupts the

occurring necrosis, reduces ultimate infarct size, preserves regional and global ventricular function, and improves survival. A subset of patients will have severe three-vessel or left main disease or anatomic features unfavorable for PCI and may be candidates for urgent or emergency CABG.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;64:e77–e137.

SECTION 3 The Gastrointestinal System

15 Intestinal Obstruction and Enhanced Recovery after Surgery

Leif Ericksen and Tong J Gan

A 73-year-old woman with an acute abdomen was scheduled to undergo an emergency exploratory laparotomy. She complained of severe abdominal pain with periodic bouts of bilious vomiting. Her past surgical history included a right hemicolectomy for colon cancer. She had a blood pressure (BP) of 85/60 mmHg, pulse of 115 beats per minute, and hematocrit of 45%.

A. Medical Disease and Differential Diagnosis

1. What is the differential diagnosis of the acute abdomen?
2. What are the causes of intestinal obstruction of the small bowel and of the large bowel?
3. Differentiate between simple and strangulated bowel obstruction.

4. Is it important to differentiate whether the bowel obstruction is located in the small bowel or large bowel? Why? How might the distinction be made?
5. What are the causes and effects of bowel distention?
6. Describe the fluid shifts during small bowel intestinal obstruction.
7. Discuss the systemic derangements that occur with intestinal obstruction.
8. What is an ileus? Discuss its causes and pathophysiology.

B. Preoperative Evaluation and Preparation

1. What is Enhanced Recovery after Surgery (ERAS)? What are the core tenants of these programs?
2. Can ERAS be used in this case?
3. What components of ERAS are applied in the preoperative phase of the care of colorectal surgery (CRS) patients?
4. Is it important to decompress the abdomen before induction of anesthesia? Why?
5. Describe the respiratory implications.
6. What are the implications of the tense abdominal wall?
7. Outline the methods of abdominal decompression.
8. Discuss the goals of fluid management.
9. What would you use as a guide to fluid volume replacement?

C. Intraoperative Management

1. What dangers are present during induction? How are they planned for?
2. Does the administration of antacids and/or histamine-2 (H_2) blockers before the induction of anesthesia have a significant value in patients with small bowel obstruction?
3. In what position would you intubate this patient?
4. What is the best muscle relaxant to use for the rapid sequence induction?
5. Would you remove or leave the nasogastric tube (NGT) in

place before inducing anesthesia?
6. Would you use nitrous oxide in this patient?
7. Are there any benefits to using a high concentration of inspired oxygen (FIO_2)?
8. What components of ERAS are applied in the intraoperative phase of the care of CRS patients?
9. What are the strengths, weaknesses, benefits, and challenges of ERAS?
10. What are the indications for ERAS?

D. Postoperative Management

1. What are the principles of postoperative care in this patient?
2. Are there any postoperative respiratory problems associated with factors other than aspiration?
3. If the patient did aspirate gastric contents, what are the possible sequelae of this event? What is the treatment?
4. What is gram-negative sepsis? Describe the clinical picture and treatment.
5. What components of ERAS are applied in the postoperative phase of the care of CRS patients?

A. Medical Disease and Differential Diagnosis

A.1. What is the differential diagnosis of the acute abdomen?

An acute abdomen refers to a number of conditions with the most prominent feature being severe abdominal pain of abrupt onset that can necessitate urgent surgical intervention. The differential is challenging because there are a number of etiologies. The most common diagnoses vary by age; many organ systems may cause an acute abdomen, and the presenting symptom is often nonspecific. Some of the most common causes are listed in **Table 15.1**. Visceral and somatic afferents are the

two systems that transmit abdominal pain. Visceral pain is dull, deep, poorly localized, and transmitted by C fibers in the mucosa, muscularis, and visceral peritoneum. Visceral pain is generated by nerve endings without specialized structures that are primarily sensitive to tissue tension typically caused by distension, spasm, and ischemia. Somatic pain is sharp and well localized and transmitted by chemical (inflammation), thermal, or mechanical irritation of the aδ fibers of the parietal peritoneum. These fibers are derived from the same origin as those innervating muscle and skin, which cause the guarding and cutaneous sensitivity that can accompany an acute abdomen. Abdominal pathology frequently has a mixed picture of visceral and somatic pain.

TABLE 15.1 Acute Abdomen Differential

Surgical	Medical	Gynecologic
Inflammation	Cardiovascular	Ectopic pregnancy
Inflammatory bowel disease	Myocardial ischemia	Ovarian cyst
Acute appendicitis	Myocardial infarction (inferior)	Torsion
Acute diverticulitis	Gastrointestinal	Rupture
Acute pancreatitis	Gastritis	Hemorrhage
Acute cholecystitis	Gastroenteritis	Infarction
Acute cholangitis	Mesenteric adenitis	Infection
Meckel diverticulitis	Hepatitis	Pelvic inflammatory disease
Obstruction	Hepatic abscess	Fibroid degeneration
Intestinal obstruction	Fitz-Hugh-Curtis syndrome	Salpingitis
Biliary colic	Primary peritonitis	Mittelschmerz
Ureteric colic	Abdominal wall conditions	Endometriosis
Acute retention of urine	Rectus sheath hematoma	
Ischemia	Genitourinary	
Mesenteric ischemia	Urinary tract infection	
Torsion of a viscus	Pyelonephritis	
Perforation	Neurologic	
Perforated peptic ulcer disease	Tabes dorsalis	
Perforated small bowel (salmonella, cytomegalovirus, and tuberculosis infection)	Hematologic	
	Sickle cell disease	
	Malaria	

Perforated diverticular disease	Hereditary spherocytosis
Perforated appendix	Endocrine
Toxic megacolon with perforation	Diabetes mellitus
	Thyrotoxicosis
Acute cholecystitis and perforation	Addison disease
	Metabolic
Perforated oesophagus	Uremia
Perforated bladder	Hypercalcemia
Perforation of a length of strangulated bowel	Porphyria
	Infective
Ruptured abdominal aortic aneurysm	Herpes zoster

The colored cells represent pathophysiologies. Non-colored cells represent specific diagnoses. The table is presented in the context of forming a differential diagnosis for an acute abdomen. The table presents categories that become more specific (e.g., surgical/medical/gynecologic, then pathophysiology, then specific diagnoses) that can be matched to a patients presenting symptoms and history.

Reprinted from Garden JO, Parks RW, eds. *Principles and Practice of Surgery*. 7th ed. Edinburgh, United Kingdom: Elsevier; 2018:159. Copyright © 2018 Elsevier. With permission.

The two processes typically implicated in an acute abdomen are inflammation and obstruction. The inflammatory milieu causes a direct chemical irritation and causes the tissue to become edematous and distended. Impeded flow-through a hollow organ causes smooth muscle to contract in an attempt to overcome the obstruction resulting in increased tension and dilation. Both of these processes can contribute to ischemia and perforation, which can in turn also cause pain.

Etiologies of the acute abdomen may require either medical and/or surgical treatment, be intra- and/or extra-abdominal, and be associated with almost any organ system. Characteristics such as intensity, chronology, location, diffuse versus localized, radiation, and comorbidities in addition to testing may help to construct a differential diagnosis.

Feldmen M, Friedman LS, Brandt LJ, eds. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management*. 10th ed. Philadelphia, PA: Elsevier Saunders; 2016:161–174.

Garden JO, Parks RW, eds. *Principles and Practice of Surgery*. 7th ed.

Edinburgh, United Kingdom; Elsevier; 2018:159–178.

A.2. What are the causes of intestinal obstruction of the small bowel and of the large bowel?

Obstruction occurs due to either an inhibition of physiologic peristalsis (ileus) or mechanical obstruction. Mechanical obstructions are broadly divided into extrinsic, intramural, and intraluminal categories.

Adhesions resulting from the inflammation and healing process of prior surgery account for the vast majority (>70%) of small bowel obstructions and are followed in order by hernias, malignancy, and then inflammatory bowel disease. Diagnoses of volvulus and hernia strangulation are less common but are surgical emergencies. Large bowel obstructions occur less frequently, but the most common etiologies are adenocarcinoma, volvulus, and sequelae from diverticulitis. Adenocarcinoma causes >50% of all large bowel obstructions.

Bower KL, Lollar DI, Williams SL, et al. Small bowel obstruction. *Surg Clin North Am*. 2018;98(5):945–971.

Feldmen M, Friedman LS, Brandt LJ, eds. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management*. 10th ed. Philadelphia, PA: Elsevier Saunders; 2016:2154–2195.

Yeo CJ, ed. *Shackelford's Surgery of the Alimentary Tract*. 8th ed. Philadelphia, PA: Elsevier; 2019:842–850.

A.3. Differentiate between simple and strangulated bowel obstruction.

A simple bowel obstruction refers to a single section of occlusion, whereas a strangulated obstruction refers to an area of compromised perfusion. It is important to recognize bowel strangulation because it increases mortality 2- to 10-fold from generally <5% to 25% depending on comorbid conditions. Strangulation is typically discussed in concert with an incarcerated segment of bowel (e.g., a hernia or hole in

omentum) but can also be due to inadequate perfusion pressure secondary to an increased intraluminal or intramural pressure. As venous outflow decreases, the walls of the bowel become edematous, obstruction worsens, pressure increases, and eventually arterial inflow is compromised. Affected sections become ischemic, infarct, and perforate after which peritonitis ensues.

The classic signs of strangulation are constant (as opposed to intermittent) pain, fever, tachycardia, leukocytosis, and peritonitic signs (e.g., guarding and rebound tenderness). However, no clinical parameter reliably rules strangulation in or out, so a thorough history and physical examination and a high index of suspicion must guide the decision to operate. Risk factors for bowel strangulation may include female sex, femoral hernia, and history of hospitalization related to groin hernia.

Doherty GM, ed. *Current: Diagnosis & Treatment: Surgery*. 14th ed. New York: McGraw-Hill; 2015:660–663, 692–695.

Garden JO, Parks RW, eds. *Principles and Practice of Surgery*. 7th ed. Edinburgh, United Kingdom: Elsevier; 2018:147–158.

Harken AH, Moore EE, eds. *Abernathy's Surgical Secrets*. 7th ed. Philadelphia, PA: Elsevier: 2018;215–218.

HerniaSurge Group. International guidelines for groin hernia management. *Hernia*. 2018;22(1):1–165.

Sutton JM, Beckwith MA, Johnson BL, et al, eds. *The Mont Reid Surgical Handbook*. 7th ed. Philadelphia, PA: Elsevier; 2018:331–344.

Townsend CM, Beauchamp RD, Evers BM, et al, eds. *Sabiston Textbook of Surgery: The Biological Basis of Modern Surgical Practice*. 20th ed. Philadelphia, PA: Elsevier; 2017:1237–1295.

A.4. Is it important to differentiate whether the bowel obstruction is located in the small bowel or large bowel? Why? How might the distinction be made?

Yes, it is important not only to differentiate between large and small bowel obstruction but also to determine the position of the

obstruction within those sections of bowel. Both small and large bowel obstructions may present with colicky abdominal pain, nausea and vomiting, distention, and obstipation. The location, however, will differentiate between the etiologies of the obstruction which will dictate the management strategy, systemic consequences, and possible special considerations. Prognosis can also vary widely. For instance, a large bowel obstruction presenting as a small bowel obstruction may have a mortality rate four times greater than from other causes.

Small bowel obstruction is associated with more bilious vomiting sooner after the obstruction occurs. Patients may continue to have bowel movements as the distal bowel continue to function. Time intervals between bouts of abdominal pain are shorter than the more proximal the obstruction is. The majority of small bowel obstructions are thought to be caused by adhesive disease, which typically resolve with nonoperative management including NGT decompression and fluid resuscitation. The small bowel is involved in a number of secretory and absorptive processes. During a trial of conservative management, a stable patient must be monitored for indications to proceed to surgery because altered function can lead to the accumulation of air and fluid, bowel distension, increased intraluminal pressure according to the law of Laplace, and possible bowel infarction and rupture. Small bowel obstruction also alters gut flora balance leading to translocation of bacteria. Vomiting occurs earlier and more frequently with a small bowel obstruction, which contributes to anesthetic concerns including decreased intravascular volume, metabolic alkalosis, and airway management. Crohn disease, irradiated bowel, and Richter hernias require additional considerations based on location and level of involvement.

Large bowel obstructions are usually slower in onset, more frequently associated with distension and lower abdominal pain,

and caused most frequently by adenocarcinoma. Surgical intervention is typically required before infarction and perforation occur. Fewer fluid shifts occur in the large bowel and vomiting occurs later in the disease process if at all, so less resuscitation and electrolyte correction is required. Plain film upright and flat x-rays are less accurate than computed tomography (CT) but are faster and may show other indications to proceed directly to surgery such as free air. CT, on the other hand, elucidates the etiology far better than x-ray. Depending on the location, surgical interventions may include resection, anastomoses, and/or ostomy, all of which have varying risks of leak and infection. Adjuvant radiation and chemotherapy may be part of the perioperative planning process. Stable patients with a sigmoid volvulus may undergo an attempt to relieve the torsion with a flexible sigmoidoscopy.

Cameron JL, Cameron AM, eds. *Current Surgical Therapy*. 12th ed. Philadelphia, PA: Elsevier; 2017:109–113, 180–183.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-Existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:359–375.

Paterson-Brown S, Paterson HM, eds. *Core Topics in General and Emergency Surgery*. 6th ed. Edinburgh, United Kingdom: Elsevier; 2019;193–215.

Weaver JL, Barnett RE, Patterson DE, et al. Large-bowel disease presenting as small-bowel obstruction is associated with a poor prognosis. *Am J Emerg Med*. 2016;34(3):477–479.

A.5. What are the causes and effects of bowel distention?

In a simple obstruction, the primary contributors to bowel distention are swallowed air and secretions from proximal sections of the gastrointestinal (GI) tract. Bacterial overgrowth may also contribute in the form of carbon dioxide and fermentation products that accumulate more rapidly due to an impaired ability to diffuse out of the bowel. Endotoxin-stimulated chemoreceptors and mechanoreceptors activated by distention activate autocrine, luminal, paracrine, and

immunoneuroendocrine systems (ALPINES) to attract neutrophils and macrophages. Prostaglandins and inflammatory mediators directly alter the activity of ion transporters (and therefore affect the flow of fluid) and the barrier function of the gut. The net result is increased secretion into the lumen of the intestine, decreased absorption, and further distention forming a feedback loop unless decompressed (**Fig. 15.1**). Interestingly, this effect is seen both proximally and distally to an obstruction and may lead to bowel movements even during a complete obstruction. Decreased intravascular volume and electrolyte imbalances are common which may present as hypotension and lactic acidosis. By the law of Laplace, as the lumen of the bowel grows larger, the pressure increases. Lymphatic drainage is impaired first, further increasing pressure which then impedes venous drainage and compromises perfusion. Ischemia, infarction, and perforation soon follow. Septic shock will ensue if it has not already been initiated by translocated bacteria.

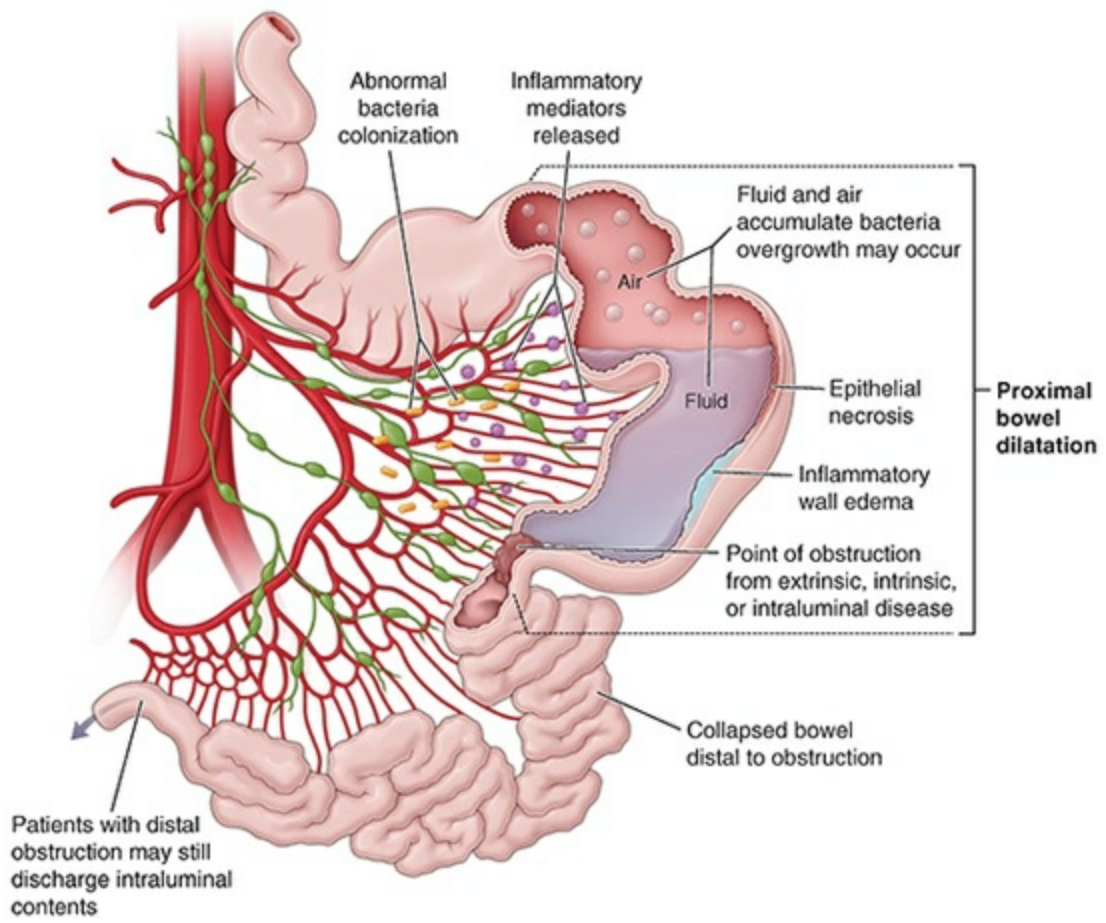


FIGURE 15.1. Pathophysiologic changes of intestinal obstruction. Note: Intraluminal obstruction is displayed. *(Republished with permission of McGraw-Hill Education, from Jameson JL, Fauci AS, Kasper DL, et al, eds*. Harrison's Principles of Internal Medicine. *20th ed. New York, NY: McGraw-Hill Education; 2018:chap 323:2296; permission conveyed through Copyright Clearance Center, Inc.)*

Closed loop obstructions result from volvulus, herniation, or a large bowel obstruction with a competent ileocecal valve. The same pathology applies but has an accelerated course due to an inability of the obstruction to be relieved proximally. Urgent operative management is typically required.

Feldmen M, Friedman LS, Brandt LJ, eds. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management*. 10th ed. Philadelphia, PA: Elsevier Saunders; 2016:1713–1735.

Jameson JL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:2294–2298.

A.6. Describe the fluid shifts during small bowel intestinal

obstruction.

A normal physiologic small bowel fluid load is 8 to 9 L per day (**Fig. 15.2**). Obstruction causing distention increases the secretory activity of the bowel and decreases the absorptive capacity leading to fluid sequestration in the lumen of the bowel. The more proximal the obstruction is, the more severe the fluid loss is. Bowel wall edema, vomiting, NG suctioning, and transudative fluid loss into the peritoneum can all also contribute to the decrease in intravascular fluid. In general, vomiting occurs when 3 L of fluid have been sequestered. Hemodynamic parameters, such as heart rate (HR) and BP, become abnormal at ≥6 L of sequestered fluid.

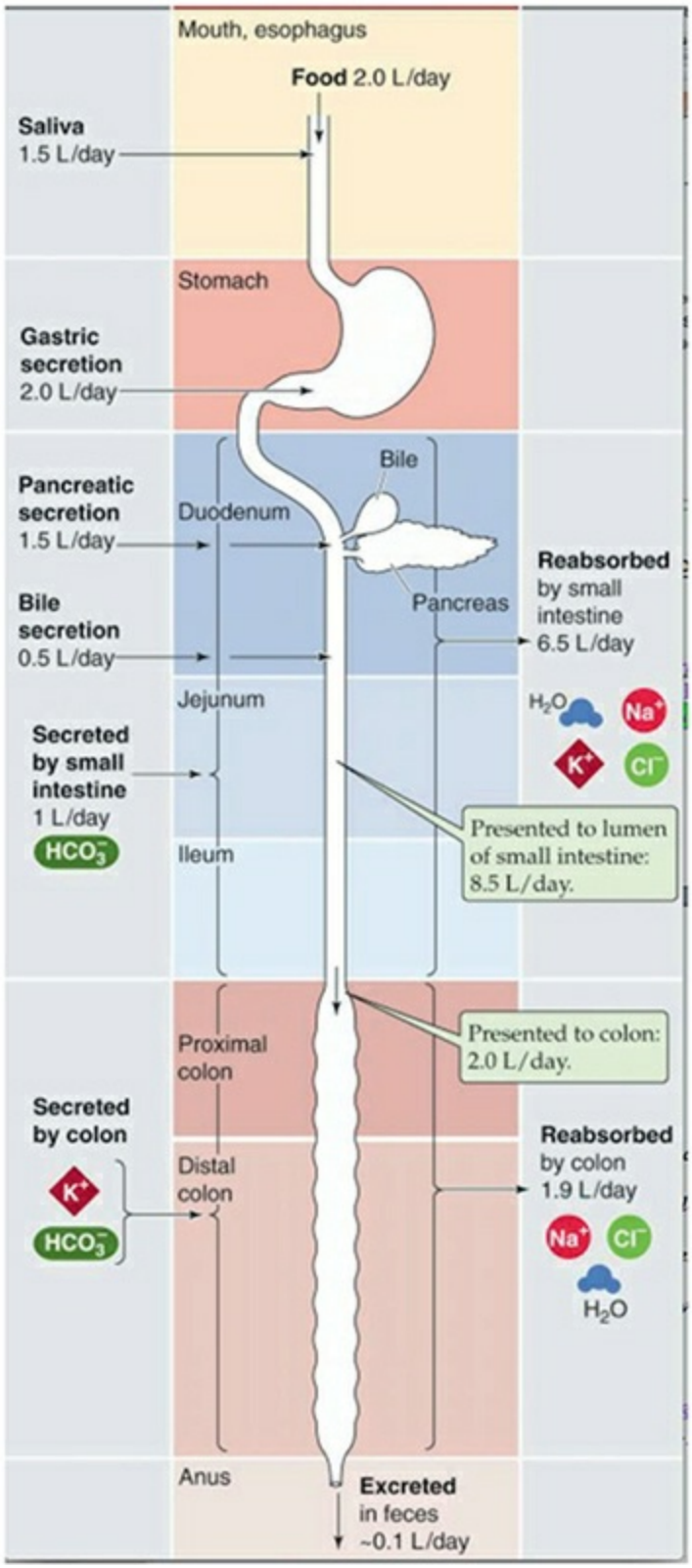


FIGURE 15.2. GI fluids. Fluid balance in the GI tract. For each segment of the GI tract, the figure shows substances flowing into the lumen on the left and substances flowing out of the lumen on the right. Of the approximately 8.5 L per day that are presented to the small intestine, the small intestine

removes approximately 6.5 L per day, delivering approximately 2 L per day to the colon. The large intestine removes approximately 1.9 L per day, leaving approximately 0.1 L per day in the feces. (*Reprinted from Boron WF, Boulpaep EL, eds*. Medical Physiology. *3rd ed. Philadelphia, PA: Elsevier; 2017:902. Copyright © 2017 Elsevier. With permission.*)

Boron WF, Boulpaep EL, eds. *Medical Physiology*. 3rd ed. Philadelphia, PA: Elsevier; 2017:899–913.

Costanzo LS. *Physiology*. 6th ed. Philadelphia, PA: Elsevier; 2018:339–394.

Freeman B, Berger J, eds. *Anesthesiology Core Review: Part Two ADVANCED Exam*. New York: McGraw-Hill; 2016:323–327.

A.7. Discuss the systemic derangements that occur with intestinal obstruction.

Systemic derangements in intestinal obstruction can be severe and even fatal if left unchecked. Hypotension results from hypovolemia secondary to fluid sequestration in the bowel lumen and wall as well as loss from vomiting/NGT suctioning. When the bowel is distended and intra-abdominal pressure is high, venous return is impaired and hypotension worsens.

Other mechanical consequences of a distended abdomen may include a reduced functional residual capacity (FRC) and an increased work of breathing.

The proximal bowel secretes a great deal of potassium, sodium, and chlorine. A very proximal obstruction may result in a hypochloremic, hypokalemic metabolic alkalosis. A more common finding is a metabolic acidosis related to compromised perfusion. Hyponatremia may further contribute to intravascular fluid loss.

Normal bowel functions as a barrier keeping bacterial flora intraluminal if any exist (many are sterile). In obstruction, intestinal flora such as *Escherichia coli*, *Enterococcus faecalis*, and *Klebsiella* increase in count profoundly. Advanced stages can lead to translocation from the gut and contribute to gram-negative sepsis, shock, and death even in the absence of perforation. Finally, inflammatory mediators and relative

hypovolemia have been shown to cause damage to remote organs.

Yeo CJ, ed. *Shackelford's Surgery of the Alimentary Tract*. 8th ed. Philadelphia, PA: Elsevier; 2019:842–850.

A.8. What is an ileus? Discuss its causes and pathophysiology.

Ileus describes a lack of physiologic peristalsis in the absence of a mechanical obstruction. Different etiologies exist including spastic and disorganized motility, but the cause most germane to the perioperative world and this case study is the adynamic ileus from the inhibition of intestinal myocytes. The most frequent cause is surgical abdominal manipulation. However, a number of other factors including inflammation, iatrogenic drugs, electrolyte imbalances, excessive crystalloid administration, and trauma may also contribute.

Two mechanisms contribute to postsurgical adynamic ileus. The first is a short-lived neurogenic phase. Incision of the peritoneum activates adrenergic afferents linked to an inhibitory spinal reflex. Subsequent more intense manipulation of the bowel activates higher order supraspinal pathways which then stimulate both adrenergic and vagal pathways to release motility impairing neurohumoral substances, such as norepinephrine and nitric oxide (NO), and vasoactive intestinal polypeptide (VIP), respectively. Corticotropin-releasing factor (CRF) has been implicated in the coordination of this pathway.

A longer lasting inflammatory phase causes uncomplicated postoperative (3 to 5 days) ileus. Surgical manipulation activates macrophages naturally living in the myenteric plexus, stimulating the innate immune response. An inflammatory milieu is generated within 3 to 4 hours after surgery. Cytokines have been shown to alter the release of enteric neurotransmitters. Prostaglandins generated by cyclooxygenase-2 (COX-2) can

activate many of the splanchnic afferents and cause reflex spinal inhibition as discussed in the neurogenic phase. NO also continues to be generated by recruited monocytes and neutrophils.

Infection, sepsis, peritonitis, and trauma cause or contribute to an inflammatory state that may cause an ileus or independently prolong a postoperative ileus (POI). Opiate administration, hypomagnesemia, hyponatremia, and hypercalcemia may also contribute and must be monitored in the perioperative period.

Chapman SJ, Pericleous A, Downey C, et al. Postoperative ileus following major colorectal surgery. *Br J Surg*. 2018;105(7):797–810.

B. Preoperative Evaluation and Preparation

B.1. What is Enhanced Recovery after Surgery (ERAS)? What are the core tenants of these programs?

ERAS is a bundle of evidence-based interdisciplinary practices emphasizing early return to functional status. Some of the main tenants include attenuating the physiologic stress response to surgery, improving metabolic responses, and preventing perioperative organ damage. Common strategies include "optimal analgesia," encouraging metabolic optimization, aggressive postoperative nausea and vomiting (PONV) prophylaxis and treatment, goal-directed fluid therapy (GDFT), minimally invasive surgical techniques, avoidance of postoperative NGT and peritoneal drains, and early enteral feeding and ambulation. ERAS programs have demonstrated accelerated recovery, reduced complication rate, reduction in length of stay, reduced readmission rate, and increased healthcare value by increasing quality while decreasing cost.

Gan TJ, Thacker JK, Miller TE, et al. *Enhanced Recovery for Major Abdominopelvic Surgery*. New York: Professional Communications;

2016:xvi–xxii, 39–48, 105–109, 151–160, 191–194, 199–212, 215–223, 227–233, 237–247, 263–275.

B.2. Can ERAS be used in this case?

ERAS pathways were developed for elective surgical procedures, including CRS. However, many of the principles may be applied to urgent/emergent procedures as well.

Gan TJ, Thacker JK, Miller TE, et al. *Enhanced Recovery for Major Abdominopelvic Surgery*. New York: Professional Communications; 2016:189, 199.

B.3. What components of ERAS are applied in the preoperative phase of the care of colorectal surgery (CRS) patients?

Multimodal analgesia helps prevent ileus through an opioid-sparing strategy. Preoperative gabapentin, nonsteroidal anti-inflammatory drugs (NSAIDs), and intravenous (IV) acetaminophen have been demonstrated to have opioid-sparing effects. Thoracic epidural analgesia (TEA) (typically placed in the preoperative period) for open procedures is associated with earlier return of bowel function, superior postoperative analgesia, and decreased cardiopulmonary morbidity. Improved GI outcomes may be due to the combination of blockade of reflex sympathetic inhibition of gut function and opioid sparing. Hypotension may be a relative contraindication for TEA. The global benefit of TEA is not as clear in laparoscopic procedures. Single-shot spinal has been shown to reduce pain scores and reduce opioid consumption. A number of peripheral blocks have also been evaluated and have all demonstrated improved pain scores and decreased opioid use. The most well studied, transversus abdominal plane (TAP) block/catheters, have improved early postoperative pain scores, opioid consumption, and length of stay.

Preoperative nutritional optimization improves functional

recovery by encouraging an anabolic, rather than catabolic, state. Patients should be screened for malnutrition and when present should receive protein-rich nutritional supplementation for at least 7 days. Screening and correction of anemia improves oxygen (O2) delivery and end-organ function. Those without specific risk for aspiration may ingest solids up to 8 hours before induction. Clear fluids are given, preferably with at least 45 g of carbohydrates, to improve insulin resistance the evening before surgery and up to 2 hours before induction of anesthesia. Metabolic conditioning may also include prehabilitation programs aimed at improving functional capacity and immunonutrition both of which have demonstrated improved clinical outcomes.

Bowel preparation in elective CRS has been researched for more than 50 years, and a number of differing opinions still exist. The most current consensus guideline from the American Society for Enhanced Recovery (ASER) and the Perioperative Quality Initiative (POQI) endorse combined isosmotic mechanical bowel preparation with oral antibiotics (MBP-OAB). MBP-OAB has been demonstrated to lower surgical site infections and is associated with decreased rates of post-op gastric dysfunction.

Nausea and vomiting prophylaxis is routinely used in ERAS even in low-risk patients because it is difficult to predict precisely who is likely to develop symptoms. Managing modifiable risk factors preoperatively and planning an anesthetic which reduces baseline risk are encouraged. Strategies may include the use of propofol for induction and maintenance, avoiding nitrous oxide and inhalational agents, minimizing opioid use, and adequate hydration while avoiding excessive fluid administration.

Maintenance of normothermia improves surgical outcomes and is affected by preoperative interventions. Ambient

temperature maintained above 26°C, dry surgical garments, and warming blankets help ensure that the initial redistribution of blood at induction does not drop a patient's core temperature. Care must be taken not to overheat a patient, which may lead to evaporative heat loss.

Favuzza J, Delaney CP. Outcomes of discharge after elective laparoscopic colorectal surgery with transversus abdominis plane blocks and enhanced recovery pathway. *J Am Coll Surg*. 2013;217(3):503–506.

Gan TJ, Thacker JK, Miller TE, et al. *Enhanced Recovery for Major Abdominopelvic Surgery*. New York: Professional Communications; 2016:39–49, 53–63, 105–109.

Guay J, Nishimori M, Kopp S. Epidural local anaesthetics versus opioid-based analgesic regimens for postoperative gastrointestinal paralysis, vomiting and pain after abdominal surgery. *Cochrane Database Syst Rev*. 2016; (7):CD001893.

Hedrick TL, McEvoy MD, Mythen MMG, et al. American Society for Enhanced Recovery and Perioperative Quality Initiative Joint consensus statement on postoperative gastrointestinal dysfunction within an enhanced recovery pathway for elective colorectal surgery. *Anesth Analg*. 2018;126(6):1896–1907.

McEvoy MD, Scott MJ, Gordon DB, et al. American Society for Enhanced Recovery (ASER) and Perioperative Quality Initiative (POQI) joint consensus statement on optimal analgesia within an enhanced recovery pathway for colorectal surgery: part 1—from the preoperative period to PACU. *Perioper Med (Lond)*. 2017;6:8.

Pöpping DM, Elia N, Van Aken HK, et al. Impact of epidural analgesia on mortality and morbidity after surgery: systematic review and meta-analysis of randomized controlled trials. *Ann Surg*. 2014;259(6):1056–1067.

Wischmeyer PE, Carli F, Evans DC, et al. American Society for Enhanced Recovery and Perioperative Quality Initiative Joint consensus statement on nutrition screening and therapy within a surgical enhanced recovery pathway. *Anesth Analg*. 2018;126(6):1883–1895.

B.4. Is it important to decompress the abdomen before induction of anesthesia? Why?

Yes. The most important reason for a preinduction NGT in obstructed and distended patients is to prevent aspiration. These patients are high risk, particularly for the need for postoperative

ventilatory support, which dramatically increases morbidity from 5% to 80%. Therefore, it is desirable to decompress the stomach while the patient has intact upper airway reflexes. NGTs have been demonstrated not to interfere with the function of the lower esophageal sphincter (LES) and do not reduce the efficacy of cricoid pressure (CP). NGTs may not be effective in removing particulate matter and may not always remove all gastric contents. In fact, it has been demonstrated that even when fully decompressed, the stomach can fill again via reverse peristalsis during intestinal obstruction. However, the volume of aspirate is one of the main determinants of morbidity, and NGTs have been shown to decrease residual volume in the stomach.

Hagberg CA, Artime CA, Aziz MF, eds. *Hagberg and Benumof's Airway Management*. 4th ed. Philadelphia, PA: Elsevier; 2018:235–248.

B.5. Describe the respiratory implications.

In addition to the increased risk of aspiration, a distended abdomen can transmit pressure via the diaphragm to reduce the compliance of the respiratory system; decrease the FRC and minute ventilation; and increase the work of breathing, atelectasis, shunt fraction, dead space, and airway pressures. Hypoxia, hypercapnia, and respiratory failure may result.

Bersten AD, Handy JM, eds. *Oh's Intensive Care Manual*. 8th ed. Philadelphia, PA: Elsevier; 2019:492–501.

Fleisher LA, Roizen MF, Roizen JD, eds. *Essence of Anesthesia Practice*. 4th ed. Philadelphia, PA: Elsevier; 2018:600.

B.6. What are the implications of the tense abdominal wall?

A tense abdominal wall can have significant hemodynamic implications. Increased abdominal pressure in both spontaneously and mechanically ventilated patients will make the inspiratory intrathoracic pressure more positive and decrease

venous return. A high-pressured abdomen will also cause venocaval compression, which decreases venous return and contributes to hypotension. A deeper level of abdominal muscle relaxation must also be targeted to optimize the surgical field.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-Existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:53–78.

Townsend CM, Beauchamp RD, Evers BM, et al, eds. *Sabiston Textbook of Surgery: The Biological Basis of Modern Surgical Practice*. 20th ed. Philadelphia, PA: Elsevier; 2017:1120–1138.

B.7. Outline the methods of abdominal decompression.

A sumping tube with a lumen for suctioning and a lumen for allowing air to be drawn into the stomach helps prevent the tube from sticking to the mucosa of the GI tract during suctioning. An NGT is advanced to approximately 50 to 60 cm for intragastric placement. The location of the tip of the tub should be confirmed before use. Inadvertent laryngeal placement of NGTs has been described with associated morbidity and mortality. Imaging is the gold standard. However, other reassuring signs may include auscultation of the stomach while insufflating air, absence of coughing and gagging during placement, pattern of resistance on placement, and commercial electromagnetic sensors have been developed. Once positioning has been confirmed, the tube must be secured (avoid the tube pressing forward on the nares causing ischemia and possibly erosion) and can then be set to gravity or suction. Tracking the output of the NGT may help to demonstrate resolution of obstruction over time.

Fleisher LA, Gaiser R, Kofke WA. Nasogastric tube placement. http://www.proceduresconsult.com/medical-procedures/nasogastric-tube-placement-AN-006-procedure.aspx. Accessed October 26, 2018.

Yeo CJ, ed. *Shackelford's Surgery of the Alimentary Tract*. 8th ed. Philadelphia, PA: Elsevier; 2019:663–672.

B.8. Discuss the goals of fluid management.

The goals of fluid management include maintaining an effective circulating volume to support O_2 delivery and avoiding organ hypoperfusion. At the same time, adverse effects of fluids, such as nonphysiologic electrolyte levels, toxicities, and excessive volume administration, must be avoided. Care is taken to prevent specific pathologic insults. For example, active bleeding decreases intravascular volume; gastric losses deplete Na^+, K^+, and Cl; small bowel losses deplete K^+, Cl^-, and HCO_3^-; and large bowel losses deplete K^+ (**Table 15. 2**). Sequestered fluid has a composition similar to plasma. Inflammation results in redistribution of fluid from the intravascular into the extracellular compartment. Sepsis impairs tissue O_2 extraction.

TABLE 15.2 Transcellular Fluid Composition

Daily Volume (L)	Daily Volume (L)	Cations				Anions		pH
Fluid		Na+	K+	Ca2+	Mg2+	Cl−	HCO3−	
Gastrointestinal tract								
Saliva	1–1.5	30–90	20–40	2.5	0.6	15–35	10–40	6–7
Gastric	1.5–2.5	20–60	10–20			20–160	0	1–3.5
Bile	0.7–1.2	130–150	5–12	10–50		25–100	10–45	7–8
Pancreatic	1–1.5	125–150	5–10			30–110	40–115	8–8.3
Small bowel (concentration from proximal to distal)	1.8	140–125	5–9			110–60	100–75	7–8
Large bowel	0.2 (lost in feces)	20–40	30–90			0–15	40	7–8

Reprinted from Miller RD, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015:1769. Copyright © 2015 Elsevier. With permission.

Both the volume and composition of resuscitative fluids must be considered. Hypovolemia predisposes to hypotension.

Hypervolemia causes the release of cardiac natriuretic peptides which degrade endothelial glycocalyx. This may contribute to capillary leakage, decreased oncotic pressure, and tissue edema. Edema of the lungs predisposes pulmonary infection, and edematous bowel can contribute to postoperative GI dysfunction. Other consequences of hypervolemia include impaired healing due to decreased oxygenation and increased myocardial work due to supraoptimal ventricular filling on the Frank-Starling curve.

The administration of different fluids with varying compositions may also lead to metabolic acidosis, renal dysfunction, and abnormalities in hemostasis. It is important to remember that clinical trials evaluating fluid administration have differing results between the healthy versus the critically ill or those with different pathologic processes. Interpatient responsiveness can also vary.

Cameron JL, Cameron AM, eds. *Current Surgical Therapy*. 12th ed. Philadelphia, PA: Elsevier; 2017:1313–1320.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1480–1523.

B.9. What would you use as a guide to fluid volume replacement?

For this patient in an urgent/emergent setting, with possible sepsis, vascular compromise, and major abdominal surgery, a dynamic physiologic variable such as cardiac output (CO), stroke volume variation (SVV), or pulse pressure variation (PPV) coupled with a marker of global perfusion like successive lactate levels are reasonable choices to guide fluid volume replacement.

Approaches to fluid therapy prescribing milliliter per kilogram fluid administration based on estimations of the deficit and maintenance requirements lead to increased complications

when more than 3.5 to 5 L are given in the perioperative period. Current data suggest that tailoring fluid therapy to physiologic endpoints results in better outcomes. There is increasing evidence that traditional markers such as HR, BP, urine output, and central venous pressure (CVP) are nonspecific and should not be used as the sole end points for resuscitation. GDFT is a strategy used to optimize flow-related hemodynamic variables to optimize end-organ function by guiding the use of fluids, vasopressors, and inotropes. Numerous studies have shown that mortality can be improved by targeting CO or end-organ O_2 delivery, and patients with the highest mortality risk benefit the most. A number of minimally invasive CO monitors are available to measure physiologic variables including esophageal Doppler, arterial waveform analysis, bioimpedance and bioreactance, and a host of other increasingly less invasive devices. Recent meta-analyses evaluating all perioperative timeframes and GDFT tools have demonstrated decreased morbidity and hospital length of stay. Common algorithms involve constant assessment of the chosen variable coupled with suggested hemodynamic interventions as in this sample (**Fig. 15.3**). Heterogeneity in prospective studies and meta-analyses has prevented researches from determining the best hemodynamic targets, monitoring tools, and interventions. However, a few key points are evident.

- Fluid therapy produces better outcomes when tailored to the patient's physiologic state.
- Dynamic- and flow-related indicators of hemodynamic status perform better than static variables.

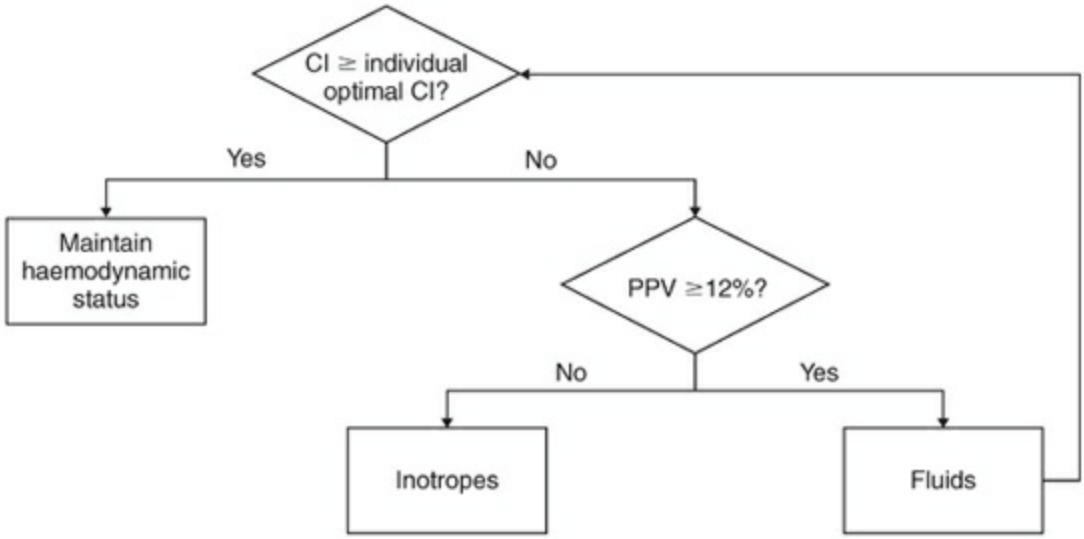


FIGURE 15.3. Sample GDFT algorithm. Intervention algorithm during mechanical ventilation. CI, cardiac index; PPV, pulse pressure variation. (*From Funcke S, Saugel B, Koch C, et al. Individualized, perioperative, hemodynamic goal-directed therapy in major abdominal surgery [iPEGASUS trial]: study protocol for a randomized controlled trial*. Trials. *2018;19[1]:273. http://creativecommons.org/licenses/by/4.0/. Copyright © The Author(s). 2018 Open Access*.)

- Timing of fluid intervention appears to affect outcomes.
- Consider early administration of vasopressors in fluid nonresponders with signs of hypoperfusion.
- As newer technology is developed, its utility in GDFT must be evaluated. New monitoring tools are valuable because they trigger intervention at critical times. The manipulation of physiologic variables is what improves outcomes, not so much the specific monitor used. This may explain why newer devices may not demonstrate a substantial benefit over existing monitors.

Funcke S, Saugel B, Koch C, et al. Individualized, perioperative, hemodynamic goal-directed therapy in major abdominal surgery (iPEGASUS trial): study protocol for a randomized controlled trial. *Trials*. 2018;19(1):273.

Kaplan JA, Cronin B, Maus TM, eds. *Kaplan's Essentials of Cardiac Anesthesia for Noncardiac Surgery*. Philadelphia, PA: Elsevier; 2019:538–577.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1480–1523.

C. Intraoperative Management

C.1. What dangers are present during induction? How are they planned for?

Aspiration of gastric contents and hypotension are the biggest dangers on induction. Mortality from aspiration ranges widely from 5% to 80%. Patients scheduled for emergency surgery are at high risk for aspiration, and intestinal obstruction is the most common predisposing condition in patients that do aspirate.

If the airway does not appear difficult, rapid sequence induction and intubation (RSII) is used to shorten the time between loss of airway reflexes and placement of a cuffed endotracheal tube to minimize the chance of aspiration. Common components of RSII are CP, administration of an IV anesthetic followed immediately by a rapid acting muscle relaxant, avoidance of sedation, and foregoing (at least initially) positive pressure ventilation.

CP has been widely adopted in RSII, but we do not currently have prospective randomized control data to rate its effectiveness. Different aspects of CP have been the focus of intense study and are well summarized in the literature. The 2015 Difficult Airway Society guidelines for unanticipated difficult intubation in adults recommend CP be applied, release of CP if laryngoscopy is difficult, and reapplication in the event of vomiting. CP prevents regurgitated contents from reaching the oropharynx. A modified RSII uses CP to prevent air from entering the stomach allowing for gentle positive pressure ventilation during induction which may be helpful in septic patients.

Patients regurgitate when barrier pressure (LES pressure − gastric pressure) is reduced below zero (**Table 15.3**). Opioids and sedatives may negatively affect barrier pressure and are avoided.

TABLE 15.3 Factors that Increase Intragastric Volume and Pressure

Increased gastric filling
Air insufflation during mask ventilation
Increased gastric acid production
Gastrin
Histamine-2 (H_2) receptor stimulation
Recent ethanol ingestion
Recent hypoglycemic episode
Decreased gastric emptying
Intestinal obstruction
Diabetic gastroparesis
Opioids
Anticholinergics
Sympathetic stimulation (pain and anxiety)

Reprinted from Hagberg CA, Artime CA, Aziz MF, eds. *Hagberg and Benumof's Airway Management*. 4th ed. Philadelphia, PA: Elsevier; 2018:237. Copyright © 2018 Elsevier. With permission.

If the airway appears difficult or the patient has a history of difficult intubation, an awake intubation must be considered. The lips, tongue, and pharynx may be anesthetized, but the larynx's innervation should be kept intact in order to maintain protective reflexes.

Hemodynamics typically dictates the choice of induction agent. Propofol is the most popular agent. Ketamine and etomidate, however, are first-line agents when a patient is already hypotensive. Both agents produce similar intubating conditions, but even one intubating dose of etomidate has been shown to cause adrenal insufficiency in acutely ill patients. Ketamine may be the best choice for septic patients.

Frerk C, Mitchell VS, McNarry AF, et al. Difficult Airway Society 2015 guidelines for management of unanticipated difficult intubation in adults. *Br J Anaesth*. 2015;115(6):827–848.

Hagberg CA, Artime CA, Aziz MF, eds. *Hagberg and Benumof's Airway Management*. 4th ed. Philadelphia, PA: Elsevier; 2018:235–248, 265–268.

Jabre P, Combes X, Lapostolle F, et al. Etomidate versus ketamine for rapid

sequence intubation in acutely ill patients: a multicentre randomised controlled trial. *Lancet*. 2009;374(9686):293–300.

Warner MA, Warner ME, Weber JG. Clinical significance of pulmonary aspiration during the perioperative period. *Anesthesiology*. 1993;78(1):56–62.

C.2. Does the administration of antacids and/or histamine-2 (H_2) blockers before the induction of anesthesia have a significant value in patients with small bowel obstruction?

H_2 blockers have a decreased value in small bowel obstruction and even less value in emergency surgery. Acidic pH is one of the main determinants of morbidity in aspiration. H_2 blockers are used in patients at high risk for aspiration to increase gastric pH by blocking the ability of histamine to induce secretion of gastric fluid with high H^+ concentration. In patients with a high GI obstruction, however, a significant amount of acidic fluid is already present. Administration of an H_2 blocker has no immediate effect on the pH of this fluid. Studies evaluating the effect of H_2 blockers typically administered them more than 1 hour before surgery. The largest benefit is from a multidose regimen starting the night before, making this prophylaxis less valuable before induction of an emergency case. Some benefit may be derived, however, during extubation.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:604.

Hagberg CA, Artime CA, Aziz MF, eds. *Hagberg and Benumof's Airway Management*. 4th ed. Philadelphia, PA: Elsevier; 2018:235–248.

C.3. In what position would you intubate this patient?

This patient is at high risk for aspiration, is hypotensive, and has a clinical picture of sepsis. Positioning the patient with 25 to 30 degrees of head elevation, her head and neck in the sniffing position, and her legs up making her into a "V" shape may be

most beneficial. This combination should improve upper airway patency and access, increase FRC, and may reduce aspiration risk; the legs up position may help prevent hypotension on induction if her body habitus does not increase gastric pressure.

Higgs A, McGrath BA, Goddard C, et al. Guidelines for the management of tracheal intubation in critically ill adults. *Br J Anaesth*. 2018;120(2):323–352.

C.4. What is the best muscle relaxant to use for the rapid sequence induction?

A rapid sequence dose of rocuronium, assuming the availability of sugammadex, may be the best option for intubation. Succinylcholine had been the preferred agent, in spite of its side effects, because of its fast offset should a difficult airway be encountered. Both produce similar intubating conditions. An emergency dose of sugammadex (16 mg per kg), however, is capable of a more rapid return of spontaneous ventilation than succinylcholine. However, spontaneous ventilation is not guaranteed because the hypnotic agent may still interfere with the patient's respiratory effort. Succinylcholine-induced fasciculations also increase O_2 consumption which may be significant in the setting of a difficult airway.

Frerk C, Mitchell VS, McNarry AF, et al. Difficult Airway Society 2015 guidelines for management of unanticipated difficult intubation in adults. *Br J Anaesth*. 2015;115(6):827–848.

Hagberg CA, Artime CA, Aziz MF, eds. *Hagberg and Benumof's Airway Management*. 4th ed. Philadelphia, PA: Elsevier; 2018:584–599.

Higgs A, McGrath BA, Goddard C, et al. Guidelines for the management of tracheal intubation in critically ill adults. *Br J Anaesth*. 2018;120(2):323–352.

C.5. Would you remove or leave the nasogastric tube (NGT) in place before inducing anesthesia?

A strong case can be made for leaving an NGT in place while inducing and intubating this patient. They are indicated for patients with obstruction and distended abdomens, and NGTs in

place on arrival to the operating room (OR) should be used to decompress the stomach before induction. Modern guidelines recommend against routine postoperative NGTs unless there is a specific indication. The decision then becomes timing of removal of the NGT. One may wish to leave an NGT in place during induction to act as a "blow off valve" for gastric pressure during induction when paralysis reduces muscle tone; removal may induce vomiting, and removal may be very stimulating and uncomfortable to an awake patient. Advocates for NGT removal point to decreased LES tone and obscured laryngoscopy from a foreign body in the airway. However, studies have shown that neither the presence nor the size of an NGT has an effect on gastric reflux, and effective CP can be maintained with an NGT in place. If an NGT is somehow obstructing laryngoscopy, it can always be removed. Of course, the presence of an NGT does not guarantee an empty stomach, and particulate matter is difficult to remove. Proper airway planning is always paramount.

Hagberg CA, Artime CA, Aziz MF, eds. *Hagberg and Benumof's Airway Management*. 4th ed. Philadelphia, PA: Elsevier; 2018:235–248.

C.6. Would you use nitrous oxide in this patient?

No. Nitrous oxide is relatively contraindicated in patients with an intestinal obstruction. Nitrous oxide can diffuse into gas-filled spaces more than 30 times faster than nitrogen can diffuse out. The increased gas and intraluminal pressure already present in the bowel during intestinal obstruction combined with the nitrous could cause ischemia and necrosis.

Zafirova Z, Sheehan C, Hosseinian L. Update on nitrous oxide and its use in anesthesia practice. *Best Pract Res Clin Anaesthesiol*. 2018;32(2):113–123.

C.7. Are there any benefits to using a high concentration of inspired oxygen (FIO_2)?

No, a high inspired concentration of O_2 does not prevent

infection or healing complications after major intestinal surgery. The dose-response curve for oxidative killing of bacterial is nonlinear. In the context of wound healing, O_2 is used as a cofactor for oxidant production rather than the energy-producing oxidative phosphorylation of aerobic respiration. Rate constants for collagen synthesis, angiogenesis, and epithelialization all fall within a physiologic range that is normally achieved with an F_{IO_2} of 30% to 40%. Normothermia, euvolemia, and appropriate prophylactic antibiotics are important determinants of infection and wound healing outcomes.

Typically, hemoglobin and CO are considered the main determinants of O_2 delivery which holds true in highly metabolically active tissue that is one cell away from a capillary. In subcutaneous tissue, the capillary distance is farther, O_2 consumption lower, and the O_2 is consumed during healing and immune function. The main determinant of oxygenation in these environments is Pa_{O_2}. Pa_{O_2} drives diffusion of O_2, especially where microvasculature has been damaged by surgical incisions. Vasoconstriction to the subcutaneous tissue will limit the O_2 delivered and diffused. Normothermia and avoidance of hypovolemia then become pillars of wound healing and immune function.

Hyperoxia can have deleterious effects. Even breathing 28% F_{IO_2} for 1 hour increases reactive O_2 species (ROS) in exhaled gas, which can damage DNA and cause lung injury. Supplemental O_2 impairs mucociliary function leading to plugging, atelectasis, and secondary infection; causes edema in large airways; and creates absorption atelectasis in healthy volunteers. There is also evidence that some specific populations may be harmed by hyperoxia, specifically patients with the comorbidities chronic obstructive pulmonary disease (COPD), postcardiac arrest, postmyocardial infarction (MI), stroke, and

traumatic brain injury (TBI). ROS may also reduce $PaCO_2$ by acting at respiratory centers in the brainstem which may lead to vasoconstriction and decreased delivery of O_2.

Ball J, Ranzani OT. Hyperoxia following cardiac arrest. *Intensive Care Med*. 2015;41(3):534–536.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:183–200.

Brown DI, Griendling KK. Regulation of signal transduction by reactive oxygen species in the cardiovascular system. *Circ Res*. 2015;116(3):531–549.

Kurz A, Kopyeva T, Suliman I, et al. Supplemental oxygen and surgical-site infections: an alternating intervention controlled trial. *Br J Anaesth*. 2018;120(1):117–126.

van Ooij PJ, Hollmann MW, van Hulst RA, et al. Assessment of pulmonary oxygen toxicity: relevance to professional diving; a review. *Respir Physiol Neurobiol*. 2013;189(1):117–128.

C.8. What components of ERAS are applied in the intraoperative phase of the care of CRS patients?

Intraoperative components of ERAS pathways focus on maintenance of euvolemia, the optimal analgesia paradigm for pain control, surgical stress response attenuation, PONV prophylaxis, optimal depth of anesthesia, and maintenance of normothermia. Both excessive and inadequate intravascular volumes are associated with poor surgical outcomes. Hypovolemia predisposes to renal injury and end-organ damage, whereas hypervolemia can lead to delayed return of gut function, decreased oxygenation, and increased myocardial work. GDFT has been shown to improve outcomes in high-risk patients and moderate-risk patients undergoing major abdominal surgery. Risk factors may include ischemic heart disease, heart failure, cerebrovascular disease, diabetes requiring insulin, and pre-op creatinine levels >2.0 mg per dL. Patient and procedure risk factors may be used to help guide the use of advanced hemodynamic monitors (**Fig. 15.4**). Patients are euvolemic at

the level portion of the Frank-Starling Curve. These protocols have reduced the variability with which fluid is administered. Some recent trials have suggested that GDFT may not show improved outcomes in the context of enhanced recovery pathways. This is likely due to redundant ERAS components that restrict fluid administration while avoiding hypovolemia within those pathways. The guiding principle of fluid therapy remains titration to dynamic physiologic endpoints rather than application of a particular GDFT tool.

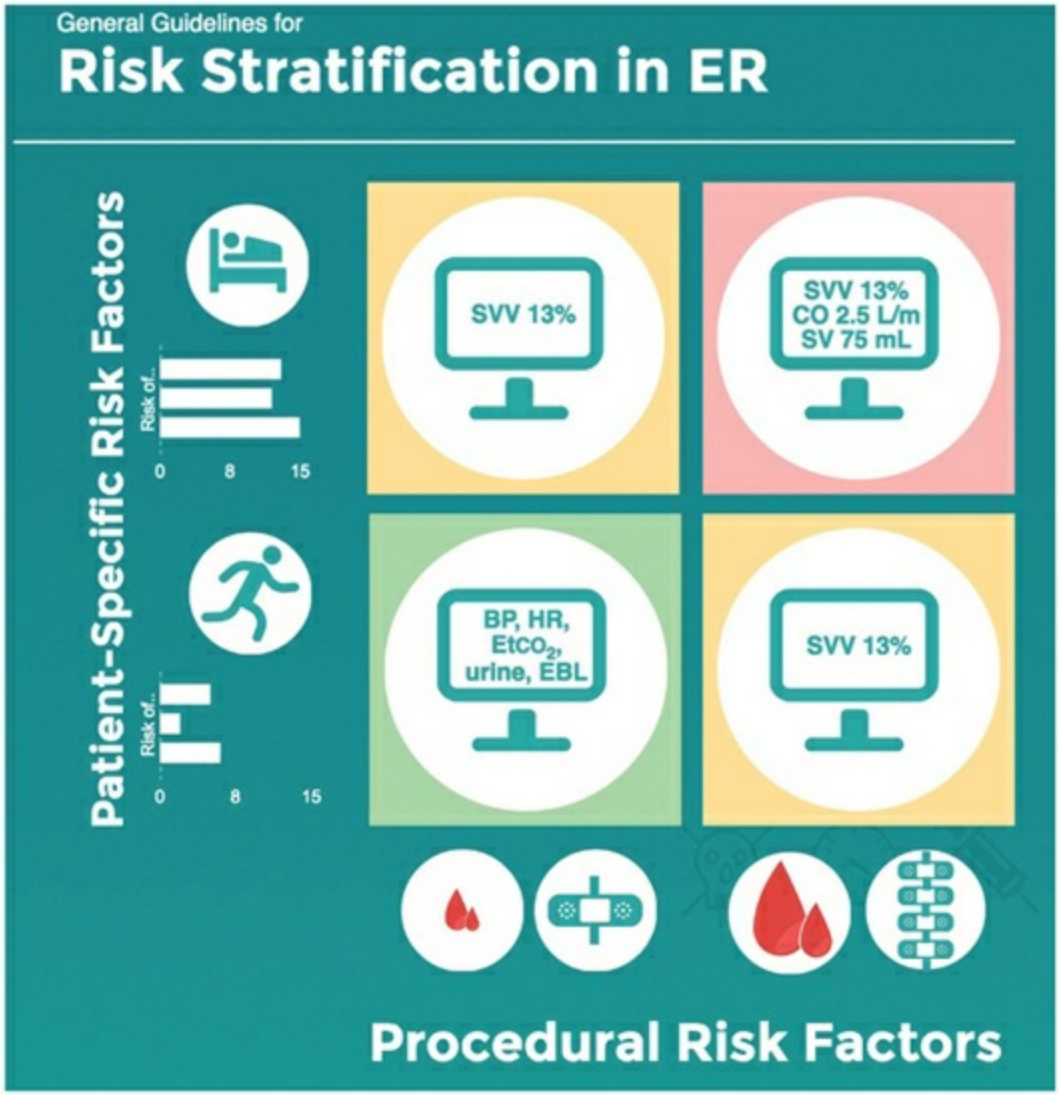
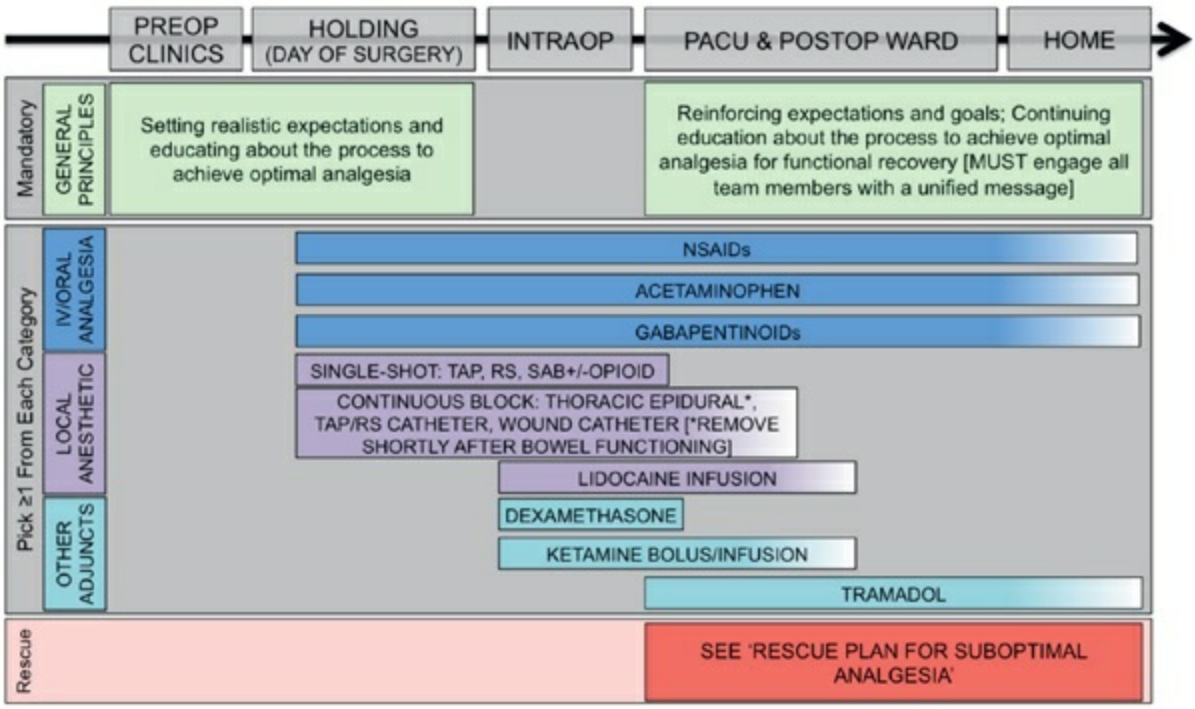


FIGURE 15.4. POQI risk stratification for monitoring in enhanced recovery protocol. Proposed risk stratification scheme for patients undergoing colorectal surgical procedures in the context of an enhanced recovery protocol. Patient-specific risk factors: poor functional status and elevated cardiac

risk **(top)**; good functional status and low cardiac risk **(bottom)**. Procedural risk factors: minimally invasive and small fluid shifts **(left)**; maximally invasive and large fluid shifts **(right)**. BP, blood pressure; CO, cardiac output; EBL, estimated blood loss; $EtCO_2$, end-tidal carbon dioxide; HR, heart rate; SV, stroke volume; SVV, stroke volume variation. (*From Thiele R, Raghunathan K, Brudney CS, et al. American Society for Enhanced Recovery [ASER] and Perioperative Quality Initiative [POQI] joint consensus statement on perioperative fluid management within an enhanced recovery pathway for colorectal surgery*. Perioper Med [Lond]. *2016;5:24. https://creativecommons.org/licenses/by/4.0/. Copyright © 2016 The Author[s].*)

Analgesia strategies intraoperatively continue to revolve around the paradigm of optimal analgesia by balancing comfort, early functional recovery, and minimizing side effects. A number of multimodal nonopioid adjuncts are efficacious and recommended in the ASER and POQI consensus statement (**Table 15.4**). They include NSAIDS, acetaminophen, gabapentinoids, single-shot and continuous nerve blocks, infusions of lidocaine, low-dose ketamine, and dexamethasone. The key point is that the combination of agents selected are not as important so long as they are effective. It is also important to note that ERAS focuses on minimizing opioid use. Pain is not perceived during general anesthesia (GA), and hemodynamic consequences of surgery can be controlled with β-blockers, calcium channel blockers, and lidocaine without increased opioid consumption postoperatively.

TABLE 15.4 Treatment Algorithm for Achieving Optimal Analgesia after Colorectal Surgery



From McEvoy MD, Scott MJ, Gordon DB, et al. American Society for Enhanced Recovery (ASER) and Perioperative Quality Initiative (POQI) joint consensus statement on optimal analgesia within an enhanced recovery pathway for colorectal surgery: part 1—from the preoperative period to PACU. *Perioper Med (Lond)*. 2017;6:8. http://creativecommons.org/licenses/by/4.0/. Copyright © The Author(s). 2017 Open Access.

Minimizing the harmful effects of the surgical stress response is a cornerstone of enhanced recovery. Patients experience stress if their typical homeostatic mechanisms are insufficient and they must alter their basic physiology. For instance, during hypoglycemia, neurohumoral mediators promote gluconeogenesis and insulin resistance in order to deliver the valuable but scarce glucose to glucose-dependent end organs. Mediators of the stress response like cortisol, glucagon, catecholamines, antidiuretic hormone (ADH), and cytokines affect multiple-organ systems and can lead to undesirable surgical outcomes including myocardial ischemia, large fluid shifts, breakdown of lean muscle, poor wound healing, and impaired immune function. Some of the challenges of perioperative homeostasis and their management are listed in the following table from the ASER (**Table 15.5**). Oxygenation,

perfusion, fluids, and nutrition can be artificially supported in the perioperative period. ERAS pathways to minimize components of the stress response focused on these variables. The most effective interventions are the ones that directly reduce a physiologic challenge, such as a laparoscopic rather than open surgical approach. A conceptual framework for the stress response is shown in **Figure 15.5**. Interventions shown to improve outcomes after surgery include TEA, high-dose corticosteroids, and intensive insulin therapy.

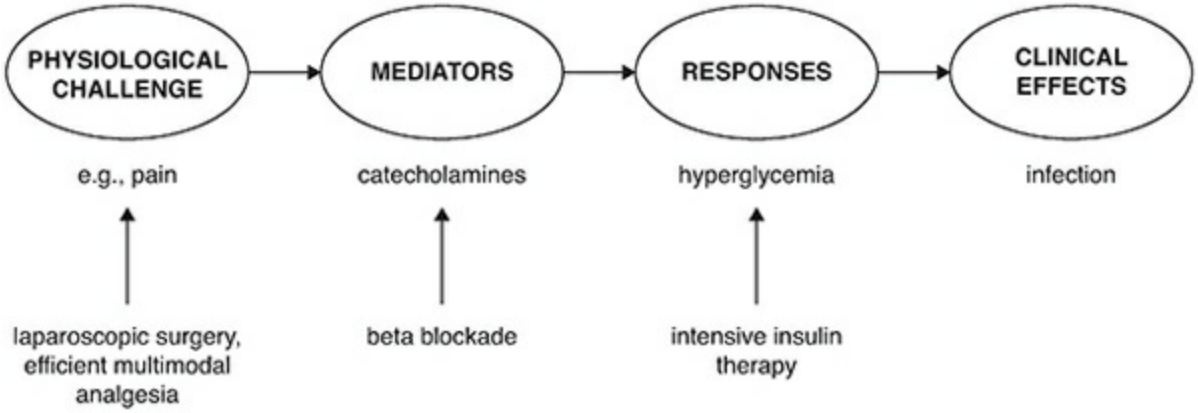


FIGURE 15.5. Conceptual framework of mechanisms of the surgical stress response. Conceptual framework of the surgical stress responses, showing potential opportunities for intervention for the example of pain, catecholamines, and hyperglycemia. Experience has shown that the most successful and feasible interventions aim to blunt the physiologic challenge in the first place (e.g., nociception), rather than blunt the release of the mediators (e.g., β-adrenergic receptor blockade) or the response itself (e.g., hyperglycemia). Successful enhanced recovery protocols (ERPs) consist of a series of interventions that target mainly the physiologic challenges. (*From Gan TJ, Thacker JK, Miller TE, et al*. Enhanced Recovery for Major Abdominopelvic Surgery. *1st ed. New York, NY: Professional Communications, Inc.; 2016:201. With permission*.)

TABLE 15.5 Physiologic Challenges to Homeostasis

Perioperative Physiologic Challenge	Management
Anxiety	Preoperative patient education Same-day admission
Preoperative dehydration	Adherence to modern preoperative fasting guidelines Avoidance of hyperosmolar oral bowel preparation
Preoperative fasting	Preoperative oral carbohydrate treatment
Preoperative transfusion	Preoperative iron infusion

Tissue injury and contamination	Minimally invasive surgical approaches Short incisions Atraumatic technique
Nociception and pain	Effective analgesia Regional analgesia Multimodal analgesia
Hypothermia	Active and passive warming
Intravenous fluid loading	Protocol-driven, balanced fluid therapy
Intra- and postoperative transfusion	Red-cell saving techniques Strict transfusion triggers
Postoperative fasting	Early oral diet Techniques to avoid or minimize ileus
Postoperative lack of physical activity	Protocol-driven postoperative mobilization

From Gan TJ, Thacker JK, Miller TE, et al. *Enhanced Recovery for Major Abdominopelvic Surgery*. 1st ed. New York, NY: Professional Communications, Inc.; 2016:203. With permission.

ERAS patients are risk stratified for PONV, and prophylaxis is tailored to risk level. A simplified Apfel risk score identifies female sex, nonsmoker, history of PONV, and postoperative opioids as factors increasing the risk of PONV. Intraoperative strategies to decrease the risk of PONV include use of regional over general anesthesia, propofol used as induction and maintenance agent, avoidance of nitrous oxide and volatile anesthetics, minimal opioid administration, adequate but not excessive fluid hydration, and administration of a number of antiemetic pharmacologic agents. ERAS pathways encourage multimodal antiemetic prophylaxis, even for low-risk patients (**Fig. 15.6**). If prophylaxis fails, a different pharmacologic class of antiemetic should be used. Dexamethasone and transdermal scopolamine do not need to be redosed within 24 to 48 hours. Other antiemetics, for example, 5HT-3 antagonists, readministered within 6 hours are ineffective (**Table 15.6**).

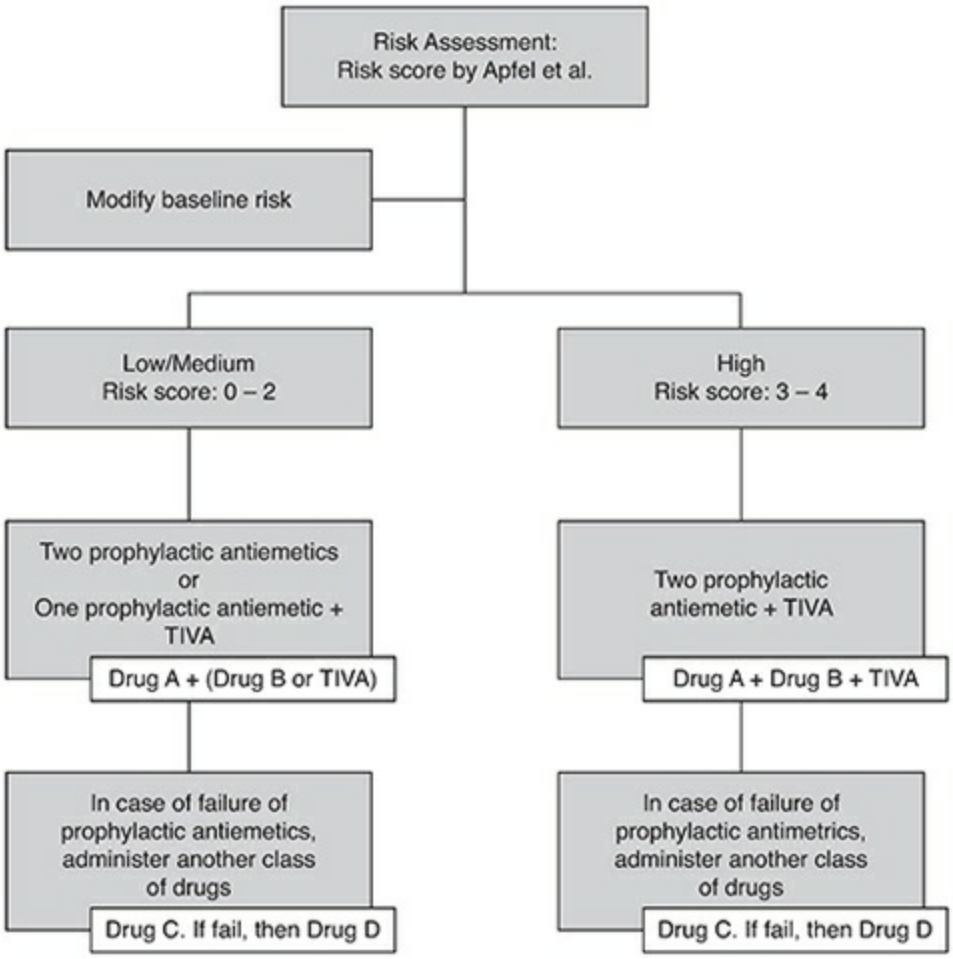


FIGURE 15.6. Flow chart for management of PONV in the context of enhanced recovery. Example interventions: drug A = dexamethasone 4 mg in adults or 0.15 mg per kg of body weight in children; drug B = ondansetron 4 mg in adults or 0.1 mg per kg of body weight in children; drug C = promethazine 6.25 mg in adults; drug D = dimenhydrinate 1 mg per kg of body weight in adults or 0.5 to 1.0 mg per kg of body weight in children. The given drug examples are used to illustrate how the algorithm may be actually implemented but may not represent the most favorable approach. The latter may be context sensitive (children, adults, or other issues). In the event of treatment failure, timely assessment is essential and an alternate antiemetic agent should be used. A multimodal treatment approach may be appropriate to increase the likelihood of success. TIVA, total intravenous anesthesia, that is, propofol induction and maintenance, no nitrous oxide. (*From Gan TJ, Thacker JK, Miller TE, et al*. Enhanced Recovery for Major Abdominopelvic Surgery. *1st ed. New York, NY: Professional Communications, Inc.; 2016:201. With permission*.)

TABLE 15.6 Choices of Antiemetic Agents in Adults: Dosage and Timing

Drugs	Dose	Evidence	Timing	Evidence
Aprepitant	40 mg PO	A2	At induction	A2
Casopitant	150 mg PO	A3	At induction	

Dexamethasone	4–5 mg IV	A1	At induction	A1
Dimenhydrinate	1 mg per kg IV	A1		
Dolasetron	12.5 mg IV	A2	End of surgery; timing may not affect efficacy	A2
Droperidol[a]	0.625–1.25 mg IV	A1	End of surgery	A1
Ephedrine	0.5 mg per kg IM	A2		
Granisetron	0.35–3 mg IV	A1	End of surgery	A1
Haloperidol	0.5–<2 mg IM/IV	A1		
Methylprednisolone	40 mg IV	A2		
Ondansetron	4 mg IV, 8 mg ODT	A1	End of surgery	A1
Palonosetron	0.075 mg IV	A2	At induction	A2
Perphenazine	5 mg IV	A1		
Promethazine	6.25–12.5 mg IV	A2		
Ramosetron	0.3 mg IV	A2	End of surgery	A2
Rolapitant	70–200 mg PO	A3	At induction	
Scopolamine	Transdermal patch	A1	Prior evening or 2 h before surgery	A1
Tropisetron	2 mg IV	A1	End of surgery	Expert opinion

IM, intramuscular; IV, intravenous; ODT, orally disintegrating table; PO, per os.
These recommendations are evidence based and not all the drugs have a US Food and Drug Administration (FDA) indication for postoperative nausea and vomiting (PONV). Drugs are listed alphabetically.

[a]See FDA black box warning.

Reprinted with permission from Gan TJ, Diemunsch P, Habib AS, et al. Consensus guidelines for the management of postoperative nausea and vomiting. *Anesth Analg*. 2014;118(1):85–113.

Postoperative delirium and postoperative cognitive dysfunction (POCD) may impair a patient's mental and motor functions preventing them from participating in their recovery, postponing their discharge, and increasing their risk of mortality. The pathophysiology is not yet well understood, but high-dose anesthetics, inflammation, stress response hormones, and other perioperative insults may contribute to neurologic dysfunction in the postoperative period. Inadequate anesthesia also prevents patients from gaining the neuroprotective benefits of anesthesia. In many situations, hemodynamic values alone are inadequate to reflect anesthetic depth. Methods to detect an optimal depth of

anesthesia using electroencephalographs (EEG), electromyographs (EMG), and auditory evoked potentials (AEP) have been shown to improve neurocognitive outcomes in older high-risk patients.

Normothermia is crucial because even mild hypothermia can increase rates of infection, platelet dysfunction, and protein catabolism; decrease drug metabolism, renal function, and wound healing; and have major cardiovascular implications such as arrhythmias, left shift of hemoglobin-O_2 saturation curve, and increased peripheral vascular resistance. Core temperature monitoring is recommended in all patients undergoing anesthesia. Interventions recommended for maintaining normothermia include warming the periphery prior to surgery to avoid the initial drop in core temperature on induction, maintaining an OR temperature above 21°C and possibly even at 26°C until the prep solution is dry and patient is draped, limiting areas of exposed skin, fluid warmers for boluses above 500 mL, heated and humidified gases, and, of course, forced air warmers over the largest available surface area.

Cameron JL, Cameron AM, eds. *Current Surgical Therapy*. 12th ed. Philadelphia, PA: Elsevier; 2017:325–334.

Gan TJ, Diemunsch P, Habib AS, et al. Consensus guidelines for the management of postoperative nausea and vomiting. *Anesth Analg*. 2014;118(1):85–113.

Gan TJ, Thacker JK, Miller TE, et al. *Enhanced Recovery for Major Abdominopelvic Surgery*. New York: Professional Communications; 2016:133–146, 165–186, 190–212, 360.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:64, 417–418.

Hedrick TL, McEvoy MD, Mythen MMG, et al. American Society for Enhanced Recovery and Perioperative Quality Initiative joint consensus statement on postoperative gastrointestinal dysfunction within an enhanced recovery pathway for elective colorectal surgery. *Anesth Analg*. 2018;126(6):1896–1907.

McEvoy MD, Scott MJ, Gordon DB, et al. American Society for Enhanced

Recovery (ASER) and Perioperative Quality Initiative (POQI) joint consensus statement on optimal analgesia within an enhanced recovery pathway for colorectal surgery: part 1—from the preoperative period to PACU. *Perioper Med (Lond)*. 2017;6:8.

Punjasawadwong Y, Chau-In W, Laopaiboon M, et al. Processed electroencephalogram and evoked potential techniques for amelioration of postoperative delirium and cognitive dysfunction following non-cardiac and non-neurosurgical procedures in adults. *Cochrane Database Syst Rev*. 2018; (5):CD011283.

Srinivasa S, Kahokehr AA, Yu TC, et al. Preoperative glucocorticoid use in major abdominal surgery: systematic review and meta-analysis of randomized trials. *Ann Surg*. 2011;254(2):183–191.

van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in critically ill patients. *N Engl J Med*. 2001;345(19):1359–1367.

Wischmeyer PE, Carli F, Evans DC, et al. American Society for Enhanced Recovery and Perioperative Quality Initiative joint consensus statement on nutrition screening and therapy within a surgical enhanced recovery pathway. *Anesth Analg*. 2018;126(6):1883–1895.

C.9. What are the strengths, weaknesses, benefits, and challenges of ERAS?

Strengths

ERAS uses evidence-based interventions that are customized to the patient and the resources of the institution. Protocols reduce the variability in care and outcomes which help to continually evaluate and improve the pathway. Multidisciplinary care allows each member of the team to focus on what they do best.

Weakness

Individual interventions included in ERAS pathways show benefit in a general population but may be redundant with other components. Attributing a benefit to a specific intervention is difficult and only the bundled program can be credited. Also, many benefits come from suppressing the surgical stress response in elective major abdominal surgeries and older patients with comorbid disease. Cardiovascular, pulmonary, and infectious complications show improvement. Advantages are not

as clear cut in surgical complications. Therefore, ERAS may not offer marked improvement in the uncomplicated laparoscopic procedure in an otherwise healthy young patient.

Benefits

ERAS programs consistently demonstrate accelerated recovery, reduced complication rate, safe reduced length of stay, reduced readmission rate, increased value by improving quality while decreasing cost, and improved patient satisfaction.

Challenges

The biggest challenges in ERAS come in implementation and maintenance. Input and consensus from members of surgery, anesthesia, nursing, and a host of other services can be difficult on an organizational level. Additional resources, such as a program coordinator or patient education materials, order sets, and data tracking systems, can be extremely useful but take time to develop and implement. Sustaining improvements can also be challenging. When implementations are made, data is tracked. Outcomes may initially improve but later decline, and the reason why is not always clear. Documentation may not accurately reflect clinical activities, new staff may not be oriented to the pathway, or experienced providers may not realize how their contributions affect downstream portions of care. Mechanisms for regularly scheduled auditing and frequent opportunities for education have to be devised for sustained improvement.

Cameron JL, Cameron AM, eds. *Current Surgical Therapy*. 12th ed. Philadelphia, PA: Elsevier; 2017:325–334.

Gan TJ, Thacker JK, Miller TE, et al. *Enhanced Recovery for Major Abdominopelvic Surgery*. New York: Professional Communications; 2016:277–309, 319–331.

Ljungqvist O, Hubner M. Enhanced recovery after surgery-ERAS-principles, practice and feasibility in the elderly. *Aging Clin Exp Res*. 2018;30(3):249–252.

C.10. What are the indications for ERAS?

Any patient may benefit from ERAS pathway elements implemented at their institution provided they do not have a contraindication to any of the components (e.g., anaphylactic acetaminophen allergy, antiplatelet therapy that cannot be interrupted for neuraxial analgesia, etc.). Larger, more invasive cases and patients with more comorbidities and more prolonged length of hospital stay may see the biggest benefit.

Gan TJ, Thacker JK, Miller TE, et al. *Enhanced Recovery for Major Abdominopelvic Surgery*. New York: Professional Communications; 2016:65.

D. Postoperative Management

D.1. What are the principles of postoperative care in this patient?

The ultimate goal of postoperative care is recovery of bowel function to the point where the patient can resume oral hydration and take in sufficient nutrition on their own. Many principles of postoperative care are the same as preoperative concerns including maintenance of euvolemia, correction of electrolyte and acid–base imbalances, nutritional support, avoiding bowel distention, and pain management. There are the additional considerations of anastomotic leak, perforation, infection, bleeding, thrombosis, and wound complications that need to be guarded against.

Tissue injury and inflammation continue after surgery which present a challenge to maintaining euvolemia. Increased endothelial permeability and damage to the glycocalyx are a result of systemic inflammation. Fluids are frequently required postoperatively. However, hypervolemia can cause release of cardiac natriuretic peptides which degrade the glycocalyx. Water and electrolytes are lost to the interstitium, which compromises

gut perfusion. When the systemic inflammatory response decreases, fluids mobilize back into the intravascular space and fluid administration must be decreased. Urine output is a poor indicator of volume status as sympathetic stimulation and increases in the renin-angiotensin-aldosterone system cause fluid retention despite adequate intravascular volume.

Bowel function must be monitored postoperatively, and physiologic POI must be differentiated from pathologic ileus. We now believe, in general, gastric and small intestinal mobility occurs within hours of surgery and colonic activity returns within 72 hours. Sections of bowel that were directly manipulated will take longer to recover and may extend to areas not directly manipulated. If the ileus is prolonged, metabolic derangements like hypokalemia, hyponatremia, and uremia can occur; iatrogenic medications, ischemia, hemorrhage, and sepsis should all be considered as contributing factors. Laparoscopic surgery can be associated with hernias and an obstructive point seen on imaging should prompt surgical reintervention.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1480–1523.

Townsend CM, Beauchamp RD, Evers BM, et al, eds. *Sabiston Textbook of Surgery: The Biological Basis of Modern Surgical Practice*. 20th ed. Philadelphia, PA: Elsevier; 2017:1237–1295.

D.2. Are there any postoperative respiratory problems associated with factors other than aspiration?

Yes, respiratory challenges exist in the immediate postoperative period as well as during the inpatient recovery phase. As with all general anesthetics, there is a decreased respiratory drive, increased airway resistance, and neuromuscular impairment caused by residual anesthetics. Immediately after surgery, the bowel may be edematous which increases the diaphragmatic work of breathing and shunt while decreasing FRC. As recovery

continues if fluids are not carefully managed, pulmonary edema can impair gas exchange and further increase the work of breathing. Carbon dioxide production can increase beyond ventilatory capacity in the face of parenteral nutrition and infection.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1538–1558.

D.3. If the patient did aspirate gastric contents, what are the possible sequelae of this event? What is the treatment?

Aspiration of gastric contents causes a chemical pneumonitis initially characterized by hypoxemia, bronchospasm, and atelectasis. Morbidity is increased with larger volumes of aspirate and/or a low pH aspirate. Particulate matter can also be more damaging because it can obstruct the airway, cause distal atelectasis, and act as a nidus for infection resulting in a superimposed pneumonia. If pneumocytes are injured and surfactant washed away, the clinical picture can resemble acute respiratory distress syndrome (ARDS) (**Table 15.7**). Pulmonary edema, decreased pulmonary compliance, increased pulmonary vascular resistance, and ventilation/perfusion ($\dot{V}/\dot{Q}$) mismatching are seen in severe cases. Radiographic evidence may not develop until 6 to 12 hours after the event.

TABLE 15.7 Pathophysiology of Aspiration

Particulate aspiration → Airway obstruction →
Granulomatous inflammation → Acid aspiration →
Neutrophilic inflammation → Hemorrhagic pulmonary edema →
Destruction of airway epithelium → Loss of type 1 alveolar cells →
Loss of surfactant → Alveolar instability and collapse →
Disruption of alveolar-capillary membrane → Plasma leakage from pulmonary capillaries →
Noncardiogenic pulmonary edema → Hypovolemia

Reprinted from Hagberg CA, Artime CA, Aziz MF, eds. *Hagberg and Benumof's Airway Management*. 4th ed. Philadelphia, PA: Elsevier; 2018:238. Copyright © 2018 Elsevier. With

permission.

If a patient begins to vomit, their head should be placed in a lateral position with head down if possible. Treatment is similar to ARDS, mainly supportive with supplemental O_2. Intubation frequently has to be continued with mechanical ventilation and positive end-expiratory pressure (PEEP) to keep O_2 levels acceptable. If particulate matter was aspirated, lavage or bronchoscopy may be considered, but neither will be helpful if the aspirate was purely an acidic fluid because it is quickly distributed, diluted, and neutralized. If bronchospasm is present, pharmacologic bronchodilation is indicated. A superimposed infection does not always occur, and no evidence exists to support prophylactic antibiotics. If an infection does occur, treatment should start with broad-spectrum antibiotics covering gram-negative rods and anaerobes including *Bacteroides fragilis* and then narrowed to the appropriate antibiotics based on culture sensitivities. Steroids do not improve the clinical picture and may increase the incidence of bacterial infection. Pulmonary edema should not be treated with diuretics unless high filling pressures or hypervolemia exist.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1538–1558.

Hagberg CA, Artime CA, Aziz MF, eds. *Hagberg and Benumof's Airway Management*. 4th ed. Philadelphia, PA: Elsevier; 2018:235–248.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-Existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:33–52.

D.4. What is gram-negative sepsis? Describe the clinical picture and treatment.

Sepsis is a clinical syndrome resulting from a dysregulated inflammatory response to infection. This response is aimed at eliminating a threat through generation of noxious O_2

metabolites and cytokines. When inflammation is systemic and long lasting, it can cause end-organ damage which may trigger further inflammation leading to a destructive positive feedback loop. Gram-negative sepsis causes the inflammatory response to certain highly conserved microbial molecules such as the lipid A moiety of lipopolysaccharides (LPS, also called endotoxin). Twenty percent to 50% of patients can progress to hypotension and shock.

Early signs of gram-negative sepsis include an abrupt onset of fever and chills, hyperventilation with respiratory alkalosis, and mental status changes. Neutropenia with increased immature polymorphonuclear leukocytes is the most common lab abnormality. Thrombocytopenia and coagulation abnormalities may also be present. As the condition progresses to septic shock, vascular endothelial damage from NO causes systemic vasodilation and fluid extravasation leading to a relative hypovolemia. Early shock is characterized by an increased CO, decreased systemic vascular resistance (SVR), hypotension, and warm extremities (warm phase). If the relative hypovolemia persists without adequate resuscitation, the resulting "cold phase" was characterized by an increased SVR and a low CO because blood flow is directed back to vital organs, and ultimately death. Both phases experience myocardial dysfunction due to circulating cytokines as evidenced by the left ventricular end systolic pressure–volume relationship (**Fig. 15.7**). Patients who survived were given fluid and were then able to maintain an adequate stroke volume through ventricular dilation without increases in pressure via the Frank-Starling mechanism. Nonsurvivors instead developed a diastolic dysfunction and were unable to maintain an adequate cardiac index. Fluid extravasation also leads to pulmonary edema and as many as 40% of patients may progress to ARDS. Adrenal insufficiency, disseminated intravascular coagulation, and

immunosuppression are also recognized complications of sepsis.

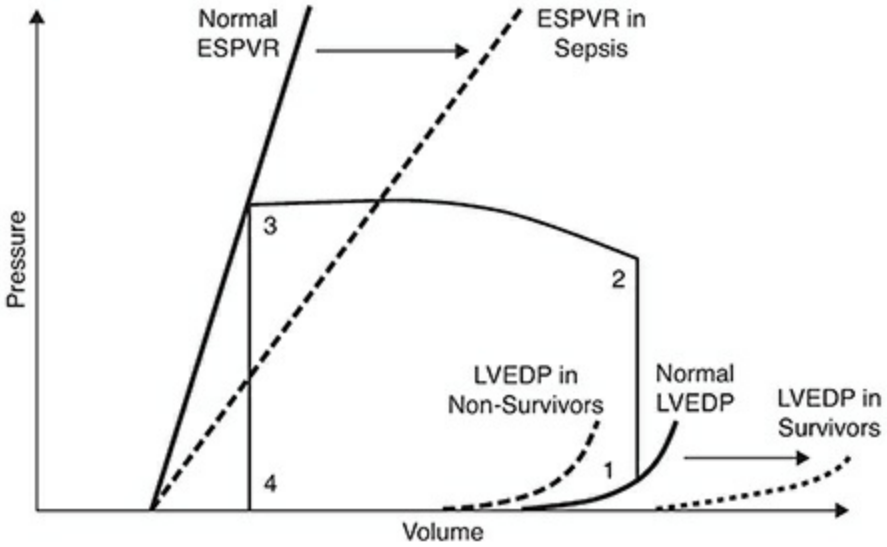


FIGURE 15.7. Myocardial dysfunction in sepsis. Left ventricular pressure–volume relationships. The *bold straight line* shows the normal end-systolic pressure–volume relationship (ESPVR), defining ventricular contraction. ESPVR is independent of changes in preload and afterload. The slope is maximal at end systole and has the units of elastance, $E = \Delta P / \Delta V$. It has therefore been designated E_{max}. The *bold curved line* shows normal end diastolic pressure–volume relationship (EDPVR). The straight section of the line represents addition of the initial volume. Whereas ventricular volume increases from 0 to approximately 50 mL, transmural pressure remains at 0. Left ventricular end diastolic pressure (LVEDP) then increases in a curvilinear manner during addition of further volume. The pressure–volume loop (1 to 4) represents one cardiac cycle (1 to 2, isovolumetric contraction; 2 to 3, stroke volume; 3 to 4, isovolumetric relaxation). The interrupted *straight line* represents E_{max} in sepsis, with depressed contractility indicated by a downward and right shift of the ESPVR. In survivors of septic shock, this is accompanied by a right shift of the EDPVR (*interrupted curved line*) caused by ventricular dilatation, enabling an increase in stroke volume. In nonsurvivors, diastolic stiffness develops represented by an upward and left shift of the EDPVR (*bold, interrupted curved line*), leading to impaired diastolic filling and a reduction in stroke volume. *Arrows* represent possible contribution of nitric oxide (NO) to the pressure–volume relationships in sepsis. Although NO may be responsible for the reduction in systolic contractility, the septic patient is able to maintain end-systolic volume because of a reduction in SVR; therefore, the overriding hemodynamic effect of NO in sepsis may be facilitation of ventricular dilatation, which acts to further stroke volume and maintain cardiac output. Potentially, NO blockade in sepsis may convert the EDPVR of a surviving septic patient to a nonsurvivor. (*Reprinted from Belcher E, Mitchell J, Evans T. Myocardial dysfunction in sepsis: no role for NO?* Heart. *2002;87[6]:508; with permission from BMJ Publishing Group Ltd.*)

Treatment guidelines are summarized in the “Surviving Sepsis” campaign bundles. Mechanical ventilation with lung protective strategies such as tidal volumes <6 mL per kg

predicted body weight and plateau pressures <30 cm H_2O are frequently required because acute lung injury is the most common complication. Circulatory support should be given in the form of an initial fluid bolus and then vasopressors. First line is usually norepinephrine, and if a goal of MAP >65 mmHg is not met, second- and third-line agents, usually vasopressin and epinephrine, may be added. Angiotensin II receptor agonists have also recently showed promise in treatment of catecholamine-resistant shock with a mechanism different from norepinephrine and vasopressin. Tissue oxygenation is not impaired in septic shock. The ability of mitochondria to use O_2 becomes impaired by bacterial endotoxins and results in lactate production. Therefore, efforts to improve tissue oxygenation with transfusions are not indicated. Broad-spectrum antibiotics should be administered within 1 hour of identifying a patient in septic shock and then be narrowed and targeted as soon as culture results are available. Corticosteroid administration has been controversial, but current guidelines recommend it be used in patients poorly responsive to vasopressors.

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Khanna A, English SW, Wang XS, et al. Angiotensin II for the treatment of vasodilatory shock. *N Engl J Med*. 2017;377(5):419–430.

Marino PL. *Marino's The ICU Book*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2014:chap 14.

Papadakis MA, McPhee SJ, Rabow MW, eds. *Current Medical Diagnosis & Treatment 2019*. 58th ed. New York: McGraw-Hill; 2019:1448–1492.

Rhodes A, Evans LE, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016. *Crit Care Med*. 2017;45(3):486–552.

D.5. What components of ERAS are applied in the

postoperative phase of the care of CRS patients?

Postoperative components of ERAS include early oral feeding, ileus prevention, restrictive use of NGTs/lines/drains, early mobilization, and optimal analgesia. These components were developed for elective procedures, but many of the concepts may still be applied to urgent/emergent procedures.

Traditional dogma of postoperative care restricted oral intake in order to protect patients from aspiration, anastomotic leak, and wound dehiscence. Contemporary practice shows early postoperative nutrition is associated with reductions in mortality, complications, anastomotic dehiscence, hyperglycemia, length of stay, and time to return of bowel function. The benefits of parenteral and enteral feeding have been well described in the literature, but oral feeding is the only form of nutritional intake that elicits all of the guts' stimulating reflexes and most closely aligns with the theme of functional recovery. Early oral nutrition in an ERAS pathway has also been shown to decrease complications and hospital length of stay even if duration of ileus was not reduced significantly. We also now know that the presence of fluid and some semidigested material in the gut does not threaten fresh anastomoses any more than natural content such as enzymes, bile juice, and stomach acids. Oral feeding is tolerated within 24 hours by 80% to 90% of CRS patients and is an inexpensive intervention not shown to be associated with adverse events. Oral intake has to be adapted to individual tolerance, surgery, and risk factors but general recommendations for postoperative care of uncomplicated cases include encouraging drinking as soon as they are fully awake, resumption of normal diet when tolerating fluids, nutritional supplement beverages, glucose monitoring and treatment, and gum chewing.

Ileus as described in the pathophysiology section earlier describes abnormal GI motility. POI is a significant challenge in

ERAS pathways because it is a major factor in determining hospital length of stay, inhibits functional recovery, and causes discomfort to patients. We do not know the exact causes of ileus because it represents complex interactions between a number of processes (**Fig. 15.8**), but treatment involves managing inflammation, autonomic dysfunction and the stress response to surgery, intestinal opioid receptors, GI hormones, electrolyte imbalances, and impaired gut contractility. Many of the recommendations to limit POI are interventions already suggested for other indications but include minimal preoperative fasting; preoperative optimization including correction of electrolyte abnormalities and anemia; minimizing insulin resistance with a carbohydrate drink 2 hours before surgery and treatment of abnormal glucose levels; minimizing fluid shifts due to iso-osmolar bowel prep by only doing it when indicated; standardized protocols for fluid management; and multimodal pain management with thoracic epidural for open cases, minimizing systemic opioid use, and use of alvimopan when postoperative opioids are used. Other interventions that have limited evidence of decreased POI and are not yet included in consensus statements include nicotine gum chewing, magnesium, coffee, Dai-Kenchu-To (DKT), and polyunsaturated fats.

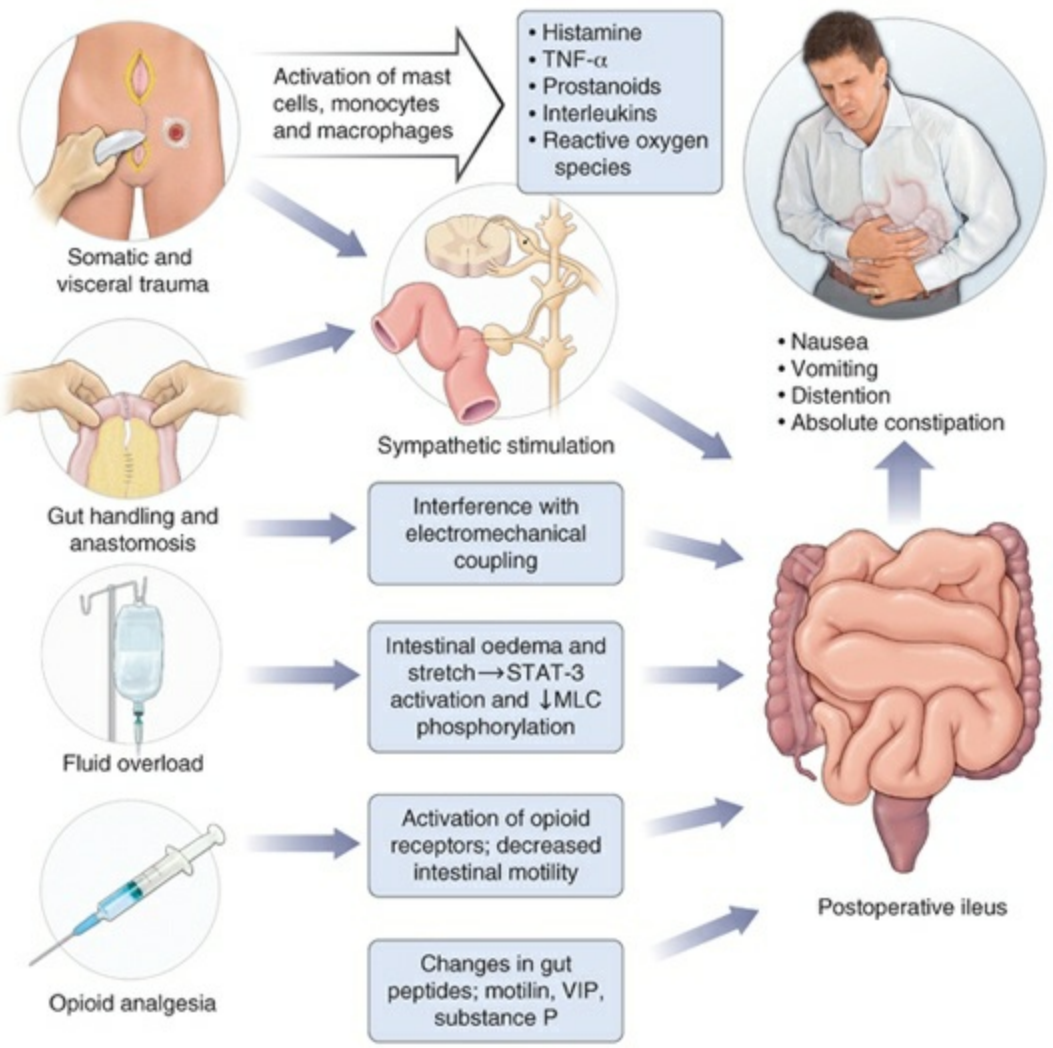


FIGURE 15.8. Proposed mechanism for POI. Schematic diagram showing proposed mechanism for the pathogenesis of POI. MLC, myosin light chain; STAT, signal transducer and activator of transcription; TNF, tumor necrosis factor; VIP, vasoactive intestinal polypeptide. (*Reprinted from Bragg D, El-Sharkawy AM, Psaltis E, et al. Postoperative ileus: recent developments in pathophysiology and management*. Clin Nutr. *2015;34[3]:367–376. Copyright © 2015 Elsevier. With permission*.)

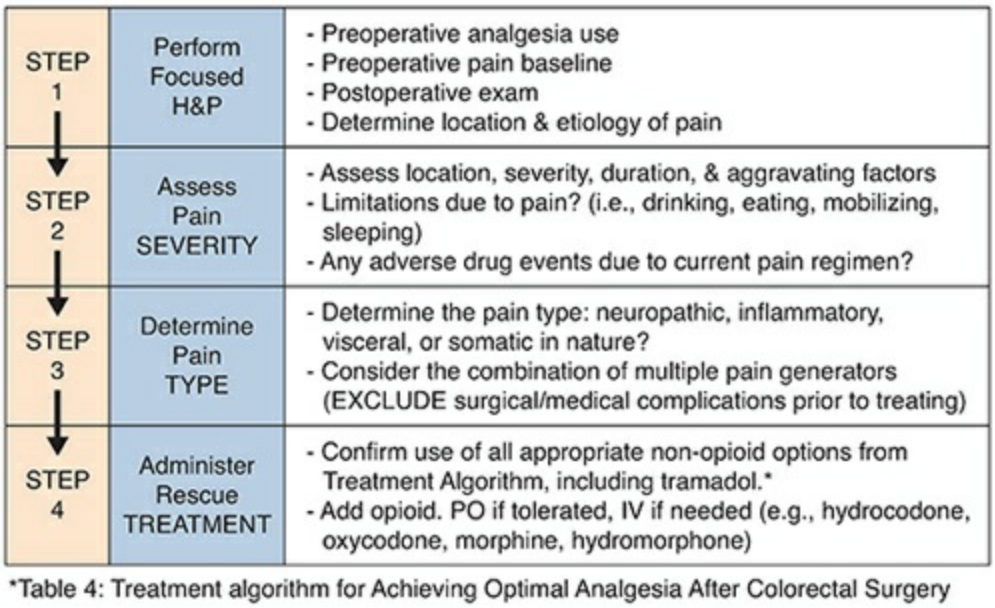
NGTs traditionally were maintained into the postoperative period until evidence of bowel function returned. The goal was to avoid an early gastric challenge and protect anastomoses by preventing distension. This practice was not evidence based. We now have good evidence that selective versus routine use of NGTs is associated with a decreased incidence of ileus, a shorter duration of ileus when it does occur, fewer fevers, less

atelectasis, and decreased incidence of pneumonia. We also know that tubes and drains are an obstacle to independent ambulation, are uncomfortable, and do not provide a benefit with regard to leaks or infections. Similarly, several reviews and meta-analyses now tell us that routine abdominal drains do not help detect leaks. Urinary catheters prevent ambulation and are not necessary to quantitate urine output. Reasonable policies in an ERAS pathway for colon surgery recommend against the routine continuation of NGTs, drains, and urinary catheters postoperatively. This recommendation refers to routine uncomplicated colon surgeries. Individual patients may have indications not present in a routine case. For instance, patients that received general anesthesia with epidural analgesia may be at increased risk for urinary retention and the catheter may be removed on postoperative day (POD) 1. Some hepatic and pancreatic procedures may require the use of early postoperative abdominal drains.

Early mobilization best exemplifies functional recovery in ERAS. Lack of physical activity suppresses cardiopulmonary and musculoskeletal systems after a short period of time. Early mobility is also correlated with a decreased incidence of atelectasis, pneumonia, thromboembolism, delirium, hospital length of stay, and an increase in muscle strength and tissue oxygenation. The amount of mobilization for each patient needs to be individualized, and the extent of mobility required to see a beneficial effect is unclear. Studies that have shown benefit have had the goals of 15 minutes of mobilization on day of surgery, and 3 hours on POD 1.

Postoperative optimal analgesia involves many of the same principles as other phases of the pathway including multimodal analgesia and minimizing opioid use. TEA is recommended for open abdominal surgery and ideally the infusion is started before the procedure. Laparoscopic surgery is typically associated with

a shorter duration of postoperative pain; routine TEA is not recommended. However, comorbid pulmonary disease or chronic opioid therapy with tolerance may be indications for TEA in laparoscopic surgery. If TEA is not used, paravertebral blocks, peripheral catheters, and TAP blocks may be helpful. IV lidocaine infusions administered in postanesthesia care unit (PACU) (or upon removal of catheter for patients receiving TEA) have been shown to lower opioid consumption, reduce nausea and vomiting, and decrease time to resumption of diet. Acetaminophen and NSAIDs are the backbone of postoperative pain control and are recommended to be scheduled, rather than ordered on as needed (PRN) basis along with the other adjuncts (**Table 15.4**). Patients still experiencing breakthrough pain *after* these interventions may be given a short-acting opioid (**Fig. 15.9**).



STEP 1	Perform Focused H&P	- Preoperative analgesia use - Preoperative pain baseline - Postoperative exam - Determine location & etiology of pain
STEP 2	Assess Pain SEVERITY	- Assess location, severity, duration, & aggravating factors - Limitations due to pain? (i.e., drinking, eating, mobilizing, sleeping) - Any adverse drug events due to current pain regimen?
STEP 3	Determine Pain TYPE	- Determine the pain type: neuropathic, inflammatory, visceral, or somatic in nature? - Consider the combination of multiple pain generators (EXCLUDE surgical/medical complications prior to treating)
STEP 4	Administer Rescue TREATMENT	- Confirm use of all appropriate non-opioid options from Treatment Algorithm, including tramadol.* - Add opioid. PO if tolerated, IV if needed (e.g., hydrocodone, oxycodone, morphine, hydromorphone)

*Table 4: Treatment algorithm for Achieving Optimal Analgesia After Colorectal Surgery

FIGURE 15.9. Rescue plan for suboptimal analgesia. (*From Scott MJ, McEvoy MD, Gordon DB, et al. American Society for Enhanced Recovery [ASER] and Perioperative Quality Initiative [POQI] joint consensus statement on optimal analgesia within an enhanced recovery pathway for colorectal surgery: part 2—from PACU to the transition home*. Perioper Med [Lond]. *2017;6:7. http://creativecommons.org/licenses/by/4.0/. Copyright © The Author[s]. 2017 Open Access*.)

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16 Liver Transplantation

Christopher H. Choi and
Vivek K. Moitra

A 66-year-old woman with a history of alcoholic cirrhosis and portal hypertension is admitted to the intensive care unit with altered mental status and low urine output. She has ascites and encephalopathy. Her kidney injury is acute with a creatinine clearance of 30 mL per minute. Her international normalized ratio (INR) is 3.0. Her hemoglobin level is 10.2 g per dL. She has a model for end-stage liver disease (MELD) score of 28 points. Her respiratory rate is 30 breaths per minute. She is scheduled for orthotopic liver transplantation.

A. Medical Disease and Differential Diagnosis

1. What are the potential graft options for liver transplantation?
2. What are the indications and contraindications for liver transplantation?
3. What is acute liver failure (ALF)?
4. What is the MELD score, and how is it used in liver transplantation evaluation?
5. What is portal hypertension? What are the sequelae of portal hypertension?
6. Describe the cardiovascular system of patients with end-stage liver disease (ESLD).
7. What causes acute kidney injury (AKI) in patients with

cirrhosis?

8. What causes hyponatremia in patients with cirrhosis?
9. Discuss the neurologic manifestations of acute and chronic liver disease.
10. Why do patients with ESLD have abnormalities of hemostasis?
11. What is the differential diagnosis for hypoxemia in patients with cirrhosis?
12. What are the risk factors and treatment guidelines for spontaneous bacterial peritonitis (SBP)?

B. Preoperative Evaluation and Preparation

1. What preoperative workup is desirable?
2. How is ascites managed preoperatively?
3. How is hyponatremia managed preoperatively?
4. What is a transjugular intrahepatic portosystemic shunt (TIPS) procedure? What is the role of TIPS in the management of patients with ESLD?
5. How are hepatic encephalopathy and elevated intracranial pressure (ICP) treated?
6. Should this patient be transfused with fresh frozen plasma prior to surgery?

C. Intraoperative Management

1. What monitors would you use? Why?
2. What are the considerations for the induction of anesthesia?
3. How does liver disease affect intraoperative medication management?
4. What happens during the first stage (preanhepatic phase) of the liver transplant operation?
5. What happens during the second stage (anhepatic phase) of the liver transplant operation?
6. What physiologic disturbances should be anticipated during the second stage (anhepatic phase) of the liver transplant operation?

7. What is venovenous bypass? What are the potential advantages and disadvantages of this procedure?
8. What surgical techniques anastomose the donor and recipient inferior vena cava (IVC)?
9. What are the potential advantages of the "piggyback" (vena cava preservation) technique?
10. What hemodynamic changes are expected after removal of vascular clamps? What is postreperfusion syndrome (PRS)?
11. How would you treat hyperkalemia?
12. Why should you anticipate hypocalcemia?
13. What happens during the third stage of the liver transplant operation?
14. What causes intraoperative bleeding during each phase of liver transplantation? How is coagulopathy monitored and treated? What are thromboelastography (TEG) and rotational thromboelastography (ROTEM)?
15. What are the complications of massive transfusion?
16. How are the complications of massive transfusion prevented?
17. How is hyperfibrinolysis managed?
18. When is intraoperative renal replacement therapy indicated?
19. What intraoperative signs suggest that the hepatic graft is working?

D. Postoperative Management

1. What are the goals of immediate postoperative care of the liver transplant patient?
2. What postoperative findings suggest that the hepatic graft is functioning?
3. What coagulation disturbances should be anticipated in the postoperative period?
4. Can renal function change after liver transplantation?
5. What vascular and biliary complications occur after liver transplantation?

6. What immunosuppressive agents will be given after liver transplantation? What are the major side effects?

A. Medical Disease and Differential Diagnosis

A.1. What are the potential graft options for liver transplantation?

Liver grafts are harvested from deceased or living donors. Cadaveric livers are procured after brain or cardiac death. Because of the increasing number of patients who die waiting for a transplant, efforts to expand the donor pool have focused on donation after cardiac death (DCD), extending donor criteria, and partial grafts from live donors. DCD is the fastest growing source of transplant organs in the United States. Upon cardiac death (defined as the irreversible cessation of circulatory and respiratory function), the liver is harvested after a mandatory waiting period of 1 to 5 minutes. Warm ischemic time begins when the waiting period starts and ends when the liver is flushed with cold preservative solution. Transplantation of a DCD-donor liver that has been exposed to a longer warm ischemic time than a graft from a brain-dead donor may be associated with ischemia-reperfusion injury leading to early graft dysfunction and potential graft loss. Ideal organs have shorter warm and cold ischemic times and are harvested from hemodynamically stable donors younger than 50 years of age who are free of hepatobiliary or renal disease, infection, and cancer.

Extending donor criteria (age older than 65 years; positive viral serology; hypernatremia; prior carcinoma, steatosis, or high-risk behaviors; split livers) to harvest organs with initial poor function or primary nonfunction also expands the donor pool. Split liver transplantation creates two transplants from one allograft. This is especially important in pediatric patients, where size-matched whole liver allografts are scarce, resulting

in increased waiting list mortality.

A related or unrelated healthy individual may donate a portion of the liver for transplantation. Usually, the right hepatic lobe is removed and transplanted into an adult recipient. Transplantation of the smaller left hepatic lobe into pediatric or very small adults may decrease the incidence of complications in the donor. This chapter focuses on cadaveric liver transplantation into adult recipients.

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Song G, Lee S. Living donor liver transplantation. *Curr Opin Organ Transplant*. 2014;19:217–222.

A.2. What are the indications and contraindications for liver transplantation?

Patients with ALF, decompensated cirrhosis, or hepatocellular carcinoma are candidates for liver transplantation. In the United States, alcoholic liver disease is the most common cause of ESLD, but cirrhosis from hepatitis C is the most common indication for orthotopic liver transplant. With the rise of the obesity epidemic, nonalcoholic steatohepatitis (NASH) is the third most common indication for liver transplantation. Specific indications for transplantation include recurrent cholangitis in patients with primary sclerosing cholangitis or intractable pruritus in patients with primary biliary cirrhosis. Uncommon indications for liver transplantation include hepatic tumors such as carcinoid tumors and hepatic adenoma, metabolic disorders such as α_1-antitrypsin deficiency, vascular disorders such as

Budd-Chiari syndrome, cystic fibrosis, hemochromatosis, amyloidosis, sarcoidosis, hyperoxaluria, and adult polycystic liver disease. Biliary atresia is the most common indication for pediatric liver transplantation.

Most surgeons will not offer transplantation to patients with severe cardiopulmonary or neurologic disease, significant hemodynamic instability, sepsis, extrahepatic malignancy, active alcohol or drug use, or unfavorable psychosocial circumstances. The decision to offer transplantation considers age and infection with human immunodeficiency virus.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1973–1986.

Martin P, DiMartini A, Feng S, et al. Evaluation for liver transplantation in adults: 2013 practice guidelines by the American Association for the Study of Liver Diseases and the American Society of Transplantation. *Hepatology*. 2014;59:1144–1165.

A.3. What is acute liver failure (ALF)?

In the absence of transplantation, ALF leads to death. ALF is defined by the absence of chronic liver disease, acute hepatitis (elevation in transaminases with an elevation in INR), encephalopathy, and illness less than 26 weeks. The most common causes of ALF are acetaminophen toxicity (39%), indeterminate (18%), idiosyncratic (19%), and acute viral hepatitis (12%, usually hepatitis B). Other etiologies include drugs (phenytoin and halothane), autoimmune disease, Wilson disease, Budd-Chiari syndrome, HELLP syndrome (hemolysis, elevated liver enzymes, low platelet count), acute fatty liver of pregnancy, toxins (i.e., trichloroethylene and tetrachloroethane in cleaning solvents and sniffed glue), and *Amanita phalloides*, the "death-cap" mushroom that grows wild in parts of the United States.

Bernal W, Wendon J. Acute liver failure. *N Engl J Med*. 2013;369:2525–2534.

Steadman RH, Van Rensburg A, Kramer DJ. Transplantation for acute liver failure: perioperative management. *Curr Opin Organ Transplant*. 2010;15:368–373.

A.4. What is the MELD score, and how is it used in liver transplantation evaluation?

Grafts from deceased donors are offered to patients with the highest risk of death. The MELD is a validated and widely used prognostic tool to prioritize organ allocation that estimates disease severity and 3-month survival in patients with chronic liver disease. Patients with a high score rank high on the transplant list and have a greater short-term risk of dying from liver disease than patients with lower scores. The MELD score ranges from 6 to 40 points and is calculated from the patient's serum bilirubin, serum creatinine, and INR. In 2016, the MELD score was modified to include sodium (MELD-Na) because hyponatremia is an important prognostic factor in patients with cirrhosis. After this change, wait-list mortality has decreased and transplant probability has increased (**Fig. 16.1**).

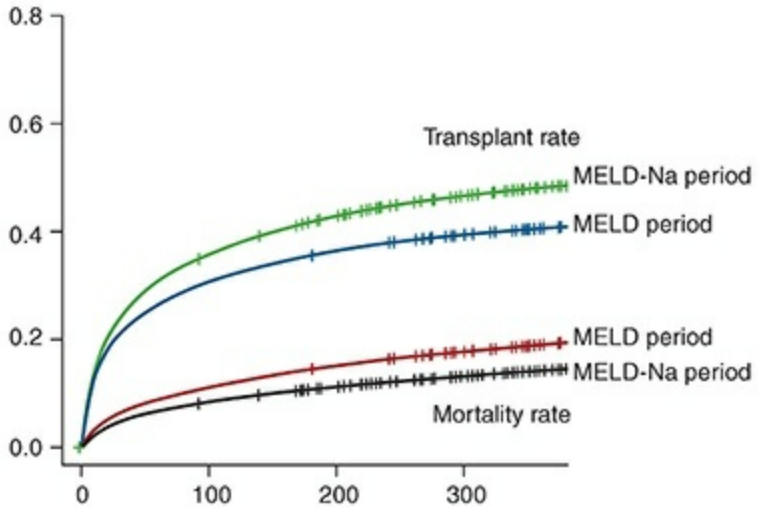

FIGURE 16.1. Comparison of waitlist mortality and transplantation rate between model for end-stage liver disease (MELD) and MELD-sodium (Na) scores in patients with cirrhotic liver disease. (*Reprinted from Nagai S, Chau LC, Schilke RE, et al. Effects of allocating livers for transplantation based on model for end-stage liver disease-sodium scores on patient outcomes*. Gastroenterology. *2018;155[5]:1451–1462. Copyright © 2018 American Gastroenterological Association Institute. With permission.*)

Formula 1

$$\text{MELD score} = 11.2 \times \ln(\text{INR}) + 9.57 \times \ln(\text{creatinine, milligrams per deciliter}) + 3.78 \times \ln(\text{bilirubin, milligrams per deciliter}) + 6.43 \text{ (an intercept)}$$

The score is rounded to the nearest whole number.

Formula 2

$$\text{MELD-Na} = \text{MELD} + 1.32 \times (137 - \text{Na}) - [0.033 \times \text{MELD} \times (137 - \text{Na})]$$

The score is rounded to the nearest whole number.

There is a lower limit of 1 for all variables.

The maximum creatinine value is 4 mg per dL. For patients who receive dialysis, creatinine is set to 4 mg per dL.

Exceptions to the MELD classification exist for patients with fulminant hepatic failure and life expectancy of less than 7 days without a liver transplant. These patients are classified as *status 1* and rank highest on the waiting list. This group includes patients who develop ALF without a history of liver disease, suffer from primary graft nonfunction or hepatic artery thrombosis within 7 days of a liver transplant, or have acutely decompensated Wilson disease. Special case exceptions also exist for patients with hepatocellular carcinoma, hepatopulmonary syndrome (HPS), familial amyloidosis, and primary oxaluria.

Pediatric patients younger than 12 years of age are ranked on the transplant waiting list according to the pediatric end-stage liver disease (PELD) model. The PELD score is similar in derivation to the MELD but does not consider creatinine and incorporates bilirubin, INR, albumin, age, and growth failure into the formula.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1467–1471.

Krowka M, Wiesner R, Heimbach J. Pulmonary contraindications, indications and MELD exceptions for liver transplantation: a contemporary view and look forward. *J Hepatol*. 2013;59:367–374.

Martin P, DiMartini A, Feng S, et al. Evaluation for liver transplantation in adults: 2013 practice guidelines by the American Association for the Study of Liver Diseases and the American Society of Transplantation. *Hepatology*. 2014;59:1144–1165.

Nagai S, Chau LC, Schilke RE, et al. Effects of allocating livers for transplantation based on model for end-stage liver disease-sodium scores on patient outcomes. *Gastroenterology*. 2018;155:1451–1462.

A.5. What is portal hypertension? What are the sequelae of portal hypertension?

The normal portosystemic gradient between the portal vein and hepatic vein is less than 5 mmHg. Greater intrahepatic vascular resistance and portal venous blood flow increases this gradient, which characterizes portal hypertension. Liver fibrosis, regenerative nodules, collagen deposition in the space of Disse, endothelial dysfunction, and an imbalance between endogenous vasoconstrictors (e.g., norepinephrine, thromboxane A, endothelin I, angiotensin II, leukotrienes) and vasodilators, such as nitric oxide, increase vascular resistance in the liver. As the pressure gradient between the portal vein and the hepatic vein increases, collaterals such as gastroesophageal and hemorrhoidal varices develop to decompress the portal system. Portal hypertension causes shear stress in the splanchnic vessels, which along with translocation of bacterial lipopolysaccharides produce endogenous vasodilators that cause vasodilation. Splanchnic vasodilation in turn increases portal blood flow and exacerbates portal hypertension.

Complications of portal hypertension include gastrointestinal bleeding from expansion and rupture of varices, intraoperative bleeding from intra-abdominal collaterals, and formation of ascites and pleural effusions.

Bloom S, Kemp W, Lubel J. Portal hypertension: pathophysiology, diagnosis

and management. *Intern Med J*. 2015:45(1):16–26.

Garcia-Tsao G, Bosch J. Management of varices and variceal hemorrhage in cirrhosis. *N Engl J Med*. 2010;362:823–832.

A.6. Describe the cardiovascular system of patients with end-stage liver disease (ESLD).

The cardiovascular system of patients with ESLD mimics the hyperdynamic circulatory changes of patients with sepsis. Tachycardia, elevated cardiac output, low arterial blood pressure, and low systemic vascular resistance are characteristic. Enhanced endogenous production or diminished hepatic clearance of vasodilating substances, such as nitric oxide, carbon monoxide, and endogenous cannabinoids, and the inflammatory response to bacterial translocation cause splanchnic arterial vasodilation. Increased venous capacitance from formation of portosystemic shunts because of portal hypertension increases venous capacitance and contributes to a hyperdynamic circulation. During the perioperative period, the patient's circulatory system may be challenged with shunt insertion or greater afterload from surgical stress, unmasking an underlying cardiomyopathy. Cirrhotic cardiomyopathy is characterized by impaired systolic and diastolic dysfunction, resistance to β-adrenergic stimulation, and QTc prolongation.

Systemic conditions such as hemochromatosis (ventricular hypertrophy with increased end-diastolic and end-systolic volumes), amyloidosis (restrictive cardiomyopathy), Wilson disease (supraventricular extrasystolic beats), and alcoholism (systolic and diastolic dysfunction) can affect liver and cardiac function. Patients with portal hypertension may develop portopulmonary hypertension, leading to right ventricular dysfunction. A mean pulmonary artery pressure greater than 25 mmHg at rest, mean pulmonary capillary wedge pressure less than 15 mmHg, and a pulmonary vascular resistance greater than 240 dynes/sec/cm^5 define portopulmonary hypertension. The

mechanism is not fully understood, and histologically, there are no clear distinguishable features from idiopathic pulmonary arterial hypertension. A mean pulmonary artery pressure greater than 50 mmHg and/or a pulmonary vascular resistance (PVR) of greater than 250 dynes/sec/cm^5 are contradictions for liver transplantation due to risk of fulminant right heart failure.

Biancofiore G, Mandell MS, Rocca GD. Perioperative considerations in patients with cirrhotic cardiomyopathy. *Curr Opin Anaesthesiol*. 2010;23:128–132.

Porres-Aguilar M, Altamirano JT, Torre-Delgadillo A, et al. Portopulmonary hypertension and hepatopulmonary syndrome: a clinician-oriented overview. *Eur Respir Rev*. 2012;21:223–233.

Rodríguez-Roisin R, Krowka MJ. Hepatopulmonary syndrome—a liver-induced lung vascular disorder. *N Engl J Med*. 2008;358:2378–2387.

Zardi EM, Abbate A, Zardi DM, et al. Cirrhotic cardiomyopathy. *J Am Coll Cardiol*. 2010;56:539–549.

A.7. What causes acute kidney injury (AKI) in patients with cirrhosis?

Patients with AKI and cirrhosis have more complications and increased risk of mortality after liver transplantation than those without renal failure. Gastrointestinal bleeding, diarrhea from infection or lactulose administration, and diuretic medications change circulatory function via hypovolemia and can cause renal injury. As cirrhosis progresses, there is compensatory activation of the renin–angiotensin and sympathetic nervous systems, which leads to ascites, severe renal vasoconstriction, and, ultimately, renal hypoperfusion. This in turn leads to electrolyte abnormalities, namely, hyponatremia and hypokalemia.

Hepatorenal syndrome (HRS) is caused by functional renal vasoconstriction in response to splanchnic arterial vasodilation. As such, histologic findings and diagnostic tests for HRS are lacking. Diagnostic criteria are used to categorize two types of HRS. Criteria for HRS include (1) cirrhosis with ascites, (2)

serum creatinine greater than 1.5 mg per dL, (3) no improvement of creatinine after 2 days of diuretic withdrawal and plasma volume expansion, (4) absence of shock, (5) no current or recent exposure to nephrotoxic drugs, and (6) absence of parenchymal kidney disease. Type I HRS involves rapid and progressive impairment of renal function (usually the result of an acute insult such as SBP or a large volume paracentesis) with a doubling of the initial serum creatinine to a level greater than 2.5 mg per dL or a 50% reduction in the 24-hour creatinine clearance to lower than 20 mL per minute in less than 2 weeks. The development of type I HRS is associated with an untreated median survival of less than 2 weeks. Patients with type II HRS have a serum creatinine greater than 1.5 mg per dL and do not meet the criteria for type I HRS; median survival in these patients is 4 to 6 months. Distinguishing between HRS and acute tubular necrosis is difficult. A fractional excretion of sodium less than 1% suggests tubular function and favors a diagnosis of HRS. The presence of renal tubular epithelial cells in urinary sediment favors a diagnosis of acute tubular necrosis.

The administration of terlipressin, a vasopressin analogue, with intravenous albumin has been shown to have benefit patients with type I HRS. The magnitude of blood pressure increase rather than a specific vasopressor type is best correlated with renal recovery. Medical management of HRS is marginally effective, but liver transplantation can reverse HRS. Kidneys transplanted from patients with HRS function normally in new hosts, suggesting the essential role of hepatic disease in the pathogenesis. Up to 40% of patients with HRS do not recover kidney function after transplantation. In these cases, systemic inflammation with hyperbilirubinemia may contribute to irreversible structural damage to the kidney.

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failure. *Semin Respir Crit Care*. 2018;39:556–565.

Fukazawa K, Lee H. Updates on hepato-renal syndrome. *J Anesth Clin Res*. 2013;4:352–368.

Ginès P, Schrier RW. Renal failure in cirrhosis. *N Engl J Med*. 2009;361:1279–1290.

Gludd LL, Christensen K, Christensen E, et al. Terlipressin for hepatorenal syndrome. *Cochrane Database Syst Rev*. 2012;(9):CD005162.

Meltzer J, Brentjens TE. Renal failure in patients with cirrhosis: hepatorenal syndrome and renal support strategies. *Curr Opin Anaesthesiol*. 2010;23:139–144.

A.8. What causes hyponatremia in patients with cirrhosis?

Patients with advanced cirrhosis have decreased effective blood volume and then circulatory dysfunction. They develop hypervolemic hyponatremia from increased secretion of antidiuretic hormone, which acts on the vasopressin-2 receptors of the renal tubular collecting duct to impair excretion of solute-free water. These patients have expanded extracellular volume, ascites, and edema.

Patients who develop hypovolemic hyponatremia via loss of extracellular fluid from the kidneys (overdiuresis) or gastrointestinal tract rarely have ascites or edema. These patients may have prerenal failure from low plasma volume and dehydration or hepatic encephalopathy from a rapid reduction in serum osmolality.

Ginès P, Guevara M. Hyponatremia in cirrhosis: pathogenesis, clinical significance, and management. *Hepatology*. 2008;48:1002–1010.

Keegan MT, Wright DR. Sodium, potassium and glucose management in organ transplantation. *Curr Opin Organ Transplant*. 2010;15:383–389.

A.9. Discuss the neurologic manifestations of acute and chronic liver disease.

Hepatic encephalopathy is a neuropsychiatric complication of acute and chronic liver disease with features that range from

mild confusion to cerebral edema with intracranial hypertension. Patients have disturbances in consciousness, cognitive abilities, behavior, neuromuscular function, concentration, reaction time, memory, and/or electroencephalogram readings. The pathogenesis of hepatic encephalopathy is not understood, but most theories implicate elevated levels of ammonia, a gut-derived neurotoxin, which is shunted to the systemic circulation from the portal system. Bacteria in the gut produce ammonia, which crosses the blood–brain barrier into astrocytes that detoxify it to glutamine. Astrocytes regulate neurotransmission, but their function is decreased when they swell because of increased concentrations of intracellular glutamine. High serum ammonia levels characterize patients with hepatic encephalopathy, even though the degree of elevation of ammonia does not correlate with neurologic severity. This observation suggests that other factors, such as hyponatremia, gastrointestinal bleeding, and infection, contribute to the development of hepatic encephalopathy. Left untreated, cerebral edema can progress to intracranial hypertension and herniation of the brain. Multiple grading scales assess the severity of hepatic encephalopathy. The most common scales are the West Haven Criteria (Conn score), which has grades 0 through 4, and the Glasgow Coma Scale (GCS).

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Ginès P, Guevara M. Hyponatremia in cirrhosis: pathogenesis, clinical significance, and management. *Hepatology*. 2008;48:1002–1010.

Sakamoto M, Perry W, Hilsabeck RC, et al. Assessment and usefulness of clinical scales for semiquantification of overt hepatic encephalopathy. *Clin Liver Dis*. 2012;16:27–42.

Teperman LW, Peyregne VP. Considerations on the impact of hepatic encephalopathy treatments in the pretransplant setting. *Transplantation*. 2010;89:771–778.

A.10. Why do patients with ESLD have abnormalities of hemostasis?

Patients with ESLD have hemostatic changes that promote both bleeding and thrombosis (**Fig. 16.2**). Inadequate synthesis of all coagulation factors (except for von Willebrand factor) thrombocytopenia, platelet function defects, dysfibrinogenemia, and elevated tissue plasminogen activator (tPA) levels cause bleeding. Elevations of von Willebrand factor and factor VIII and decreased levels of a disintegrin and metalloproteinase, with a thrombospondin type 1 motif, member 13 (ADAMTS-13), protein C, protein S, antithrombin, α_2-macroglobulin, plasminogen, and heparin cofactor II, favor thrombosis.

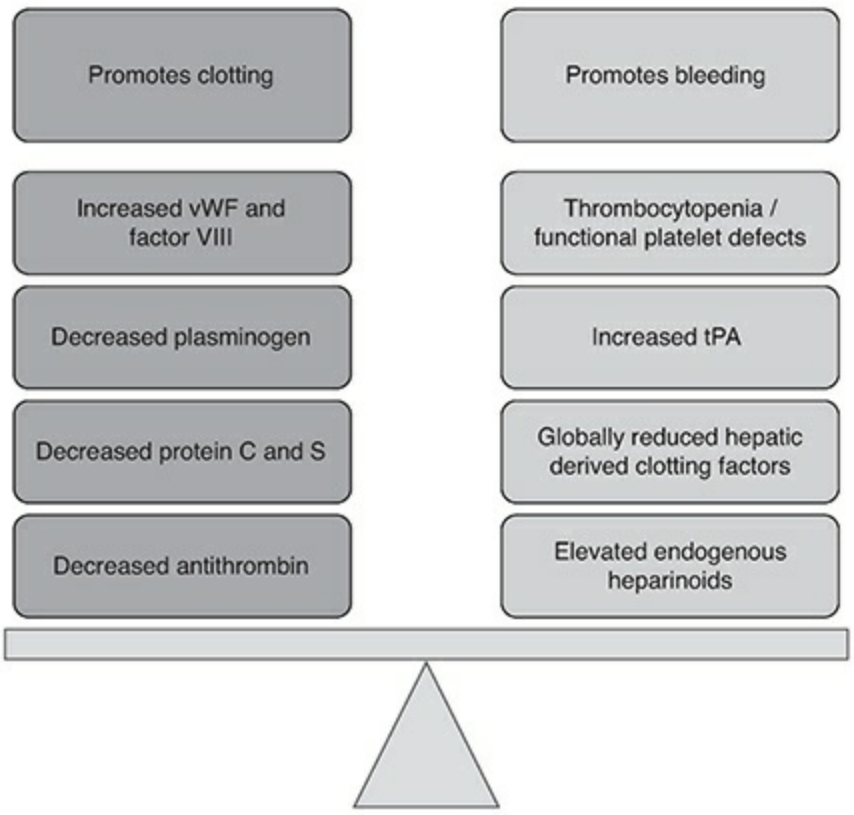

FIGURE 16.2. Changes of the coagulation and fibrinolytic system in ESLD. tPA, tissue plasminogen activator; vWF, von Willebrand factor. (*Modified from Intagliata NM, Davis J, Caldwell SH. Coagulation pathways, hemostasis, and thrombosis in liver failure*. Semin Respir Crit Care Med. *2018;39[5]:598–608. Copyright © Georg Thieme Verlag KG.*)

Factors VII, X, V, II (prothrombin), and I (fibrinogen) have a short half-life (hours to days) and are synthesized solely in the hepatocytes making possible a “semi-real time” evaluation of the liver’s synthetic function. Although patients with liver disease can have abnormal prothrombin times (PTs) from decreased production of procoagulant factors, the rebalanced state of pro- and anticoagulants in patients with liver disease makes the PT an unreliable tool for evaluating tendency to bleed or clot.

Levels of fibrinogen, an acute phase reactant, are normal or increased in liver disease. Patients with severe hepatic dysfunction, however, may synthesize fibrinogen poorly, which increases the risk of bleeding. Although high concentrations of fibrinogen are found in patients with chronic hepatitis, cholestatic jaundice, and hepatocellular carcinoma, clot formation is not enhanced because the fibrinogen is dysfunctional. Hyperfibrinolysis (from increased levels of tPA and reduced levels of thrombin-activatable fibrinolysis inhibitor [TAFI] and plasmin inhibitor) has been observed in cirrhotic patients, but its association with bleeding is unclear. Hypofibrinolysis (from increased levels of plasminogen activator inhibitor [PAI] and reduced levels of plasminogen) may restore the balance of fibrinolysis.

Thrombocytopenia and platelet dysfunction are also characteristic of ESLD. Thrombocytopenia results from several factors: hypersplenism, which sequesters platelets; consumption of platelets during systemic intravascular coagulation; and impaired hepatic synthesis of thrombopoietin, which produces platelets in the bone marrow. Defective signal transduction; uremia from AKI; and intrinsic defects of adenosine diphosphate (ADP), arachidonic acid, collagen, and thrombin prevent platelet aggregation.

There may be little evidence of deranged coagulation when

normal hepatic parenchyma is preserved, such as in an isolated hepatoma.

Northup P, Caldwell S. Coagulation in liver disease: a guide for the clinician. *Clin Gastroenterol Hepatol*. 2013;11:1064–1074.

Tripodi A, Mannucci PM. The coagulopathy of chronic liver disease. *N Engl J Med*. 2011;365:147–156.

Weeder P, Porte R, Lisman T. Hemostasis in liver disease: implications of new concepts for perioperative management. *Transfus Med Rev*. 2014;28:107–113.

A.11. What is the differential diagnosis for hypoxemia in patients with cirrhosis?

Potential causes of preoperative hypoxemia and respiratory failure in patients with cirrhosis include atelectasis from the compressive effects of ascites, hepatic hydrothorax, HPS, and underlying chronic pulmonary disease. Muscle wasting and intra-abdominal hypertension from ascites increase the work of breathing.

Ascites fluid can enter the pleural space through small channels in the diaphragm to cause a hepatic hydrothorax (usually on the right side). Negative intrathoracic pressure during inspiration facilitates movement of fluid from the peritoneum to the pleural space to minimize ascites. A pleural fluid culture with polymorphonuclear cell count greater than 250 cells per μL or isolated polymorphonuclear cell count greater than 500 cells per μL diagnose spontaneous bacterial empyema.

A diagnosis of HPS is considered in patients without cardiopulmonary disease who have a room air Pa_{O_2} less than or equal to 70 mmHg in any position. The triad of liver disease and/or portal hypertension, widened age-corrected alveolar–arterial oxygen gradient (more than 15 or 20 mmHg) while breathing room air, and documented intrapulmonary vascular dilation (IPVD) define HPS. Enhanced production or impaired

hepatic clearance of endogenous vasodilators (i.e., nitric oxide, carbon monoxide, vasodilator prostaglandins, substance P) or inhibition of vasoconstrictive substances (i.e., tyrosine, serotonin, and endothelin) by a damaged liver may cause IPVD. IPVD causes hypoxemia via ventilation/perfusion mismatching, intrapulmonary shunt physiology, and diffusion limitation. Patients with HPS often complain of dyspnea and fatigue; they may have clubbing and spider angiomata on physical examination. Patients may experience platypnea (dyspnea in the upright position relieved by recumbency) or have orthodeoxia (arterial oxyhemoglobin desaturation in the upright position). Preferential perfusion of IPVD (while the patient is upright) may cause these clinical manifestations. Contrast-enhanced echocardiography or perfusion lung scanning with technetium-99m-labeled macroaggregated albumin detects intrapulmonary shunting suggestive of IPVD. There is no established medical therapy for HPS other than supplemental oxygen to correct hypoxemia. The only known treatment for HPS is liver transplantation, which improves oxygenation in almost all patients.

Hemprich U, Papadakos PJ, Lachmann B. Respiratory failure and hypoxemia in the cirrhotic patient including hepatopulmonary syndrome. *Curr Opin Anaesthesiol*. 2010;23:133–138.

Rodríguez-Roisin R, Krowka MJ. Hepatopulmonary syndrome—a liver-induced lung vascular disorder. *N Engl J Med*. 2008;358:2378–2387.

Zhang J, Fallon MB. Hepatopulmonary syndrome: update on pathogenesis and clinical features. *Nat Rev Gastroenterol Hepatol*. 2012;9:539–549.

A.12. What are the risk factors and treatment guidelines for spontaneous bacterial peritonitis (SBP)?

The American Association for the Study of Liver Diseases recommends paracentesis for all hospitalized patients with ascites because infection of ascitic fluid is common. Delaying paracentesis and initiation of antibiotics is associated with

higher in-hospital and 3-month mortality (each hour delay increases in-hospital mortality by 3.3%). SBP is diagnosed by polymorphonuclear cell counts greater than 250 cells per μL without evidence of an intra-abdominal surgically treatable source of infection.

Cirrhotic patients have a disproportionate growth of pathogenic bacteria for numerous reasons. They have a smaller bile pool and less conversion of primary to secondary bile acids, which have bactericidal properties. This causes dysbiosis from an overgrowth of Enterobacteriaceae. Reduced gut motility and proton pump inhibitor use stimulates small intestinal overgrowth and may increase intestinal permeability and rate of bacterial translocation.

A minimum of 5 days of empiric treatment with a third-generation cephalosporin is usually adequate coverage for the typical organisms known to cause SBP (i.e., *Escherichia coli*, *Klebsiella*). There is little data to support the use of large-volume paracentesis for SBP. Administration of intravenous albumin as part of the routine treatment for SBP, however, can decrease overall mortality and incidence of HRS. A repeat paracentesis should be considered with ascitic fluid analysis in patients with inadequate response to treatment, an atypical organism in the culture, or suspected secondary peritonitis.

Cheung A, Tanna S, Ison MG. Infectious complications in critically ill liver failure patients. *Semin Respir Crit Care Med*. 2018;39:578–587.

Pericleous M, Sarnowski A, Moore A, et al. The clinical management of abdominal ascites, spontaneous bacterial peritonitis and hepatorenal syndrome: a review of current guidelines and recommendations. *Eur J Gastroenterol Hepatol*. 2016;28(3):e10–e18.

B. Preoperative Evaluation and Preparation

B.1. What preoperative workup is desirable?

Anesthesiologists face several preoperative challenges when patients with ESLD need surgery. Surgical and anesthetic management is complicated for patients who often have preoperative encephalopathy, AKI, electrolyte abnormalities, ascites, myocardial and pulmonary dysfunction, and/or coagulopathy. To anticipate and prevent complications from transplantation, underlying conditions should be thoroughly evaluated before surgery. A multidisciplinary team including an anesthesiologist, hepatologist, psychologist, and surgeon should be involved in preoperative preparation. Consultations may be requested with cardiology, pulmonary, infectious diseases, and nephrology for patients with comorbidities.

Electrolyte levels, blood urea nitrogen, creatinine levels, albumin levels, bilirubin levels, transaminases, complete blood count, coagulation studies, and glucose values should be routinely obtained. An electrocardiogram and chest radiograph to rule out pulmonary edema or cardiomegaly should also be obtained. Blood group and antibody screening needs to be done in advance for crossmatching large amounts of blood products, especially in those patients who have received prior transfusions. Echocardiography is useful to detect cardiac dysfunction and right ventricular systolic pressure as a marker for pulmonary hypertension. If elevated, pretransplant right heart catheterization may be warranted.

In cases of altered mental status, a head computed tomography (CT) scan often is indicated to evaluate intracranial bleeding, herniation, and/or the extent of cerebral edema. Pulmonary function studies may be indicated in smokers or patients with preexisting pulmonary disease.

The American Association for the Study of Liver Diseases recommends that patients older than 50 years, with clinical or family history of heart disease, or with diabetes undergo dobutamine stress echocardiography because cardiovascular

disease accounts for a majority of non–graft-related deaths. Of note, a vasodilatory (e.g., adenosine, dipyridamole [Persantine]) myocardial stress test is less useful because in patients with ESLD, the resting vascular tone is so low that provoking vasodilation with drugs is difficult. Other risk factors for adverse cardiac outcomes after liver transplantation include a history of stroke and increased intraventricular thickness.

If intraoperative renal replacement (continuous venovenous hemofiltration) therapy is a consideration, a nephrologist should be consulted.

Hall T, Dhir A. Anesthesia for liver transplantation. *Semin Cardiothorac Vasc Anesth*. 2013;17:180–194.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1973–1986.

B.2. How is ascites managed preoperatively?

Ascites is initially managed with a low-sodium diet (<2 g per day) and diuretic therapy. Spironolactone as a sole agent or in combination with furosemide is typically used. Patients with ascites refractory to treatment with diuretics may require large volume paracentesis. If more than 5 L of ascites are drained, albumin is replaced to prevent hypotension and HRS. Patients with ascites should avoid nephrotoxic agents such as nonsteroidal anti-inflammatory drugs (NSAIDs), aminoglycosides, angiotensin-converting enzyme (ACE) inhibitors, and α_1-blockers. Patients may be treated with a TIPS in refractory cases of ascites or hepatic hydrothorax.

Liou I. Management of end-stage liver disease. *Med Clin North Am*. 2014;98:119–152.

Pericleous M, Sarnowski A, Moore A, et al. The clinical management of abdominal ascites, spontaneous bacterial peritonitis and hepatorenal syndrome: a review of current guidelines and recommendations. *Eur J Gastroenterol Hepatol*. 2016;28(3):e10–e18.

B.3. How is hyponatremia managed preoperatively?

Hyponatremia is associated with HRS, ascites, death from liver disease, and postoperative mortality after transplantation. Cirrhotic patients typically have hypervolemic hyponatremia due to overstimulation of their renin–angiotensin–aldosterone system (RAAS), which is managed with fluid restriction (1 to 1.5 L per day) and withholding of diuretics. Vaptans, medications that block the vasopressin-2 receptor, are reserved for severe episodes of hyponatremia; they increase solute-free water excretion dose dependently and may preclude water restriction so that diuretics can be continued. Patients with hypovolemic hyponatremia are given saline instead of diuretics to increase plasma volume.

Patients who undergo orthotopic liver transplantation are at risk for perioperative osmotic demyelination syndrome (ODS), former known as central pontine myelinolysis. ODS is a neurologic condition characterized by myelinolysis or destruction of astrocytes, which can occur in the pons and other areas of the brain. The etiology of ODS is uncertain, but osmotic stress on central nervous system cells is theorized, and ODS correlates with rapid correction of hyponatremia. Rapid changes in concentration of serum sodium cannot be predicted and a "safe" rate of correction of hyponatremia has not been definitively established; some experts recommend sodium correction at a rate less than 12 mEq/L/day.

The incidence of ODS ranges from 0.5% to 1.5% in liver transplantation. Preoperative correction of hyponatremia may prevent a rapid rise in serum sodium intraoperatively and postoperatively. During intraoperative fluid replacement, high sodium loads may cause rapid swings in serum sodium, or even hypernatremia, by the end of the case. Sodium bicarbonate should be administered cautiously because it has a high concentration of sodium. Tris-hydroxymethyl aminomethane

(THAM), although a weaker base, is an alternative because of its lower sodium content.

Bernal W, Auzinger G, Dhawan A, et al. Acute liver failure. *Lancet*. 2010;376:190–201.

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Zafirova Z, O'Connor M. Hepatic encephalopathy: current management strategies and treatment, including management and monitoring of cerebral edema and intracranial hypertension in fulminant hepatic failure. *Curr Opin Anaesthesiol*. 2010;23:121–127.

B.4. What is a transjugular intrahepatic portosystemic shunt (TIPS) procedure? What is the role of TIPS in the management of patients with ESLD?

During a TIPS procedure, an expandable stent is deployed into the liver parenchyma to bridge the hepatic and portal vein and to decrease portal hypertension. Therefore, it reduces the portosystemic pressure gradient by acting as a side-to-side portocaval shunt. The strongest evidence for TIPS intervention is for secondary prevention of variceal bleeding and management of refractory ascites. The procedure is performed under local or general anesthesia as a "bridge" to liver transplantation in patients with severe liver disease. General anesthesia may be preferred because of the duration of the procedure and the potential for life-threatening events such as bleeding, hemobilia, arrhythmias, liver ischemia, and stent migration. Preoperative evaluation of cardiac function (particularly right ventricular function and presence of pulmonary hypertension) is essential because stent placement

can rapidly increase venous return and unmask an underlying cardiomyopathy. Unlike older, surgically created portosystemic and peritoneovenous shunts, a TIPS does not require abdominal operation or vascular diversion, both of which impose technical hazards to future liver transplantation.

Encephalopathy may worsen in 30% to 46% of patients from increased systemic delivery of biogenic amines normally cleared by the liver. The long-term patency of a TIPS is poor, especially prior to the introduction of polytetrafluoroethylene-covered stents, and multiple revisions may be required.

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Fidelman N, Kwan, SW, LaBerge JM, et al. The transjugular intrahepatic portosystemic shunt: an update. *AJR Am J Roentgenol*. 2012;199(4):746–755.

Gaba RC, Khiatani VL, Knuttinen MG, et al. Comprehensive review of TIPS technological complications and how to avoid them. *AJR Am J Roentgenol*. 2011;196:675–685.

Sher C. Anesthesia for transjugular intrahepatic portosystemic shunt. *Int Anesthesiol Clin*. 2009;47:21–28.

B.5. How are hepatic encephalopathy and elevated intracranial pressure (ICP) treated?

Initial therapy for hepatic encephalopathy identifies and treats reversible triggers (i.e., gastrointestinal bleeding and infection) of this neuropsychiatric syndrome. Nonabsorbable disaccharides such as lactulose decrease absorption of ammonia from the gut via catharsis. Excessive dosing of lactulose causes dehydration. Oral antibiotics (rifaximin, neomycin, vancomycin, paromomycin, or metronidazole) reduce ammonia-producing enteric bacteria. Rifaximin, in combination with lactulose, may prevent episodes of hepatic encephalopathy. L-ornithine L-aspartate also decreases ammonia levels by providing an

alternative substrate for the urea cycle.

Patients who develop fulminant hepatic failure are at risk for hepatic encephalopathy, cerebral edema with increased ICP, and a threat of herniation. A venous ammonia level of 255 to 340 μg per dL is a known risk factor for increased ICP in patients with fulminant hepatic failure. In cases of altered mental status, a head CT scan is often indicated to evaluate for intracranial bleeding, herniation, and/or the extent of cerebral edema. ICP monitoring should be considered for these patients with severe encephalopathy, even given the bleeding risks associated with invasive monitors. Bleeding risk seems to be the greatest deterrent to ICP monitoring; there is a risk of approximately 10% for intracranial hemorrhage with insertion of a monitor in this population. To minimize the risk, epidural transducers are recommended rather than intradural monitors. With or without ICP monitoring, 30-day outcomes are similar. Alternate noninvasive ultrasonographic modalities such as transcranial Doppler and optic nerve sheath diameter measurements can be used to estimate ICP.

Sustained ICP elevations greater than 20 mmHg should be treated with mannitol or hypertonic saline to achieve hyperosmolarity. Preoperative hyperventilation has not been shown to improve outcome, and corticosteroids are not indicated. Pentobarbital coma may be indicated for patients unresponsive to mannitol, but coma may worsen cerebral hypoperfusion by causing systemic hypotension and confound the neurologic exam. Extracorporeal albumin dialysis with the molecular adsorbent recirculating system (MARS) system has been studied as bridge to liver transplant; however, it can also lead to electrolyte disturbances and a worsening coagulopathy. Many centers consider sustained cerebral hypoperfusion (cerebral perfusion pressure <40 mmHg) a contraindication to transplant because of the high risk for brain death. In the future,

transcranial Doppler ultrasonography and near-infrared spectrophotometry may offer means of monitoring for elevated ICP in these patients. For anesthesia, drugs or conditions that exacerbate elevations in ICP should be avoided. Recent evidence shows that moderate hypothermia (32°C to 33°C) may reduce cerebral edema and intracerebral hypertension; however, the side effects of the maneuvers are a greater risk of infection, cardiac dysrhythmias, and coagulopathy.

Bass NM, Mullen KD, Sanyal A, et al. Rifaximin treatment in hepatic encephalopathy. *N Engl J Med*. 2010;362:1071–1081.

Dmello D, Cruz-Flores S, Matuschak GM. Moderate hypothermia with intracranial pressure monitoring as a therapeutic paradigm for the management of acute liver failure: a systematic review. *Intensive Care Med*. 2010;36:210–213.

Mohsenin V. Assessment and management of cerebral edema and intracranial hypertension in acute liver failure. *J Crit Care*. 2013;28:783–791.

Wijdicks EFM. Hepatic encephalopathy. *N Engl J Med*. 2016;375:1660–1670.

Zafirova Z, O'connor M. Hepatic encephalopathy: current management strategies and treatment, including management and monitoring of cerebral edema and intracranial hypertension in fulminant hepatic failure. *Curr Opin Anaesthesiol*. 2010;23:121–127.

B.6. Should this patient be transfused with fresh frozen plasma prior to surgery?

Management of the coagulopathy is challenging because conventional blood tests such as PT and activated partial thromboplastin time (aPTT) do not predict transfusion requirements during liver transplantation.

Patients who need an orthotopic liver transplant usually have severe perturbations in coagulation, but it is neither necessary nor possible to correct them preoperatively. In patients with active sites of bleeding, it is reasonable to administer fresh frozen plasma, packed red blood cells, cryoprecipitate, or platelets as dictated by clinical assessment and laboratory tests, including TEG. In addition, desmopressin (1-deamino-8-D-

arginine vasopressin [DDAVP]) may be considered for patients with concomitant renal dysfunction and uremic bleeding. Potentially curative transplant surgery should not be postponed to correct coagulation defects.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1973–1986.

Massicotte L, Beaulieu D, Thibeault L, et al. Coagulation defects do not predict blood product requirements during liver transplantation. *Transplantation*. 2008;85:956–962.

C. Intraoperative Management

C.1. What monitors would you use? Why?

In addition to the monitors recommended by the American Society of Anesthesiologists (electrocardiogram, pulse oximetry, capnography, temperature, and noninvasive blood pressure), a radial arterial catheter is placed for beat-to-beat blood pressure monitoring and frequent sampling of blood. Pulse pressure variation, calculated from the invasive arterial tracing, assesses fluid responsiveness. A second arterial catheter should be placed in the femoral artery to measure central aortic blood pressure. Peripheral arterial pressures may not be reliable in a patient with vasoconstriction, vasodilation, or compression of the subclavian artery with rib retraction.

Central line access is established to measure right atrial pressure and to administer drugs. Central venous pressure monitoring does not reliably measure blood volume or change in blood volume. The use of a pulmonary artery catheter depends on local practice and the physiologic state of the patient. Thermodilution measurements for cardiac output may be inaccurate with large-volume administration of intravenous fluids and the rapid return of cooled blood during reperfusion. Mixed venous oxygen saturation values are measured to assess

cardiac output, but these measurements also are influenced by changes in oxygen-carrying capacity and oxygen consumption.

Transesophageal echocardiography (TEE) assesses ventricular filling, contractility, and function in real time. Numerous case reports have reported its usefulness in diagnosing portopulmonary hypertension, ischemic heart disease, cirrhotic cardiomyopathy, and intraoperative thromboembolic events. While grade IV varices may be a contraindication, risk of rupture of grade I and II esophageal varices with TEE is rare.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1973–1986.

Krenn C, DeWolf AM. Current approach to intraoperative monitoring in liver transplantation. *Curr Opin Organ Transplant*. 2008;13:285–290.

Rudnick MR, Marchi LD, Plotkin JS. Hemodynamic monitoring during liver transplantation: a state of the art review. *World J Hepat*. 2015;7(10):1302–1311.

C.2. What are the considerations for the induction of anesthesia?

If there is evidence of tense ascites, recent food ingestion, or a propensity for delayed gastric emptying, a rapid sequence induction of general endotracheal anesthesia is performed. AKI with elevated potassium levels or prolonged immobilization may preclude the use of succinylcholine. Compressive atelectasis from ascites and pleural effusions reduce functional residual capacity and decrease the time to oxygen desaturation. Vasodilating anesthetic agents may cause hypotension if intravascular volume is depleted (i.e., overdiuresis or gastrointestinal losses).

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1973–1986.

C.3. How does liver disease affect intraoperative

medication management?

The metabolic activity and clearance of anesthetic medications is impaired in patients with liver disease. Without adjusted doses of medications, duration of drug actions is extended and toxic levels result. Emergence from anesthesia may be delayed.

In the liver, metabolism takes place via two pathways: biotransformation via the cytochrome P450 system (which requires delivery of oxygen molecules via hepatic perfusion) and glucuronide conjugation. The first is decreased in liver disease; the second pathway is relatively spared when dysfunction begins. Many anesthetic drugs (i.e., opioids, barbiturates) bind to albumin in the circulation. Low albumin levels increase the free fraction of drug and can theoretically exaggerate the drug's effect. ESLD, however, alters many other aspects of normal pharmacokinetics such as drug volume of distribution, hepatic extraction and metabolism, renal excretion, and levels of serum proteins other than albumin. The net effect of these changes is unpredictable, making general recommendations for drug administration difficult. A safe approach in these patients is to titrate the drugs to their desired effects.

Patients with hepatic dysfunction may be sensitive to sedatives such as midazolam and diazepam. In contrast, the pharmacokinetics of lorazepam, which undergoes glucuronidation, is less likely to be affected by liver disease. Benzodiazepines may precipitate hepatic encephalopathy, and flumazenil can reverse this condition. Conversely, patients who have a history of alcohol abuse may require large doses of benzodiazepines. Rapid redistribution of bolused propofol determines its duration of action, which is not affected by impaired liver metabolism.

The adverse effects of morphine may be more pronounced in patients with severe liver disease. Morphine is metabolized by glucuronidation in the liver, and its intermediate metabolites are

eliminated renally. Although the pharmacokinetics of morphine may be unaltered in patients with mild hepatic disease, a prolonged half-life is associated with a prolonged PT, hypoalbuminemia, encephalopathy, ascites, and jaundice. The elimination of morphine's metabolites can also be prolonged in patients with HRS. Metabolism of fentanyl, sufentanil, and morphine, which have a high hepatic extraction ratio, is slowed by impaired hepatic blood flow.

In patients with liver disease and edema, muscle relaxant doses are increased because fluid retention increases volume of distribution. The duration of action of muscle relaxants that are metabolized by the liver (i.e., vecuronium and rocuronium) is prolonged. Liver disease reduces plasma cholinesterase activity, and prolonged neuromuscular blockade after succinylcholine has been reported.

Vasodilating anesthetic agents such as propofol and volatile anesthetics may cause hypotension if intravascular volume is depleted (i.e., overdiuresis or gastrointestinal losses) and reduce liver perfusion. In addition to perioperative hemorrhage and hypotension, volatile anesthetics can reduce hepatic blood flow and hepatic oxygen uptake. Compared to the vasoconstrictive effects of halothane, isoflurane and desflurane may improve hepatic blood flow and splanchnic perfusion via hepatic vasodilation.

Patients with ESLD often exhibit coagulation disorders. The presence of a coagulopathy is a contraindication to regional anesthesia, particularly epidural anesthesia.

Kiamanesh D, Rumley J, Moitra VK. Monitoring and managing hepatic disease in anaesthesia. *Br J Anaesth*. 2013;111(suppl 1):i50–i61.

Wiklund RA. Preoperative preparation of patients with advanced liver disease. *Crit Care Med*. 2004;32:S106–S115.

C.4. What happens during the first stage (preanhepatic

phase) of the liver transplant operation?

The preanhepatic phase begins with induction of anesthesia and ends with clamping of the hepatic artery. The diseased liver is mobilized; the suprahepatic and infrahepatic vena cava, portal vein, and hepatic artery are isolated; and the bile duct is divided. The anesthesia team manages disorders of coagulation and hemodynamic disturbances. Large losses of ascites cause hypotension and require early fluid resuscitation. Albumin solution and fresh frozen plasma are often used to replete intravascular volume.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1973–1986.

C.5. What happens during the second stage (anhepatic phase) of the liver transplant operation?

The second stage of the liver transplant operation, the anhepatic phase, begins after removal of the diseased liver and ends with reperfusion of the new liver. If the IVC and portal vein are clamped, venous return to the heart and cardiac output decrease. In preparation for clamping and dividing the IVC, a test clamp maneuver (occlusion of the suprahepatic IVC) is performed to assess the resilience of the circulatory system. Hypotension is managed with vasoactive medications, fluid repletion, adjustment of anesthetic agents, correction of hypocalcemia, and venovenous bypass. Anastomoses between the recipient and donor liver are performed in the following order: caval, portal, hepatic artery, and biliary.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1973–1986.

Polak WG, Peeters PM, Slooff MJ. The evolution of surgical techniques in clinical liver transplantation. A review. *Clin Transplant*. 2009;23:546–564.

C.6. What physiologic disturbances should be anticipated

during the second stage (anhepatic phase) of the liver transplant operation?

Without a liver, the patient may develop acidosis and hypocalcemia due to lack of lactate and citrate metabolism. Acidemia as well as reduced urine output leads to hyperkalemia. In the anhepatic phase, hepatic gluconeogenesis is absent; therefore, blood glucose levels are monitored regularly for both hyperglycemia and hypoglycemia.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1973–1986.

C.7. What is venovenous bypass? What are the potential advantages and disadvantages of this procedure?

Some centers routinely use venovenous bypass to divert blood flow from the portal circulation and IVC to the right atrium. Standard venovenous bypass uses a Y-shaped tubing. One limb of the tubing is inserted into the recipient's portal vein to drain the splanchnic beds. Another limb of the tubing is placed, through a groin cut, down into an iliac vein or the distal IVC. The outflow tubing passes through a pump. Blood returns to the patient through a cutdown access to an axillary vein or through percutaneous access to an internal jugular or subclavian vein (**Fig. 16.3**).

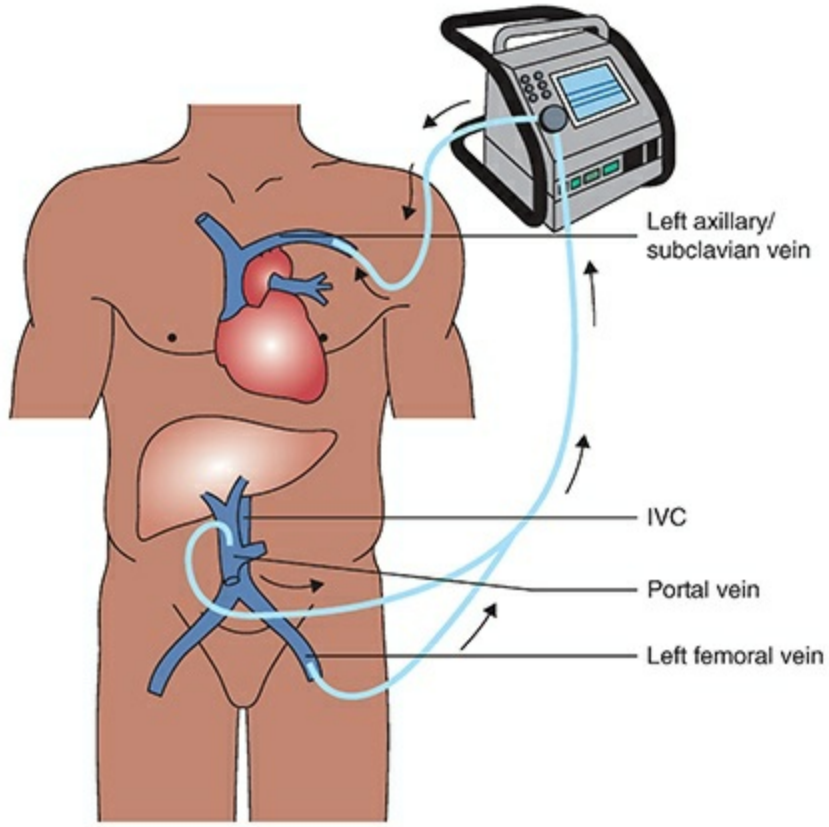

FIGURE 16.3. Schematic diagram of venovenous bypass circuit during liver transplantation. Venous return comes from the femoral and portal veins with the tubing connected together into a single venous return line. The centrifugal pump returns the blood into the axillary or subclavian vein. IVC, inferior vena cava.

Potentially, venovenous bypass can decompress the portal circulation and reduce congestion of the gut, decrease hemodynamic instability during clamping of the IVC, maintain normothermia via continuous warming of the bypass circuit, manage blood volume overload, preserve renal perfusion pressure, and improve surgical exposure during dissection. Disadvantages include the complications of venous cannula placement (bleeding, air, or thrombotic embolism); release of proinflammatory mediators; activation of complement, which may contribute to tissue injury and organ failure; and the time and cost of an expensive procedure.

The efficacy and benefits of routine use of venovenous bypass remain controversial. However, portal decompression

clearly improves surgical visualization in certain circumstances. Other centers reserve venovenous bypass for situations in which interrupted venous return through the IVC depresses the recipient's circulating system; with the increase in popularity of the piggyback anastomosis technique, this indication is less common. Budd-Chiari syndrome is a contraindication for bypass because there is an increased risk of pulmonary embolism and poor shunt flow rates.

Barnett R. Pro: veno-veno bypass should routinely be used during liver transplantation. *J Cardiothorac Vasc Anesth*. 2006;20:742–743.

Hilmi IA, Planinsic R. Con: venovenous bypass should not be used in orthotopic liver transplantation. *J Cardiothorac Vasc Anesth*. 2006;20:744–747.

Hoffmann K, Weigand MA, Hillebrand N, et al. Is veno-venous bypass still needed during liver transplantation? A review of the literature. *Clin Transplant*. 2009;23:1–8.

Polak WG, Peeters PM, Slooff MJ. The evolution of surgical techniques in clinical liver transplantation. A review. *Clin Transplant*. 2009;23:546–564.

C.8. What surgical techniques anastomose the donor and recipient inferior vena cava (IVC)?

There are several techniques to anastomose the donor and recipient IVC. Conventionally, blood flow through the IVC is completely interrupted and a cylinder of the recipient's IVC is removed with the diseased liver. An end-to-end anastomosis is created between the donor's and the recipient's IVC (**Fig. 16.4A**). In the piggyback method, the diseased liver is dissected off the IVC. The recipient's IVC is preserved, and blood flow is not completely interrupted. One end of the graft's segment of IVC is oversewn, and the orifice of the hepatic veins (the liver's venous outflow) is anastomosed to the preserved recipient's suprahepatic IVC (**Fig. 16.4B**). A third technique creates a side-to-side cavo-caval anastomosis (**Fig. 16.4C**).

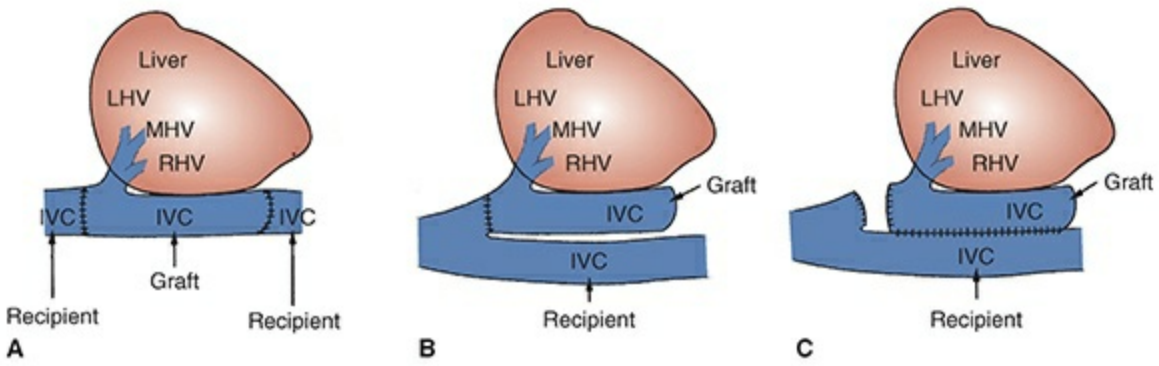

FIGURE 16.4. Three different techniques to reconstruct the hepatovenous outflow. A. End-to-end interposition of the donor vena cava to the recipient vena cava. **B.** End-to-end anastomosis of the vena cava to the hepatic veins. **C.** Side-to-side cavo-cavostomy. IVC, inferior vena cava; LHV, left hepatic vein; MHV, middle hepatic vein; RHV, right hepatic vein. (*Modified by permission from Springer: Hesse UJ, Berrevoet F, Troisi R, et al. Hepato-venous reconstruction in orthotopic liver transplantation with preservation of the recipients' inferior vena cava and veno-venous bypass*. Langenbecks Arch Surg. *2000;385[5]:350–356. Copyright © 2000 Springer-Verlag.*)

Mehrabi A, Fonouni H, Müller SA, et al. Current concepts in transplant surgery: liver transplantation today. *Langenbecks Arch Surg*. 2008;393:245–260.

Polak WG, Peeters PM, Slooff MJ. The evolution of surgical techniques in clinical liver transplantation. A review. *Clin Transplant*. 2009;23:546–564.

C.9. What are the potential advantages of the "piggyback" (vena cava preservation) technique?

Potential advantages of the piggyback technique for vascular reconstruction include hemodynamic stability because cardiac filling is preserved; protected perfusion pressure; no need for the surgical interventions associated with venovenous bypass; reduced need for retrocaval dissection, which lessens the likelihood of damage to the adrenal vein; and shorter anhepatic time and warm ischemia time. A disadvantage of the technique is that outflow obstruction results in hepatic congestion. Unfavorable anatomy in the recipient may preclude the use of the piggyback technique.

Polak WG, Peeters PM, Slooff MJ. The evolution of surgical techniques in clinical liver transplantation. A review. *Clin Transplant*. 2009;23:546–564.

C.10. What hemodynamic changes are expected after removal of vascular clamps? What is postreperfusion syndrome (PRS)?

Removal of the suprahepatic IVC clamp is not associated with hemodynamic changes. Unclamping the infrahepatic IVC restores venous return.

After unclamping of the portal vein, desaturated blood from the obstructed portal circulation, inflammatory mediators such as interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α), potassium, protons, and cold components are released into the systemic circulation. Hemodynamic instability, characterized by a decrease in blood pressure, heart rate, systemic vascular resistance, stroke volume index, and an increase in pulmonary arterial pressures, may follow unclamping of the portal vein and reperfusion of the liver. After reperfusion, an increase in serum potassium and a decrease in serum calcium are seen. A sustained 30% decrease in mean arterial blood pressure for more than 1 minute during the first 5 minutes after reperfusion defines PRS. A prolonged cold ischemic time, age of the donor, and mismatch in size between the recipient and grafted organ are associated with the development of PRS. Careful flushing of the graft just before completion of the anastomoses attenuates reperfusion disturbances by removing the cold hyperkalemic preservative solution as well as mediators of ischemia-reperfusion injury. Although venovenous bypass provides improved hemodynamic stability, it is not protective for PRS.

Before reperfusing the new graft, the following measures should be considered: (1) preemptive administration of calcium to correct hypocalcemia; (2) sodium bicarbonate, dichloroacetate, or THAM to adjust pH; and (3) inotropes or vasopressors for circulatory support. The surgical and anesthesia teams must be prepared to diagnose and treat dysrhythmias or

cardiac arrest.

Paugam-Burtz C, Kavafyan J, Merckx P, et al. Postreperfusion syndrome during liver transplantation for cirrhosis: outcome and predictors. *Liver Transpl*. 2009;15:522–529.

Siniscalchi A, Gamberini L, Laici C, et al. Post reperfusion syndrome during liver transplantation: from pathophysiology to therapy and preventive strategies. *World J Gastroenterol*. 2016;22(4):1551–1569.

C.11. How would you treat hyperkalemia?

Hyperkalemia is treated with diuretics, aldosterone agonists, β-adrenergic agonists, insulin in combination with glucose, and alkalinization via hyperventilation. Calcium should be administered to temporarily stabilize the myocardium and prevent arrhythmias. Rarely, when hyperkalemia is refractory to the preceding treatments, dialysis with continuous venovenous hemofiltration may reduce the elevated serum potassium level.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1973–1986.

C.12. Why should you anticipate hypocalcemia?

The principal reason to anticipate hypocalcemia is a failure to clear citrate, which normally is metabolized by the liver. This calcium-chelating agent accumulates in patients who receive transfusions of citrated blood products.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1973–1986.

C.13. What happens during the third stage of the liver transplant operation?

The third stage of the liver transplant operation, the neohepatic phase, follows reperfusion of the new liver. In the neohepatic phase, the biliary drainage system is constructed. Reconstruction may be straightforward, with an anastomosis between the graft's common bile duct and the biliary stump of the recipient. More

complex reconstructions are sometimes required, such as the creation of a choledochojejunostomy. A donor cholecystectomy generally is performed. A T-tube is placed in the reconstructed biliary outflow system with external drainage. An intraoperative cholangiogram, with contrast dye instilled through the T-tube, is used to assess the patency and integrity of the biliary reconstruction. The third stage ends with closure of all wounds and transport to the intensive care unit.

During the third stage of the procedure, an insidious coagulopathy may develop, requiring transfusion.

Polak WG, Peeters PM, Slooff MJ. The evolution of surgical techniques in clinical liver transplantation. A review. *Clin Transplant*. 2009;23:546–564.

C.14. What causes intraoperative bleeding during each phase of liver transplantation? How is coagulopathy monitored and treated? What are thromboelastography (TEG) and rotational thromboelastography (ROTEM)?

The etiology of intraoperative bleeding during liver transplantation is multifactorial. Patients with ESLD have serious hemostatic defects, and coagulation is affected by alterations in body temperature, tissue perfusion, acid–base balance, and fluid balance.

During the preanhepatic phase, bleeding from the surgical technique is influenced by the patient's underlying coagulopathy. Excessive fluid administration may cause a dilutional coagulopathy and increase venous congestion of the splanchnic area, leading to more bleeding at the surgical site. Bleeding may be minimal in a hypercoagulable state such as hepatocellular carcinoma or cholestatic cirrhosis.

During the anhepatic phase, there is a net increase in systemic tPA derived from endothelial cells, which is normally cleared by

the liver. Although PT and aPTT values may not change, hyperfibrinolysis is possible. Hyperfibrinolysis is confirmed by a decrease in α_2-antiplasmin and plasminogen activity and an increase in fibrin and fibrinogen degradation products.

Nonsurgical and insidious bleeding during reperfusion can be profound. Disseminated intravascular coagulation, increased fibrinolysis, release of heparin or heparin-like substances, and trapped platelets in the graft cause coagulopathy. After reperfusion, platelet counts drop due to sinusoidal obstruction and entrapment by the new liver, generalized platelet aggregation, and a consumptive disseminated intravascular coagulation-like process.

The coagulation status should always be monitored by inspection of the surgical field. Routine laboratory tests (PT, aPTT, platelet count, fibrinogen levels) are used in some centers for evaluating the coagulation status and directing treatment. Multiple studies have shown that routine laboratory tests have limited utility in the ESLD population because of complex changes in hemostasis. Viscoelastic tests (TEG or ROTEM) assess the viscoelastic properties of a whole blood sample as a function of time to reflect the function and interaction of the plasma, blood cells, and platelets. These measurements detect a hypercoagulable state and distinguish hyperfibrinolysis from other causes of coagulopathy, such as factor depletion or thrombocytopenia, to offer a dynamic and rapid composite picture of the entire clotting cascade. Heparinase may be used to help diagnose coagulopathy resulting from the presence of heparinoids (also see Chapter 12, sections B.8, B.9, and B.10; Chapter 31, section A.1; and Chapter 57, section C.25).

Bezinover D, Dirkmann D, Findlay J, et al. Perioperative coagulation management in liver transplant recipients. *Transplantation*. 2018;102(4):578–591.

Clevenger B, Mallett SV. Transfusion and coagulation management in liver

transplantation. *World J Gastroenterol*. 2014;20:6146–6158.

Dalmau A, Sabaté A, Aparicio I. Hemostasis and coagulation monitoring and management during liver transplantation. *Curr Opin Organ Transplant*. 2009;14:286–290.

Krzanicki D, Sugavanam A, Mallett S. Intraoperative hypercoagulability during liver transplantation as demonstrated by thromboelastography. *Liver Transpl*. 2013;19:852–861.

Tripodi A, Mannucci PM. The coagulopathy of chronic liver disease. *N Engl J Med*. 2011;365:147–156.

C.15. What are the complications of massive transfusion?

Uncontrolled hemorrhage and massive transfusion may cause the lethal triad of acidosis, coagulopathy, and hypothermia. Left uncorrected, each of these abnormalities can exacerbate the other, creating a "blood vicious cycle." Additional early complications of massive transfusion include (1) acute hemolytic transfusion reactions, (2) febrile nonhemolytic transfusion reactions, (3) transfusion-related acute lung injury, (4) transfusion-associated circulatory overload, (5) allergic reactions, (6) bacterial sepsis, (7) hypocalcemia, (8) hyperkalemia, and (9) transfusion-related immunomodulation.

Sihler KC, Napolitano LM. Complications of massive transfusion. *Chest*. 2010;137:209–220.

C.16. How are the complications of massive transfusion prevented?

Warming the room, applying forced warming systems to the patient's body, administering blood products and fluids through a fluid warmer, and heating and humidifying inspired gases reduce the risk of hypothermia. Dilutional coagulopathy and thrombocytopenia traditionally were prevented by transfusing packed red blood cells, fresh frozen plasma, and platelets in a 1:1:1 ratio. Because of increased morbidity and mortality with blood product transfusion in liver transplantation, bedside-guided transfusion with TEG/ROTEM is encouraged. Platelet

transfusion has been implicated in overall mortality as well as decreased graft survival in liver transplants. Occasionally, prothrombin complex concentrate can be used to correct refractory coagulopathy. Potassium, magnesium, and calcium levels are frequently monitored to correct abnormal levels. Metabolic acidosis is managed by improving hemodynamic parameters, adjusting minute ventilation, and administering sodium bicarbonate or tromethamine for severe metabolic acidosis. The risk of transfusion-related acute lung injury may be reduced by minimizing transfusions and transfusing packed red blood cells with a short storage time and fresh frozen plasma from men or nulliparous women.

Hartmann M, Szalai C, Saner FH. Hemostasis in liver transplantation: pathophysiology, monitoring, and treatment. *World J Gastroenterol*. 2016;22(4):1541–1550.

Sihler KC, Napolitano LM. Complications of massive transfusion. *Chest*. 2010;137:209–220.

C.17. How is hyperfibrinolysis managed?

The tPA has been implicated as a causal agent in hyperfibrinolysis. A functioning graft liver will eventually clear excess tPA from the circulation; however, levels seem to peak at reperfusion and are associated with greater intraoperative blood loss. Pharmacologic therapy with antifibrinolytic agents (tranexamic acid, ε-aminocaproic acid) blocks fibrin degradation by plasmin, but the full spectrum of their actions remains incompletely defined. The use of prophylactic antifibrinolytic agents in liver transplant surgery may reduce transfusion requirements, but this remains controversial because of concern for development of thromboses that may be catastrophic.

Badenoch A, Sharma A, Gower S, et al. The effectiveness and safety of tranexamic acid in orthotopic liver transplantation clinical practice: a propensity score matched cohort study. *Transplantation*. 2017;101(7):1658–1665.

Kim E, Ko JS, Gwak M, et al. Incidence and clinical significance of hyperfibrinolysis during living donor liver transplantation. *Blood Coagul Fibrinolysis*. 2018;29(3):322–326.

Ortmann E, Besser MW, Klein AA. Antifibrinolytic agents in current anaesthetic practice. *Br J Anaesth*. 2013;111:549–563.

C.18. When is intraoperative renal replacement therapy indicated?

Managing patients with low urine output, renal dysfunction, or preoperative hyperkalemia, who undergo liver transplantation, is challenging. Continuous renal replacement therapy may be used intraoperatively to manage volume shifts, acid–base balance, and electrolyte disturbances. Patients who are receiving dialysis and patients who have AKI should have intraoperative continuous renal replacement therapy.

Townsend DR, Bagshaw SM, Jacka MJ, et al. Intraoperative renal support during liver transplantation. *Liver Transpl*. 2009;15:73–78.

C.19. What intraoperative signs suggest that the hepatic graft is working?

Good texture and color of the graft, evidence of bile production, and hemodynamic stability are signs that the graft is working. Hypocalcemia often resolves quickly, even with rapid fresh frozen plasma administration. Metabolic alkalemia can develop as a result of citrate metabolism. Potassium levels tend to normalize with the onset of hepatocyte function. A number of recipients exhibit hyperglycemia resistant to insulin.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1467–1471.

D. Postoperative Management

D.1. What are the goals of immediate postoperative care of the liver transplant patient?

After liver transplantation, patients are admitted to the intensive care unit for monitoring of organ function, management of intraoperative complications, correction of coagulopathy, evaluation of graft function, and initiation of immunosuppression. Although many patients are extubated within 6 hours after the operation, the lungs of liver transplant patients often are mechanically ventilated for 24 to 48 hours.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1973–1986.

D.2. What postoperative findings suggest that the hepatic graft is functioning?

Clearance of lactic acid, production of glucose, resolution of encephalopathy, normothermia, normalization of coagulopathy, decreasing total bilirubin levels, production of bile (through the biliary tube), and adequate urine output suggest a functioning graft. Preservation injury causes transaminases to rise immediately after surgery, but enzyme levels usually fall within 24 to 48 hours. New synthesis of coagulation factors will not correct factor depletion for hours to days after the transplant.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1973–1986.

D.3. What coagulation disturbances should be anticipated in the postoperative period?

Typically, heparin effects, disseminated intravascular coagulation, or hyperfibrinolysis has been resolved in the operating room. However, dilutional coagulopathy, along with ongoing platelet and factor consumption in the early postoperative phase and poor graft function, may contribute to clinical bleeding. Postoperative uremia also compromises platelet function. A functioning graft liver may not produce substantial levels of clotting factors for several days. Therefore,

plasma, cryoprecipitate, and/or platelets may be needed in the early postoperative period.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1973–1986.

D.4. Can renal function change after liver transplantation?

Postoperative renal function is correlated with preoperative glomerular filtration rate, and approximately 10% of liver transplant patients require postoperative dialysis. For patients on renal replacement therapy prior to surgery, rate of renal recovery is negatively associated with increasing age, presence of diabetes, and duration of renal replacement therapy greater than 8 weeks. For patients with cirrhosis who have HRS resistant to diuretics, renal function may improve after transplantation. Postoperatively, sepsis and the nephrotoxic calcineurin inhibitors, such as cyclosporin A and FK-506 (tacrolimus), may contribute to renal dysfunction. Balanced immunosuppression with steroids, mycophenolate mofetil, anti-CD25 (basiliximab/daclizumab), and antithymoglobulin can minimize posttransplant renal dysfunction. Chronic allograft nephropathy in patients who have received liver, heart, lung, or kidney transplants is now the third most common reason for patients to be on the waiting list for a kidney transplant.

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D.5. What vascular and biliary complications occur after

liver transplantation?

Arterial and venous vascular complications include anastomotic bleeding leading to hypovolemia, acute stenosis or occlusion from thrombosis or kinking of the graft vessels, and development of an aneurysm or pseudoaneurysm. Thrombosis of the portal vein or hepatic artery compromises viability of the graft. Abdominal Doppler ultrasound is used to assess the hepatic vessels. Hepatic artery thrombosis, which is more common than portal vein thrombosis, may cause severe liver failure from necrosis. Portal vein thrombosis may cause liver dysfunction, tense ascites, and variceal bleeding.

Biliary complications include bile leak, bile duct stricture, ductal stones, and sphincter of Oddi dysfunction and are associated with the use of T-tubes, Roux-en-Y anastomoses, ischemia-reperfusion injury, cytomegalovirus infection, and hepatic artery thrombosis (leading to duct ischemia). Patients with bile leaks experience fever, abdominal pain, and peritoneal irritation. Bile leaks develop early in the postoperative course and may be identified by ultrasonography showing abdominal fluid collections or cholangiography. Bile leaks are managed with endoscopic placement of a biliary stent or relaparotomy.

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Mehrabi A, Fonouni H, Müller SA, et al. Current concepts in transplant surgery: liver transplantation today. *Langenbecks Arch Surg*. 2008;393:245–260.

D.6. What immunosuppressive agents will be given after liver transplantation? What are the major side effects?

The risk of organ rejection is balanced against the adverse side effects (i.e., neurotoxicity, nephrotoxicity, infection, metabolic abnormalities, malignancy, and recurrence of pretransplant

conditions such as hepatitis C virus, hepatocellular carcinoma, and sclerosing cholangitis) of immunosuppressive medications. Although protocols vary from center to center, newer regimens have reduced the degree of immunosuppression. A usual induction regimen includes a calcineurin inhibitor such as cyclosporine or FK-506 (tacrolimus), an antimetabolite such as azathioprine or mycophenolate mofetil, and a steroid such as methylprednisolone or prednisone. Antibodies directed against T-cell lymphocytes (e.g., OKT3 or antithymocyte globulin) or the interleukin-2 (IL-2) receptor (basiliximab) or mammalian target of rapamycin (mTOR) inhibitors (e.g., everolimus or sirolimus) may be substituted for cyclosporine or tacrolimus in patients with renal dysfunction or used in short courses to treat rejection. After 6 months to a year, many patients can be weaned to calcineurin inhibitor monotherapy. New drugs for immunosuppression in liver transplantation are monoclonal antibodies to IL-2 receptors (CD25) of T lymphocytes (basiliximab and daclizumab). The adverse effects of these medications are listed in **Table 16.1**.

TABLE 16.1 Adverse Effects of Immunosuppressant Medications

Medication	Adverse Effects
FK-506 (tacrolimus)	Nephrotoxicity Hypertension Neurotoxicity (tremors, seizures, posterior leukoencephalopathy)
Cyclosporine	Nephrotoxicity Hypertension
Mycophenolate mofetil	Hypertension Bone marrow suppression Abdominal pain Diarrhea Vomiting
Azathioprine	Leukopenia Anemia Thrombocytopenia

Glucocorticoid	Glucose intolerance Osteoporosis Peptic ulcer disease Adrenal suppression
OKT3	Symptoms of cytokine release (fever, chills, dyspnea, wheezing, chest pain) Leukopenia
Basiliximab	Gastrointestinal upset
Daclizumab	Gastrointestinal upset

Gotthardt D, Bruns H, Weiss KH, et al. Current strategies for immunosuppression following liver transplantation. *Langenbecks Arch Surg*. 2014;399:981–988.

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SECTION 4 The Nervous System

17 Brain Tumor and Craniotomy

June M. Chan, Elena V. Christ, and Kane O. Pryor

A 47-year-old woman who was previously healthy presents with a 4-month history of headache, with intermittent diplopia and gait disturbance developing over the last month. She is admitted after her family witnesses an acute episode of profound lethargy, altered cognition, and vomiting. Neurologic examination is remarkable for abnormal right-sided cranial nerve V, VII, and VIII function; nystagmus; and ataxic gait. Magnetic resonance imaging (MRI) shows a large, right posterior fossa mass that is only slightly hyperintense on T2-weighted images but is clearly demarcated after the intravenous injection of gadolinium contrast. The impression is of a petroclival meningioma, with mass effect on the pons and fourth ventricle. Magnetic resonance angiogram shows a highly vascular tumor drawing principal blood supply from the ascending pharyngeal branch of the ipsilateral external carotid artery. The patient improves clinically following the administration of dexamethasone and mannitol and the infusion of 2% sodium chloride and is monitored in the neurosurgical intensive care unit (ICU). The day after admission,

the patient undergoes uneventful cerebral angiography and partial embolization of the tumor under general anesthesia. She is now scheduled for posterior fossa craniotomy and resection of the tumor.

A. Medical Disease and Differential Diagnosis

1. What is the pathology of intracranial tumors?
2. What is intracranial pressure (ICP), and what are its determinants?
3. How does the presence of a mass alter the ICP in this patient, and what are the clinical manifestations of these alterations?
4. What is cerebral blood flow (CBF), and what are its determinants?
5. What are the cerebral steal syndromes?
6. Are there any issues specific to posterior cranial fossa pathology?
7. What is the role of preoperative embolization therapy?

B. Preoperative Evaluation and Preparation

1. What are the special considerations in preoperative evaluation of the patient scheduled for posterior fossa craniotomy?
2. In a patient who presents with intracranial hypertension, what management might have already been initiated preoperatively, and what are the implications for anesthetic management?
3. What are the types of intraoperative neurophysiologic monitoring (IOM) that would likely be used for this procedure, and how will they affect the anesthetic management plan?
4. What are the options for patient positioning during posterior fossa surgery?
5. What are the principal disadvantages associated with the common posterior fossa craniotomy positions?
6. How does the sitting position affect your preoperative assessment and planning?

7. How should the patient position ultimately be determined?
8. Should this patient receive premedication?

C. Intraoperative Management

1. What are the anesthetic goals for craniotomy?
2. What monitors should be used during craniotomy?
3. Would you monitor for venous air embolism (VAE)? What are the monitoring options?
4. What specific risks are associated with induction of anesthesia?
5. How would you induce anesthesia?
6. What are the effects of anesthetics on cerebral metabolic rate of oxygen ($CMRO_2$), CBF, and ICP? With this in mind, how would you maintain anesthesia?
7. How would you manage ventilation and maintain arterial carbon dioxide (CO_2)?
8. How would you approach diuretic therapy?
9. How would you manage serum glucose?
10. How would you approach fluid management?
11. Once the bone plate is removed and the dura retracted, the surgeon reports that the brain is still "tight." What would be your response?
12. If deliberate hypotension is indicated, how will you achieve it?
13. While the surgeon is resecting tumor from near the brainstem, the patient's heart rate suddenly drops to 20 beats per minute. What is your assessment and management?
14. Are there any measures you can take to prevent VAE?
15. During the procedure, the precordial Doppler becomes loud and turbulent. The end-tidal CO_2 ($EtCO_2$) drops from 31 to 13 mmHg, and the systemic pressure from 121/63 to 64/32 mmHg. What is your assessment and management plan?
16. What is your approach to emergence? What if the patient does not regain consciousness?

D. Postoperative Management

1. What postoperative complications are of greatest concern? What level of monitoring is required?
2. What is your approach to postoperative pain control?
3. In the ICU, the patient's neurologic status deteriorates and ICP monitoring is instituted. What are the different methods of monitoring ICP, and what are their limitations?

A. Medical Disease and Differential Diagnosis

A.1. What is the pathology of intracranial tumors?

Intracranial tumors may be primary neoplasms or secondary to metastases, infection, inflammation, or vascular disruption. Primary cancers can be classified according to their cell origin, or according to their anatomic location (**Table 17.1**). The most common tumors in children are pilocytic astrocytomas and medulloblastomas compared with meningiomas, pituitary tumors, and glioblastomas in adults. Secondary metastases are far more common than primary intracranial tumors, although the exact incidence is unknown, and most likely originate from lung cancer, breast cancer, and melanoma.

TABLE 17.1 Classification of Intracranial Tumors

Anatomic Classification	Supratentorial • Glioma • Pituitary • Craniopharyngioma • Pineal • Lymphoma • Metastases	Infratentorial • Schwannoma • Medulloblastoma • Ependymoma • Hemangioblastoma • Glioma
Cell Origin	Primary • Neuroepithelial – Astrocytoma – Oligodendroglioma – Ependymoma • Neuronal/mixed neuronal-glial	Secondary • Metastases – Lung – Breast – Genitourinary – Melanoma

- Pineal
- Embryonal
  - Medulloblastoma, PNET
- Cranial and paraspinal nerves
  - Schwannoma, neurofibroma
- Meningioma
- Primary CNS lymphoma
- Germ cell
  - Gastrointestinal
- Infection
  - Abscess
  - Toxoplasmosis
  - Tuberculosis
- Inflammation
  - Sarcoidosis
- Vascular
  - Hemorrhage
  - Giant aneurysm

CNS, central nervous system; PNET, primitive neuroectodermal tumor.

Although the cause of primary intracranial neoplasms remains unclear, there are genetic conditions that predispose to tumor development. There is, for instance, a clear association between meningiomas and neurofibromatosis type 2. Other conditions linked with the development of brain tumors include neurofibromatosis types 1 and 2, von Hippel-Lindau syndrome, tuberous sclerosis, Li-Fraumeni syndrome, and Turcot syndrome. These conditions are associated with extra-tumor manifestations that should be carefully considered during preoperative evaluation (**Table 17.2**).

TABLE 17.2 Genetic Conditions Associated with Intracranial Tumors

Syndrome	Chromosome	Characteristic Tumor	Other Pathognomic Lesions
NF-1	17q11	Optic glioma Brainstem glioma	Café-au-lait spots, Lisch nodules
NF-2	22q12	Bilateral acoustic neuromas Multiple meningiomas	Subcutaneous schwannomas
Retinoblastoma	13q14	Trilateral retinoblastoma	
von Hippel-Lindau	3p25	Cerebellar, retinal, and spinal hemangioblastoma	
Tuberous sclerosis	9q34	Subependymal astrocytoma Retinal astrocytoma	Ash-leaf spots Shagreen patch Adenoma sebaceum

Sturge-Weber	9q21	Leptomeningeal angiomatosis Choroidal hemangioma	Port-wine nevus Glaucoma
Turcot	5q21	Glioblastoma Medulloblastoma	
Li-Fraumeni	17q	Malignant glioma PNET	

NF-1, neurofibromatosis type 1; NF-2, neurofibromatosis type 2; PNET, primitive neuroectodermal tumor.

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A.2. What is intracranial pressure (ICP), and what are its determinants?

Normal ICP is 5 to 15 mmHg (6 to 20 cm H_2O). This pressure results from the physiologic interactions of intracranial structures within the rigid skull. Anatomically, these structures are enclosed within a cranial vault that is divided by tough dural partitions, the falx and tentorium cerebelli. Functionally, intracranial structures can be conceptualized as three compartments within a minimally compliant space:

- *Parenchyma*, consisting of cellular, extracellular, and intracellular fluid components, occupying 80% to 85% of total intracranial volume (approximately 1,400 mL in the average adult)
- *Cerebrospinal fluid (CSF) (circulatory component)*, occupying 10% of total intracranial volume (approximately 75 mL in the cisterns, 50 mL in the subarachnoid space, and 25 mL in the ventricles)

- *Intracranial blood volume (vascular component)*, consisting of both arterial and venous blood, which occupies 5% to 10% total intracranial volume (averaging 150 mL in the adult)

Without compensation, alterations in any one of these compartments will lead to increases in ICP, which may impede blood flow and result in ischemia. Monro (1783) and Kellie (1824) first hypothesized that an increase in the volume of one compartment results a compensatory decrease in the other compartments, thereby preserving normal ICP. Initially, CSF can drain to the spinal CSF reservoir and venous blood to the extracranial veins. This minimizes the change in ICP during the early phases of intracranial volume expansion. However, this compensation is limited, especially if the expansion is rapid. At a critical point, these compensatory mechanisms are exhausted, and even small increases in intracranial volumes will result in significant increases in ICP.

Early signs of increased ICP include headache (classically occipital), vomiting, behavioral changes, sedation, and cognitive slowing. Papilledema on funduscopy is an important sign that is often missed on examination. Further increases in ICP can eventually lead to compressive cranial neuropathies (typically cranial nerve VI, causing unilateral mydriasis) and herniation of brain tissue through a noncompliant partition—rapidly resulting in irreversible regional and global neuronal injury.

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A.3. How does the presence of a mass alter the ICP in this patient, and what are the clinical manifestations of these alterations?

Within the constraints of the intracranial compliance model outlined earlier, there are certain characteristics of an intracranial mass that influence the degree of ICP alteration:

- *Size*: An intracranial mass exerts effects through its own intrinsic volume and any surrounding edema. Any space-occupying lesion within a relatively fixed intracranial compartment is compensated for through decreases in volume of other intracranial contents.
- *Rate of growth*: A rapidly expanding mass outpaces the rate in which compensatory volume shifts can occur, which leads to an increase in ICP.
- *Anatomic location*: The infratentorial space is notable for being highly susceptible to mass-related alterations in ICP. The area bound by the tentorium cerebelli and occiput is much lower in volume and compliance when compared with the supratentorial space. It also contains vital structures involved in CSF bulk flow between different compartments:

the fourth ventricle, which communicates with the supratentorial ventricles and subarachnoid cisterns, and the foramen magnum, which communicates with the spinal column. Any volume shift within the infratentorial space may therefore precipitate a noncommunicating hydrocephalus, which further compromises compensatory mechanisms for intracranial hypertension.

- *Local tissue dysfunction*: The presence of an intracranial tumor causes local effects on surrounding tissue through invasive destruction, induction of neoangiogenesis through the release of oncogenic factors, or compression with ischemic cellular disruption. This results in an inflammatory response that causes further tissue edema and increases in ICP.

Taken together, these considerations account for the differences in the clinical presentation of intracranial masses. A slow-growing mass, particularly in the peripheral supratentorial space, can become sizable with minimal symptoms due to compensatory volume remodeling, whereas a small infratentorial lesion can obstruct the fourth ventricle and rapidly cause significant intracranial hypertension.

In this patient, a slow-growing meningioma has been able to attain a large size before becoming symptomatic. The patient's earliest signs and symptoms were most likely due to a localized mass effect. The more acute decompensation, with rapidly developing signs and symptoms of elevated ICP, probably represents the added component of CSF outflow obstruction at the fourth ventricle. Even with the clinical improvement achieved by steroid therapy and osmotic diuresis, this patient has very little volume reserve and intracranial compliance so even small increases in volume—such as an increase in cerebral blood volume (CBV) precipitated by a minimum alveolar concentration (MAC) of volatile anesthetic—have the potential

to cause a precipitous spike in ICP.

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A.4. What is cerebral blood flow (CBF), and what are its determinants?

Despite only constituting about 2% of the total body weight, the brain receives approximately 15% to 20% of resting cardiac output as CBF via the carotid and vertebral arteries. This disproportionately high blood flow is due to the brain's metabolic requirement of oxygen (MRO_2), which consumes approximately 3.5 mL O_2/min/100 g brain tissue, or 20% of total body MRO_2. CBF is approximately 750 mL per minute in the adult, or 50 mL/min/100 g averaged across gray and white matter. Gray matter, which contains neuronal nuclei, is metabolically more active than white matter and consumes 75 versus 45 mL/min/100 g brain tissue.

CBF is determined by cerebral perfusion pressure (CPP), which describes the pressure gradient for blood flow across the cerebral vascular bed, and cerebral vascular resistance (CVR):

$$CBF = CPP / CVR$$

On a global level, CPP is the difference between the inflow and outflow pressures of the brain's blood supply. However, the cerebral circulation behaves as a Starling resistor: Its enclosure within the rigid cranial vault allows extravascular pressure (ICP) to compress and compromise venous outflow. Hence, CBF can be expressed as:

CBF = (mean arterial pressure [MAP] – outflow pressure) /

where outflow pressure = CVP or ICP, whichever is higher.

CBF is highly regulated to ensure substrate delivery matches the metabolic demands of neural tissue in a phenomenon known as *flow-metabolism coupling*. Depending on neuronal activation and metabolic demands, regions of the brain may be either hypoperfused or hyperperfused. A sudden decrease in CBF (such as during the occlusion of a cerebral artery) results in an ischemic stroke with neurologic deficits and potentially irreversible tissue damage. An excess of blood flow leads to hyperemia and potential increases in ICP leading to tissue compression and damage. Therefore, it is essential to maintain brain homeostasis; this is achieved through alterations in CVR via four overlapping mechanisms occurring on a regional and global cerebral level:

- *Vascular myogenic autoregulation*
  - CBF is maintained constant across MAPs of approximately 50 to 150 mmHg. Based on recent studies in humans, the extremes of this range should be approached with caution, especially the lower boundary; CBF can decrease at MAPs of 60 or even 70 mmHg. Chronic hypertension causes a rightward shift in the CBF–MAP relationship. Hypocapnia has been demonstrated to broaden the autoregulatory range, whereas hypercapnia and elevated ICP decreases the responsiveness of pressure autoregulation.
- *Metabolic autoregulation*
  - CO_2: CO_2 is a potent cerebral vasodilator. It exerts its effects on the cerebral vasculature primarily by altering CSF pH, although there is evidence that CSF P_{CO_2} also has a direct effect on cerebral vascular smooth muscle. At normotensive ranges, CBF has a linear relationship with

acute changes in $Paco_2$ between 20 and 80 mmHg, with CBF changing by 2% to 4% for every mmHg change in $Paco_2$. Beyond this range, further changes are limited by extremes in vascular diameter. This response is blunted by systemic hypotension and volatile anesthesia. It is important to note that prolonged hypocarbia or hypercarbia (beyond 6 to 8 hours) will ultimately have little effect on CVR, as CSF pH normalizes with active transport of bicarbonate over the blood–brain barrier (BBB). Furthermore, subsequent correction of $Paco_2$ would likely result in rebound cerebral hyper- or hypoperfusion.

- Oxygen (O_2): Acute exposure to hypoxia causes an immediate increase in CBF in a curvilinear relation with respect to arterial PO_2 and linear with respect to hemoglobin saturation. Acute hypoxemia below 50 mmHg causes cerebral vasodilation, rapidly reaching maximal response at approximately 30 mmHg. The exact mechanism of how this occurs is unclear, but it likely involves the direct effects of by-products from anaerobic metabolism and cellular ischemia, such as lactic acid and adenosine. This mechanism is also impaired in the presence of volatile anesthesia.

- *Neurogenic autoregulation*
  - Compared with myogenic and metabolic mechanisms, the autonomic nervous system plays a minor role in cerebral autoregulation. Both sympathetic innervation of cerebral arterioles and circulating sympathomimetics attenuate increases in CBF during severe hypertension, hypoxia, and hypercapnia.

As stated earlier, the presence of an intracranial mass induces dysfunction in surrounding neural tissue resulting in ischemia

and inflammation. This acidic microenvironment promotes local vasodilatation and vasoplegia with subsequent narrowing of the pressure autoregulatory range. Regional CBF becomes dependent on MAP and ICP, with little ability to compensate for changes in systemic blood pressure. Mass effect alone can increase ICP enough to critically compromise CPP with apparently normal MAP.

A conservative approach to the management of CPP would suggest that it should not be allowed to fall below 70 mmHg for any extended period in the baseline normotensive patient. Although a more moderate approach targeting CPPs in the 60- to 70-mmHg range is commonly used, most neuroanesthesiologists agree that sustained CPP values under 60 mmHg place the brain at risk, despite the possible neuroprotection afforded by the presence of a gamma-aminobutyric acid (GABA)ergic anesthetic agent.

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A.5. What are the cerebral steal syndromes?

Any intracranial pathology, including marginal ischemia and inflammation surrounding a mass lesion, can cause localized dysfunction of normal cerebral autoregulation and an impaired response to vasoactive agents. The microvasculature in the pathologic region can have an essentially fixed resistance. In this case, if vasodilation occurs in other normal regions of the brain, the decreased vascular resistance in the normal tissue can theoretically shunt blood flow away from the pathologic regions, which are already most vulnerable. This phenomenon is known as *cerebral steal*.

In anesthesia management, cerebral steal is most relevant in the context of hypercapnia and the use of volatile anesthetics. Both cause vasodilation of normal vasculature and potentially decrease regional CBF in pathologic areas. For volatile anesthesia, cerebral vasodilatation is usually considered to be significant when given in doses of 1 MAC or greater, but as a dose-dependent effect, it may be clinically apparent at 0.5 MAC. During hypocapnia, when there is vasoconstriction in normal tissue, the opposite may occur. In this case, blood flow to pathologic regions can actually increase. This phenomenon is known as *inverse steal* or the *Robin Hood effect*. Although both steal effects have been well reported in human literature, the clinical relevance of steal and inverse steal phenomena is unclear. Nonetheless, it is prudent to consider it in anesthetic management.

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A.6. Are there any issues specific to posterior cranial fossa pathology?

Surgery for tumors in the posterior fossa presents several challenges not seen with supratentorial surgery (**Table 17.3**). The posterior fossa extends from tentorium cerebelli superiorly to foramen magnum inferiorly, housing the cerebellum and most of the brainstem—specifically the pons and medulla. The posterior fossa is a tightly enclosed space in which tumors are often in direct contact with critical brainstem structures, including the cranial nerves and brainstem nuclei. The smaller volume of the posterior fossa means that less mass effect is needed to produce symptoms from compression of the cerebellum, brainstem, or fourth ventricle, with the potential risk of superior vermian or inferior tonsillar herniation. The patient with a posterior fossa tumor, especially one close to the brainstem, can worsen neurologically in the hours following surgery as a result of postsurgical inflammation causing edema.

TABLE 17.3 Specific Anesthetic Considerations in Posterior Fossa Craniotomy

Specific Challenges	Management Considerations
Need for adequate surgical access	• High likelihood of nonsupine positioning – Sitting position – Prone/semiprone position • Reduced access to airway and precordium in case of emergency • Risk of disrupting airway, vascular access, and

	monitors during position changes • Specific hemodynamic effects of nonsupine positioning – Venous air embolism risk – Venous pooling in sitting position – External abdominal compression in prone position • Positioning-related nerve and soft tissue injury
Brainstem dysfunction	• Intraoperative autonomic instability • Postoperative central respiratory failure
Intraoperative neuromonitoring	• Limitations in the administration of volatile agents and neuromuscular blockade • Need to understand implications of pathologic alterations in intraoperative monitoring signals and the appropriate management response

In addition to the risk of neuronal damage, surgery in proximity to brainstem nuclei can trigger significant intraoperative autonomic and collateral hemodynamic instability, which can be extremely challenging to manage. The most common autonomic event is an acute increase in vagal tone, which can lead to a prolonged period of asystole, and can be immediately followed by a reflexive surge in sympathetic tone. Furthermore, the risk to cranial nerves and other structures often demands IOM—such as somatosensory evoked potentials (SSEPs), brainstem auditory evoked potentials, or electromyography (EMG)—all of which can substantially restrict and dictate anesthetic management.

Finally, the posterior fossa cannot be accessed with the patient in the conventional supine position. In the past, the sitting position was highly favored by neurosurgeons and presented marked anesthetic challenges because of the increased risk of VAE. Although still common in some centers, the sitting position has fallen out of favor; nonetheless, all of the positions that permit access to the posterior fossa pose management difficulties that must be considered. The risk of VAE, although reduced, often still exists. Other considerations include loss of

jugular outflow, deterioration of pulmonary compliance, strain on the cervical spine and brachial plexus, and a lack of access to central venous lines and the airway. In patients who are critically ill or otherwise at risk for life-threatening intraoperative events, it must be remembered that cardiopulmonary resuscitation will always require that the patient be rapidly returned to the supine position.

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A.7. What is the role of preoperative embolization therapy?

Highly vascular tumors, especially those that are anatomically difficult to access, present a high risk for substantial intraoperative bleeding. In addition to the systemic risks associated with gross blood loss, peritumor bleeding can severely compromise surgical exposure and exacerbate neuronal and neurovascular inflammation.

To reduce this risk, patients often undergo embolization of the vessels feeding the tumor in the days immediately before surgery. An arterial catheter is inserted, usually in the femoral artery, and fluoroscopically guided until it rests in any of the vessels that have evolved to supply only the tumor and not normal brain. Low-dose systemic heparinization to achieve activated clotting times of 200 to 300 seconds is required to

prevent the formation of microthrombi. At this point, an embolic agent is slowly delivered to occlude the vessel, reducing the tumors vascular supply and thus the degree of bleeding during subsequent operative resection. Currently, the embolic agents available can be considered as two groups: particulate (using a variety of substances such as coils, gelatin sponges, fibrin glue, and polyvinyl alcohol) and liquid (ethylene vinyl alcohol, hyperosmolar mannitol). The choice of agent is determined by angiographic anatomy, tumor vascularity, and tumor histology. Because of collateralization and reestablishment of blood supply, embolization is effective for only a short period and is usually performed within 48 hours of the intracranial resection.

Tumor embolization comes with its own risks and challenges: Vascular anatomy might not always permit embolization, and the embolization itself can precipitate peri-tumor edema and hyperemic changes in blood flow dynamics. These changes are particularly relevant in this patient with a posterior fossa tumor proximate to the brainstem. Deposition of embolic agent into vessels supplying normal brain amounts to an embolic stroke and can have catastrophic consequences. Catheter-related complications including vessel dissection and rupture, and access site hematomas are well described. Furthermore, embolizations often require general anesthesia and thus assume all of the associated general and neuro-specific risks. Current literature reports embolization-related complication rates for meningiomas at between 2.9% and 4.6% but with significant decreases in intraoperative blood loss.

Ashour R, Aziz-Sultan A. Preoperative tumor embolization. *Neurosurg Clin N Am*. 2014;25(3):607–617.

Carli DF, Sluzewski M, Beute GN, et al. Complications of particle embolization of meningiomas: frequency, risk factors, and outcome. *AJNR Am J Neuroradiol*. 2010;31:152–154.

Raper DM, Starke RM, Henderson F Jr, et al. Preoperative embolization of

intracranial meningiomas: efficacy, technical considerations, and complications. *Am J Neuroradiol*. 2014;35(9):1798–1804.

Young WL. Anesthesia for endovascular neurosurgery and interventional neuroradiology. *Anesthesiol Clin*. 2007;25:391–412.

B. Preoperative Evaluation and Preparation

B.1. What are the special considerations in preoperative evaluation of the patient scheduled for posterior fossa craniotomy?

In addition to the routine thorough preoperative evaluation, the evaluation of the patient for craniotomy should answer several questions that critically influence anesthesia management:

- What is the ICP? If ICP is still in the normal range, how much intracranial compliance reserve is likely to exist?
- How is autoregulation likely to be affected by the pathology and chronic changes in blood pressure? What range of arterial pressures will be required to preserve adequate CPP and CBF?
- Does the patient have any of the electrolyte and endocrine abnormalities associated with intracranial pathology or treatment, such as neurogenic diabetes insipidus, or hypernatremia resulting from hypertonic saline therapy?
- Is the lesion highly vascular, difficult to access, or situated proximate to one of the large draining veins—all of which increase the probability of significant bleeding?
- What is the likely positioning, and does it incur a risk of VAE, obstruction of jugular venous outflow, or neck hyperextension? Are there preoperative patient conditions that would significantly increase the risk of or preclude certain positions, such as patent foramen ovale and right to left intracardiac shunts?
- Is the tumor located in a position close to the brainstem such

that severe autonomic dynamics are likely?

- Will the baseline neurologic status affect the ability to extubate or to establish an early neurologic assessment after general anesthesia?
- Will the anesthetic technique need to accommodate specific monitoring requirements, such as electroencephalography (EEG), electrocorticography, brainstem auditory evoked responses (BAERs), or SSEPs?

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Jellish WS, Murdoch J, Leonetti JP. Perioperative management of complex skull base surgery: the anesthesiologist's point of view. *Neurosurg Focus*. 2002;12:E5.

Lieb K, Selim M. Preoperative evaluation of patients with neurological disease. *Semin Neurol*. 2008;28:603–610.

B.2. In a patient who presents with intracranial hypertension, what management might have already been initiated preoperatively, and what are the implications for anesthetic management?

A patient with evidence of intracranial hypertension will be aggressively monitored and treated preoperatively; it is likely that the preoperative assessment will occur in an intensive care setting. The anesthesiologist must be familiar with the management of intracranial hypertension as various therapies will likely need to be initiated or continued in the operating room. Furthermore, the anesthesiologist must be mindful of potential sequelae that can arise from various perioperative therapies and interventions such as:

- *Corticosteroids*. Treatment can lead to hyperglycemia, which should be aggressively treated to maintain plasma glucose less than 150 to 180 mg per dL while taking care to avoid

hypoglycemia.

- *Head elevation*. Care should be taken to maintain 30-degree head elevation, where possible, and to avoid rapidly lowering the head during transport.
- *Diuretics (mannitol, furosemide)*. These can result in electrolyte or acid–base abnormalities. Decreased preload can increase the risk of hypotension in the peri-induction period.
- *Isotonic or hypertonic saline therapy*. This can result in hypernatremia or a hyperchloremic, non–anion gap metabolic acidosis.
- *Intubation and institution of hyperventilation*. If prolonged, the CBF response to CO_2 can become diminished or absent, with a risk for dangerous increases in CBF and ICP if hyperventilation is rapidly ceased. It can also lead to a compensatory loss of bicarbonate and other basic metabolic buffers leading to the development of acidosis if ventilation was normalized. Care should be taken to avoid hypoventilation during transport.
- *Ventriculostomy*. This is usually clamped during transport to or from the ICU, as the level of the drain relative to the head is critical, and accidental changes in position can result in excessive draining of CSF. It should be attended to on arrival to the operating room because even relatively short periods of clamping can result in elevations of ICP.
- *Manipulation of systemic pressures to optimize CPP*. Care should be taken to ensure drug infusions are maintained during transport to avoid rebound hypertension or hypotension.
- *Drug-induced cerebral vasoconstriction and coma*. Propofol infusion and pentobarbital are the typical agents currently used in the United States, following the decline in the availability of thiopental. This signifies a critical neurologic status. The therapy is often continued as the primary

anesthetic.

- *Deliberate hypothermia*. This signifies a critical neurologic status and requires discussion of intraoperative temperature management goals with the neurosurgeon and neurointensivist because the neuroprotective benefits may be countered by hypothermia-induced coagulopathy.

Li LM, Timofeev I, Czosnyka M, et al. Review article: the surgical approach to the management of increased intracranial pressure after traumatic brain injury. *Anesth Analg*. 2010;111:736–748.

Perez-Barcena J, Llompart-Pou JA, O'Phelan KH. Intracranial pressure monitoring and management of intracranial hypertension. *Crit Care Clin*. 2014;30(4):735–750.

Stevens RD, Bhardwaj A. Evolving paradigms in the management of severe traumatic brain injury. *Crit Care Med*. 2005;33:2415–2417.

Vincent JL, Berré J. Primer on medical management of severe brain injury. *Crit Care Med*. 2005;33:1392–1399.

B.3. What are the types of intraoperative neurophysiologic monitoring (IOM) that would likely be used for this procedure, and how will they affect the anesthetic management plan?

IOM uses a combination of stimulators and sensing electrodes to detect the functional integrity of sensory, motor, and cranial nerves and their associated nerve tracts and/or muscles. The primary monitoring modalities are EMG, evoked potentials (EPs), and EEG. EEG is rarely used for craniotomies for tumor resection and will not be considered in detail in this chapter.

EMG records the electrical activity within muscle in response to the stimulation of its innervating cranial or peripheral nerve. The most common EMG monitoring during posterior fossa surgery is for cranial nerve VII, although monitoring of cranial nerves V, IX, X, and XI is frequently encountered. Usually, the surgeon will deliver a very low current to a structure he or she believes could be the cranial nerve of interest, and muscular

activity is monitored in the distribution of the nerve. Mechanical manipulation of a nerve will often also cause muscular activity, which may herald potential inadvertent injury. EMG is relatively unaffected by volatile and intravenous anesthetic agents but requires intact functioning of the neuromuscular junction. Therefore, neuromuscular blockers cannot be used for EMG monitoring beyond anesthetic induction. Some anesthesiologists advocate the use of succinylcholine for intubation; however, with the use of sugammadex becoming more widely available, an intubating dose of a medium-duration nondepolarizing agent such as rocuronium, vecuronium can be used if needed and quickly reversed to allow adequate return of muscular function by the time monitoring is relevant.

EPs measure electrical activity generated within the nervous system in response to a stimulus. The most common EP monitoring encountered during resection of posterior fossa tumors is the BAER, which monitors cranial nerve VIII and auditory pathway function (including portions of the brainstem, midbrain, and the primary auditory cortex) in response to sounds generated in the auditory canal. SSEPs can also be used to monitor dorsal column-medial lemniscus tract integrity, which is useful for posterior fossa surgery given the superficial location of the medial lemniscus in the brainstem and pons. These are elicited via electrical stimulation of peripheral sensory nerves (most commonly median and posterior tibial nerves) and recorded via scalp needle electrodes directed over the somatosensory cortex. Similarly, motor evoked potentials (MEPs) are obtained through transcranial stimulation of cortical pyramidal cells and recorded distally along the spinal cord, motor nerves, and muscle.

EPs are recorded as positive and negative deflections from baseline. The time delay from stimulus to first recorded deflection is termed the latency, and the maximal deflection

from baseline is the amplitude. A significant increase in latency or decrease in amplitude of EPs can reflect injury along the nerve tract, or dysfunction due to physiologic or pharmacologic factors. Anesthetic agents can dramatically alter EPs in the absence of other abnormalities (**Table 17.4**). Although BAERs are reasonably robust, MEPs (and SSEPs to a lesser but still significant degree) are exquisitely sensitive to volatile anesthetics, which cause decreases in amplitude and increases in latency in a dose-dependent manner. Furthermore, neuromuscular blockers cannot be used if MEPs are proposed. Volatile agents should be kept at less than 0.5 MAC, and nitrous oxide (N_2O) should not be used. The anesthetic plan will often rely heavily on opioids; propofol and dexmedetomidine infusions are also often incorporated, the latter of which may also offer improvements in overall hemodynamic stability. Perhaps more important than the specific anesthetic regimen is that a maintenance equilibrium is established for the baseline neurophysiology measurements and is then kept constant throughout the procedure. Pseudo-equilibrated steady-state continuous infusions are key to this strategy.

TABLE 17.4 Anesthetic Effects on Intraoperative Neuromonitoring

	Affected By	Resistant To
SSEP	Volatile agents (goal <0.5 MAC) Nitrous oxide Intravenous agents	Muscle relaxants Opioids
BAEP		Volatile agents Nitrous oxide Muscle relaxants Intravenous agents Opioids
MEP	Muscle relaxants Volatile agents (avoid; use TIVA)	Opioids
EMG	Muscle relaxants	Volatile agents Propofol

	Nitrous oxide Opioids

BAEP, brainstem auditory evoked potential; EMG, electromyography; MAC, minimum alveolar concentration; MEP, motor evoked potential; SSEP, somatosensory evoked potential; TIVA, total intravenous anesthesia.

Although anesthetic agents are major influences on the accuracy of IOM, it should be remembered that physiologic factors such as hypothermia, acidosis, excessive hemodilution, and hypotension can also influence EPs as well as neuronal integrity and should be avoided (**Table 17.5**).

TABLE 17.5 Physiologic Effects on Intraoperative Neuromonitoring

	Effects
Temperature	• Progressive hypothermia predictably increases latency in SSEPs but has variable effects on amplitude (can increase in mild hypothermia and decreases with moderate hypothermia). • VEPs are completely lost at 25°C–27°C. • BAEPs are more resistant to hypothermia, but changes reflect those of SSEPs at lower temperature thresholds. • Hyperthermia to 40°C decreases latency but with further increases slowing occurs, likely reflecting neuronal injury.
Hematocrit	• Changes similar to ischemia in SSEPs and VEPs are seen with acute isovolemic hemodilution to hematocrit of 10%–15% in animals, with resolution when hematocrit was increased to 20%–22%.
Oxygen	• Mild hypoxemia has minimal effects on SSEPs and BAEPs. • Severe ischemia increases latency and decreases amplitude of SSEPs, with cortical responses being more sensitive than spinal responses. BAEPs are similarly affected.
Carbon dioxide	• Hypocarbia ($PaCO_2$ 20–25 mmHg) decreases latency in SSEPs. • Hypercarbia (to $PaCO_2$ 55 mmHg) has minimal effects on SSEPs.

BAEPs, brainstem auditory evoked potentials; SSEPs, somatosensory evoked potentials; VEPs, visually evoked potentials.

Bala E, Sessler DI, Nair DR, et al. Motor and somatosensory evoked potentials are well maintained in patients given dexmedetomidine during spine surgery. *Anesthesiology*. 2008;109:417–425.

Banoub M, Tetzlaff JE, Schubert A. Pharmacologic and physiologic influences affecting sensory evoked potentials: implications for perioperative monitoring. *Anesthesiology*. 2003;99(3):716–737.

Deiner S. Highlights of anesthetic considerations for intraoperative neuromonitoring. *Semin Cardiothorac Vasc Anesth*. 2010;14:51–53.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1868–1910.

Harper CM. Intraoperative cranial nerve monitoring. *Muscle Nerve*. 2004;29:339–351.

Lotto ML, Banoub M, Schubert A. Effects of anesthetic agents and physiologic changes on intraoperative motor evoked potentials. *J Neurosurg Anesthesiol*. 2004;16:32–42.

B.4. What are the options for patient positioning during posterior fossa surgery?

- *Sitting position*. Although used far less often now than two decades ago, it is critically important for the anesthesiologist to understand the sitting position partly because it could still have specific surgical advantages in some situations and partly because it provides the archetype for the risks and management of VAE. The patient is in a reclined sitting posture such that the feet are at or near the level of the heart. The head is held in a flexed position with a skull fixation device, and the arms are crossed over the chest.
- *Modified sitting position*. Due to concerns about the sitting position, a modified sitting position has been described. This involves the same reclining position as described earlier but with careful position of the hips and legs so that the feet and knees are above the level of the heart. The head is anteriorly flexed and held in place with a fixation device, and the arms are padded and placed on arm boards by the patient's side.
- *Prone position*. This is especially suitable for lesions in the midline but can be adapted for more lateral approaches by having the head slightly rotated. Depending on body habitus, supporting rolls are placed horizontally across the chest and hips or in parallel along the longitudinal axis of the body. The head is held with a skull fixation device with the neck in a neutral to flexed position.

- *Lateral decubitus position*. This position is suited to cerebellopontine angle tumors and cerebellar hemispheric lesions.
- *Park bench (semiprone) position*. The patient is turned toward a more prone position, moving the upper shoulder out of the surgeon's view and permitting better access to midline lesions.
- *Supine position*. This can sometimes be used with the patient's head rotated. To reduce the amount of rotation of the neck, which can obstruct venous outflow, a supporting roll can be placed under the ipsilateral shoulder and the whole bed rotated away from the surgeon.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1868–1910.

Jadik S, Wissing H, Friedrich K, et al. A standardized protocol for the prevention of clinically relevant venous air embolism during neurosurgical interventions in the semisitting position. *Neurosurgery*. 2009;64(3):533–538.

Rozet I, Vavilala MS. Risks and benefits of patient positioning during neurosurgical care. *Anesthesiol Clin*. 2007;25(3):631–653.

B.5. What are the principal disadvantages associated with the common posterior fossa craniotomy positions?

The greatest concern for the sitting position is the increased risk of VAE. In this position, the head is elevated above the right atrium and beyond the height of the central venous fluid column. This will reduce venous bleeding; it will also enable large volumes of air to be entrained into the central venous circulation, especially through the large dural sinuses, which are tented open. When propagated to the right heart and pulmonary circulation, VAE can range in severity from subclinical to severe, precipitating acute hemodynamic collapse and death. In a patient with a patent foramen ovale—which is present in 25% of the general population and is often undetected—air can traverse to the arterial circulation, causing embolic stroke.

Although VAE can occur with other positions, the risk and severity are substantially higher in the sitting position, with recent reported incidences detected by precordial Doppler as high as 50% for minor and major VAE, and significant VAE causing hypotension at 2% to 6% (other literature using transesophageal echocardiography (TEE) for detection have reported even higher rates). Furthermore, the sitting position complicates the effective treatment of VAE, as it is difficult to rapidly lower the patient's head below heart level, and precludes easy access for airway manipulation and cardiopulmonary resuscitation maneuvers when required. The sitting position is also associated with a greater degree of hypotension (thus compromising CPP), an increased risk of pneumocephalus causing postoperative drowsiness, and compression of vulnerable structures including cervical spinal cord from neck flexion causing quadriplegia, oropharyngeal structures causing macroglossia, and peripheral nerves causing nerve palsies and pressure areas.

In the prone position, the head is usually slightly elevated above the heart; therefore, the risk of VAE remains present, although the risk of massive entrainment is reduced. Prone positioning can cause a significant decrease in pulmonary compliance and will increase ventilation/perfusion mismatch, leading to atelectasis, venous admixture, and shunting. Virtually no access is available to the airway, chest, or limbs, and in the event of an airway, pulmonary, or cardiovascular emergency, the prone position places the anesthesiologist in a substantially compromised position.

The supine position alleviates many of these issues. Nevertheless, to access even the lateral posterior fossa from the supine position usually requires substantial rotation of the neck. This can cause obstruction of jugular venous outflow, leading to cerebral venous engorgement, with potentially undesirable

effects on ICP, CPP, surgical exposure, and bleeding. The neck rotation can also cause brachial plexus injury as well as significant pressure on laryngeal structures with potential vocal cord injury. Placing supports to elevate the ipsilateral shoulder can reduce rotation at the neck.

Fathi AR, Eshtehardi P, Meier B. Patent foramen ovale and neurosurgery in sitting position: a systematic review. *Br J Anaesth*. 2009;102:588–596.

Feigl GC, Decker K, Wurms M, et al. Neurosurgical procedures in the semisitting position: evaluation of the risk of paradoxical venous air embolism in patients with a patent foramen ovale. *World Neurosurg*. 2014;81:159–164.

Ganslandt O, Merkel A, Schmitt H, et al. The sitting position in neurosurgery: indications, complications and results. A single institution experience of 600 cases. *Acta Neurochir*. 2013;155:1887–1893.

Lindroos AC, Niiya T, Silvasti-Lundell M, et al. Stroke volume-directed administration of hydroxyethyl starch or Ringer's acetate in sitting position during craniotomy. *Acta Anaesthesiol Scand*. 2013;57(6):729–736.

Rath GP, Bithal PK, Chaturvedi A, et al. Complications related to positioning in posterior fossa craniectomy. *J Clin Neurosci*. 2007;14:520–525.

B.6. How does the sitting position affect your preoperative assessment and planning?

In addition to the standard preanesthetic and neurologic assessment, preoperative evaluation should be focused on the following:

- *Presence of intracardiac shunts*. The presence of a patent foramen ovale, right-to-left intracardiac shunts, and pulmonary arteriovenous malformations are generally considered absolute contraindications to the sitting position due to the risk of VAE and subsequent paradoxical air embolism (PAE), which can have disastrous clinical consequences. In the era of increasing litigation, preoperative contrast echocardiography with Valsalva has become part of routine workup for those considered for elective sitting position craniotomy. However, there is a significant drop-off between the incidences of diagnosed VAE, PAE, and

subsequent neurologic sequelae. Therefore, in the rare patient with a demonstrated shunt that still requires sitting position craniotomy, it is not routine to proceed to percutaneous shunt closure. Rather, it serves to heighten the surgeon's awareness for absolute, meticulous control of venous bleeding because it is the presence of open entraining vessels that ultimately determines the risk of VAE.

- *Other complications of the sitting position and their impact on the patient*. General anesthesia in the sitting position is associated with a greater degree of hypotension compared with other positions. This is in large part due to venous pooling in the dependent portions of the body causing a fall in preload, coupled with anesthetic depressant effects on systemic vascular resistance and inotropy. This results in a fall in stroke volume and cardiac output, which is compensated in otherwise healthy patients with increases in heart rate and vasoconstriction. Conditions that exaggerate this fall in MAP include hypovolemia and preoperative diuresis, cachexia, advanced age, and therapeutic β-blockade, all of which can blunt compensatory autonomic responses. The concern with aggressive fluid loading intraoperatively is that it could run counter to the therapeutic goals of diuresis and ICP reduction, and the subsequent redistribution when returned to the supine position can cause an exaggerated increase in cardiac filling pressures. Furthermore, the use of vasoconstrictors to maintain adequate MAP in the face of a preload deficit increases the risk of end-organ hypoperfusion and dysfunction, particularly the kidneys. This is particularly relevant if electrolyte derangements coexist because they may worsen with perioperative renal injury.

The additional hydrostatic gradient between the heart and cerebral vasculature in the sitting position places the brain at a greater risk of hypoperfusion, particularly in patients who have

underlying carotid or vertebrobasilar atherosclerosis. This history should be actively sought because these patients may require higher MAPs intraoperatively to maintain adequate CPP, and intraoperative MAP measurements should be made at the level of the circle of Willis. There is also a hydrostatic gradient in lung perfusion when under positive pressure ventilation, with the lung apices being susceptible to hypoperfusion. Functionally termed West Zone 1, after the physician and physiologist John West, this area becomes alveolar dead space. A hallmark of increasing alveolar dead space is a broadening arterial–Et_{CO_2} gap, which places the patient at risk of hypercarbia and increased ICP if Et_{CO_2} is used as a surrogate for Pa_{CO_2} monitoring. Increases in alveolar dead space also place a greater ventilatory burden on the rest of the lung, which may be of particular concern in patients with obstructive airway disease, despite the gains in functional residual capacity and ventilation/perfusion matching in the dependent portions of the lung in the upright position.

Patients with cervical spinal stenosis and occult atlantoaxial instability are at an increased risk of cervical spinal cord ischemia from compression in the anterior flexed neck position and cord hypoperfusion for the reasons discussed earlier. Quadriplegia is a rare but well-documented complication of the sitting position. The patient should be carefully examined for motion that elicits neurologic symptoms, and these findings discussed with the neurosurgeon. Similarly, patients with macroglossia and obstructive sleep apnea should be identified because they are at risk of further airway swelling and potential obstruction postextubation due to direct compression and potential decrease in venous drainage. Finally, the presence of pressure sores and preexisting peripheral neuropathies should be evaluated because these can potentially worsen even with careful padding in the sitting position.

- *Invasive monitoring*. This involves planning for the detection and management of potential VAE as well as routine invasive arterial pressure monitoring. Patients with neck pathology, scarring from prior central access or irradiation, and morbid obesity can increase the difficulties of central venous or right atrial catheter placement and render emergency placement impossible. This may influence the decision to place a central line preoperatively under radiologic guidance. Collateral flow for arterial catheterization should also be assessed, and the patient interviewed for contraindications for TEE if it is a part of the management plan.

Gale T, Leslie K. Anaesthesia for neurosurgery in the sitting position. *J Clin Neurosci*. 2004;11:693–696.

Gracia I, Fabregas N. Craniotomy in sitting position: anesthesiology management. *Curr Opin Anaesthesiol*. 2014;27(5):474–483.

Kwapisz MM, Deinsberger W, Müller M, et al. Transesophageal echocardiography as a guide for patient positioning before neurosurgical procedures in semi-sitting position. *J Neurosurg Anesthesiol*. 2004;16:277–281.

Stendel R, Gramm HJ, Schröder K, et al. Transcranial Doppler ultrasonography as a screening technique for detection of a patent foramen ovale before surgery in the sitting position. *Anesthesiology*. 2000;93:971–975.

B.7. How should the patient position ultimately be determined?

This requires careful patient evaluation and clear communication between the surgeon and anesthesiologist. Surgical exposure should be a primary determinant for patient positioning; however, the vigilant anesthesiologist should be aware of specific patient conditions that may preclude certain positions, anticipate any physiologic insult that may result, and ensure adequate access and planning to treat these occurrences. If there are significant safety concerns, the anesthesiologist is obliged to discuss these with the neurosurgeon and advocate for

alternative positioning if appropriate. One such safety concern is the presence of patent foramen ovale or right-to-left intracardiac shunt. Other conditions may be amenable to a trial of positioning prior to anesthetic induction or surgery. For example, a patient with cervical spinal canal stenosis should be evaluated for neck and shoulder positions that precipitate neurologic symptoms. A patient with compromised pulmonary compliance or reserve can be positioned prone and monitored during other preparations, with alternative positioning sought if the trial fails.

It bears repeating that the risk of VAE is such that we are very reluctant to use the sitting position except where there are overwhelming surgical exposure considerations.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1868–1910.

B.8. Should this patient receive premedication?

Although preoperative anxiety is common among neurosurgical patients, pharmacologic premedication in patients with intracranial mass lesions presents risks that can result in neurologic decompensation, outweighing any benefit in reducing the sympathetic stress response and increasing patient satisfaction. It is prudent, therefore, to avoid sedative premedication outside of the operating room in these patients. Emphasis should instead be placed on nonpharmacologic methods to address anxiety, including a professional, empathetic preoperative visit from the neuroanesthesiologist. Psychoactive medications can unmask subclinical neurologic symptoms and can have lingering effects at the end of surgery, which at best confuses the postoperative neurologic examination, and at worse can contribute to a failure to emerge from anesthesia. Opioids can cause sedation, partial upper-airway obstruction, and hypoventilation, all of which lead to hypercarbia and increases

in intracranial blood volume. In patients with limited intracranial compliance reserve, this small degree of hypoventilation can lead to dangerous increases in ICP. For these reasons, it is imperative that sedating premedication only be administered in a fully monitored setting and under the direct supervision of an anesthesiologist who is able to rapidly intervene and take over ventilation. Once the patient is transferred to the operating room and monitored, we would then administer small doses of short-acting agents to facilitate placement of invasive monitors prior to induction as needed.

Oral dosing of gabapentin and clonidine will attenuate the hemodynamic instability resulting from laryngoscopy and head pinning when given before anesthetic induction and potentially decrease postoperative pain and nausea. The effects of clonidine can likely be mimicked by starting an infusion of dexmedetomidine—also an α_2-adrenergic agonist—as soon as the patient arrives in the operating room.

Misra S, Koshy T, Suneel PR. Oral clonidine attenuates the fall in mean arterial pressure due to scalp infiltration with epinephrine-lidocaine solution in patients undergoing craniotomy: a prospective, randomized, double-blind, and placebo-controlled trial. *J Neurosurg Anesthesiol*. 2009;21:297–301.

Misra S, Koshy T, Unnikrishnan KP, et al. Gabapentin premedication decreases the hemodynamic response to skull pin insertion in patients undergoing craniotomy. *J Neurosurg Anesthesiol*. 2011;23(2):110–117.

Misra S, Parthasarathi G, Vilanilam GC. The effect of gabapentin premedication on postoperative nausea, vomiting, and pain in patients on preoperative dexamethasone undergoing craniotomy for intracranial tumors. *J Neurosurg Anesthesiol*. 2013;25(4):386–391.

C. Intraoperative Management

C.1. What are the anesthetic goals for craniotomy?

It goes without saying that the anesthetic goals for craniotomy include the basic principles of physiologic stability that are

common to all anesthetic management. Additionally, craniotomy incurs several specific goals that follow from the effects—both helpful and unhelpful—of anesthetic drugs on the brain. In short, the anesthetic goals specific to craniotomy are to protect the brain from injury resulting from mechanical or physiologic insult during the perioperative period. *Direct* protection (often referred to simply as *neuroprotection*) can be conceptualized as actions that facilitate the ability of neural tissue to withstand ischemic episodes without inflammation or activation of the apoptotic cascade leading to infarction. Less discrete is the concept of *indirect* protection, which aims to minimize the anteceding ischemic episodes. The principal elements are as follows:

- Management of CBF and CPP
- Management of ICP while the skull is intact
- The provision of a "relaxed" brain. This optimizes surgical exposure, which is critically important in many cases because the field of view available to the surgeon in many craniotomy approaches can be extremely narrow. Furthermore, relaxation reduces the parenchymal pressure exerted by the retraction devices on underlying brain tissue.
- Implementation and timing of pharmacologic measures specifically intended to effect direct neuroprotection, traditionally involving anesthetic-induced burst-suppression pattern on the EEG (although experimental data suggest that anesthetics can be protective without burst suppression)
- Strict management of physiologic parameters that may contribute to brain injury, such as serum glucose, osmolarity, and acid–base balance
- Minimize the effect of anesthetic pharmacology, cerebral perfusion, and temperature on neurophysiologic monitoring, such as EEG, BAERs, or SSEPs.
- Facilitate early neurologic assessment.

Bhagat H, Dash HH, Bithal PK, et al. Planning for early emergence in neurosurgical patients: a randomized prospective trial of low-dose anesthetics. *Anesth Analg*. 2008;107:1348–1355.

Chui J, Mariappan R, Mehta J, et al. Comparison of propofol and volatile agents for maintenance of anesthesia during elective craniotomy procedures: systematic review and meta-analysis. *Can J Anesth*. 2014;61(4):347–356.

Citerio G, Franzosi MG, Latini R, et al. Anaesthesiological strategies in elective craniotomy: randomized, equivalence, open trial—the NeuroMorfeo trial. *Trials*. 2009;10:19.

Mantz J, Degos V, Laigle C. Recent advances in pharmacologic neuroprotection. *Eur J Anaesthesiol*. 2010;27:6–10.

Miura Y, Kamiya K, Kanazawa K, et al. Superior recovery profiles of propofol-based regimen as compared to isoflurane-based regimen in patients undergoing craniotomy for primary brain tumor excision: a retrospective study. *J Anesth*. 2012;26:721–727.

Pasternak JJ, Lanier WL. Neuroanesthesiology update. *J Neurosurg Anesthesiol*. 2010;22:86–109.

Schifilliti D, Grasso G, Conti A, et al. Anaesthetic-related neuroprotection: intravenous or inhalational agents? *CNS Drugs*. 2010;24(11):893–907.

C.2. What monitors should be used during craniotomy?

In addition to electrocardiography (ECG), noninvasive blood pressure, pulse oximetry, temperature, and capnography monitoring, an arterial line is considered mandatory for all except the most superficial and nonvascular supratentorial tumors, even in those without significant comorbidity. The real-time dynamic assessment of arterial pressure is of paramount importance in patients with intracranial pathology and impaired autoregulation, as CPP and CBF become entirely dependent on MAP. There are multiple occasions of high hemodynamic stress that require rapid measurement and management of blood pressure such as induction, intubation, head pinning, epinephrine infiltration of scalp, and emergence (intraoperative emergencies notwithstanding). It also allows for repeated arterial blood monitoring of CO_2, glucose, acid–base physiology, hematocrit, and electrolytes, all of which critically affect patient

management. A key concept in neuroanesthesia practice is to ensure the measured arterial blood pressure reflects cerebral inflow pressure. In the prone or sitting position, the head may be significantly higher than the level of the heart, so care must be taken to position the arterial pressure transducer at the level of the circle of Willis, which corresponds approximately to the level of the tragus.

The use of central venous and right heart catheters is less common in craniotomies, except in cases where the sitting position is planned, or where preexisting comorbidity or therapies require it. A central venous catheter allows the safe infusion of hypertonic saline and allows for air aspiration in the event of VAE, although its performance is variable. Beyond these reasons, there is little additional advantage in patient management. Because of this and the potential for complications in its placement, the placement of central lines is not routine in our practice.

Depth of anesthesia monitors, if surgical access allows, is commonly used in some institutions to allow for titration of anesthetic agent and for possible induction of burst suppression. It is rarely used in our practice, mostly because of our frequent use of intraoperative neuromonitoring, which provides similar useful data from the cortical tracing on SSEPs. The use of neurophysiology monitoring such as EEG, EMG, BAERs, or SSEPs is determined by the location of the tumor; although these methods are often performed by neurophysiologists, the anesthesiologist must understand the principles behind them and be aware of the effects of anesthetics, other drugs, and physiologic variables on their integrity.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1868–1910.

C.3. Would you monitor for venous air embolism (VAE)?

What are the monitoring options?

VAE can potentially occur whenever there is an open venous channel beyond the venous fluid column to the heart. The sitting position confers the highest risk of VAE, although it is also been described in prone and lateral position craniotomies where the head is typically slightly elevated above the heart. An additional consideration is that the posterior fossa contains several major dural venous sinuses and their confluences, which are noncollapsible, drain into the internal jugular vein. For these reasons, any posterior fossa craniotomy, regardless of position, should be considered for VAE monitoring.

- TEE is the most sensitive monitor for VAE and PAE, able to detect volumes of 0.02 mL per kg in both the right and left heart, but is invasive and requires expertise in interpretation. Furthermore, it requires constant vigilance and can divide attention from other essential monitoring.
- *Precordial Doppler ultrasound* is noninvasive, highly sensitive (able to detect air volumes of 0.05 mL per kg), and is a part of our routine monitoring for posterior fossa craniotomies. It provides audible feedback, thereby minimizing distraction from other monitoring. However, the requirement for precise placement of the Doppler probe over the right heart becomes challenging when the variety of surgical positioning is considered and is particularly difficult in the prone position. This limits its sensitivity when applied in real-world scenarios. We find that rapid intravenous injection of 5 to 10 mL of saline is useful to ensure adequate detection of turbulent flow, which causes a characteristic coarse change in the basal “swishing” sound of normal pulsatile blood flow.
- *Pulmonary artery catheters* are a less sensitive detector of VAE (0.25 mL per kg air), and invasiveness generally limits use in patents with no other indication for right heart

monitoring. Characteristically, a sudden increase in pulmonary artery pressures occurs with VAE, first from reflex pulmonary vasoconstriction and later from the air lock formed by the embolus at right ventricular outflow tract.

- *End-tidal nitrogen (N_2) monitoring* is not routinely available on anesthesia gas monitors but is noninvasive and highly specific for air embolism. It is superior to Et_{CO_2} despite the latter's ubiquity, being more sensitive, specific, and rapidly responsive to air in the pulmonary circulation, but can be difficult to interpret when using air–oxygen carrier gas mixtures. Both end-tidal N_2 and CO_2 can be affected by pulmonary hypoperfusion.
- *Esophageal stethoscope* is discussed here for its historical interest in producing a characteristic mill wheel murmur but is too low in sensitivity (1.7 mL per kg air) and of limited use in detecting late, large VAE.

In our experience, the combination of precordial Doppler, Et_{CO_2}, and arterial pressure monitoring is minimally invasive and extremely effective at detecting clinically significant VAE.

The use of a right atrial catheter as a means to aspirate air should be considered in any situation when the risk of VAE is high. Catheter tip position, type, and size have been extensively studied over the years, but consensus on the ideal approach remains disputed. Large-bore (14 gauge), single-lumen, multiorifice catheters have performed best in animal and human studies. Traditionally, the ideal catheter tip position is 2 cm distal to the superior vena canal–right atrial junction. This can be established through TEE, radiographic or intravascular ECG guidance. In the last method, the patient is attached to standard three-lead ECG and the catheter inserted in the usual manner. The lumen is then flushed with sodium bicarbonate ($NaHCO_3$) to reduce electrical impedance along the catheter, and the right-

arm ECG lead is attached to a conductive connector placed on the line. The catheter should then be advanced into the right ventricle, which can be detected by transducing the pressure waveform. It should then be drawn back until the P wave on the catheter lead is biphasic (midatrium) and then back further to the point at which the P wave and QRS complex are of equal amplitude. The catheter is then pulled back another centimeter and secured. The right atrial catheter can confirm the presence of VAE through the aspiration of air, but its principal utility is therapeutic: It enables significant volumes of air to be rapidly extracted from the right atrium, thus breaking the "air lock" that causes the loss of cardiac output. Nonetheless, even under controlled conditions using ideal equipment, the success rate of air aspiration is 30% to 60% at best, and the catheter is liable to migrate as patient position is changed.

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C.4. What specific risks are associated with induction of anesthesia?

The key considerations for anesthetic induction in the patient with marginal intracranial reserve include the onset of apnea and the hemodynamic effects of anesthetic agents and intubation. With prolonged apnea and hypercarbia, CBV and CBF increase, worsening ICP. Hypoxemia also has similar effects on ICP, although unless it is in the extremes, hypoxemia causes more

deleterious effects by impacting oxygen delivery to the brain.

Hypotension from induction agents compromises CPP, whereas hypertension with laryngoscopy and coughing from inadequate neuromuscular blockade abruptly increases CBF and CBV further. The end point of all these events is a tendency to increase ICP and reduce CPP, leading to decreased cerebral oxygen delivery, ischemia, and potentially herniation in a patient with minimal intracranial compliance.

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C.5. How would you induce anesthesia?

In the absence of potential airway difficulty, the most common choice of anesthetic agents will involve an opioid, induction agent, and neuromuscular blocker. Benzodiazepines are not recommended due to their prolonged elimination and disinhibiting effects, especially in the elderly, and can delay awakening and cloud the postoperative neurologic examination. If preinduction anxiolysis is required, dexmedetomidine can be given as a preinduction infusion in the operating room during monitor placement and invasive access. It has advantages over benzodiazepines including preservation of respiratory effort, minimal disinhibition, and reduced interference with EP monitoring. The infusion can be continued through the case, with the additional benefits of MAC reduction and improved intraoperative hemodynamic stability.

A common induction technique is to coadminister large doses of opioid. This reduces the ED50 of intravenous anesthetic

dosing (thereby limiting postinduction hypotension), blunts the responses to intubation, and diminishes the hypertensive spike seen with head pinning. Fentanyl (slowly titrated to a total dose of 5 to 10 μg per kg), remifentanil bolus and infusion (1 μg per kg bolus, followed by infusion at 0.1μg/kg/min or a target effect site concentration of 3 ng per mL), and alfentanil (30 μg per kg bolus) are all effective regimens. Fentanyl has the advantage of achieving these characteristics without the inconvenience and technical risks of a continuous infusion but at the expense of titratability. All contribute to a relatively hemodynamically stable induction (especially with an appropriately decreased dose of the intravenous anesthetic agent) and steady maintenance levels, thereby extending MAC- and ED50-sparing effects through the procedure. If volatile agents are used, this allows us to run at less than 1 MAC (and typically at 0.5 to 0.6 MAC) with greater confidence in adequate anesthesia while limiting deleterious effects on ICP. Despite these advantages, high-dose opioids can cause significant sympatholysis, particularly in patients with a dominant sympathetic tone (such as the elderly), necessitating small doses of phenylephrine (40 to 120 μg) or ephedrine (5 to 10 mg) to support the cardiac output. All opioids given in high dose, particularly the more potent drugs such as remifentanil and alfentanil, can precipitate chest wall rigidity, which can compromise ventilation and increase ICP. Finally, it should be reiterated that this technique is only safe if there is certainty that immediate control of ventilation can be achieved.

Propofol is the induction agent of choice, given its favorable effects on CBF, $CMRO_2$, and ICP. However, its vasodilating and negative inotropic effects can cause significant hypotension even in the dose-sparing presence of opioids. With the loss of thiopental from our regular armamentarium, etomidate should be considered in patients where the cardiodepressant effects of

propofol are considered dangerous. Ketamine is inappropriate at induction doses in patients with marginal intracranial compliance due to increases in CBF, $CMRO_2$, and ICP, despite promising data of its protective effects in neurotrauma literature. An alternative is to add lidocaine 1.5 mg per kg to a high-dose opioid induction, which can further reduce the ED50 of the induction agent further.

Although succinylcholine is not contraindicated in patients with increased ICP, the risks and benefit should be assessed prior to its use. It is preferred in situations where a rapid sequence induction is required and IOM is proposed. However, because fasciculations can transiently increase ICP, it is recommended to administer a small precurarizing dose of nondepolarizing agent or lidocaine 1.5 mg per kg prior to the administration of succinylcholine. In recent years, with the increased availability of sugammadex, it would also be acceptable to consider using a rapid sequence induction dose of rocuronium with immediate reversal upon securing the airway. Sugammadex 16 mg per kg can be used for the reversal of neuromuscular block 3 minutes after administration of rocuronium allowing for adequate IOM. In most other situations, the use of nondepolarizing neuromuscular blockers is generally preferred.

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C.6. What are the effects of anesthetics on cerebral metabolic rate of oxygen ($CMRO_2$), CBF, and ICP? With this in mind, how would you maintain anesthesia?

Volatile Anesthetics

Volatile anesthetics have the characteristic of being direct cerebral vasodilators while reducing $CMRO_2$ in a dose-related fashion. This has been described as an "uncoupling" the flow-metabolism relationship; however, autoregulation remains largely intact at doses of up to 1 MAC. It is more accurate to say that it is a balance between the reductions in $CMRO_2$ with the concomitant decrease in CBF, and the direct vasodilator effect, which causes an increase in CBF. At 1 MAC or greater, autoregulation is lost and the vasodilating effect becomes dominant. In most patients, this increased CBF would be potentially beneficial to the extent that it improves the supply–demand balance (termed *luxury perfusion*), with minor, compensated effects on ICP. In patients with intracranial pathology, however, this increase in CBF causes an increase in CBV and can potentially elevate ICP while the cranial bone is intact, or impede surgical exposure once the bone plate is removed. At doses below 1 MAC in the normal brain, this increase in CBV and ICP can be fully reversed by hypocapnia, as cerebrovascular CO_2 reactivity is preserved. However, as previously discussed, this is impaired or absent in pathologic states.

At equivalent doses, isoflurane causes the greatest decrease in

$CMRO_2$, which mitigates some of its direct cerebral vasodilator effect leading to a proportionately modest increase in CBF and ICP. Desflurane has effects similar to isoflurane but appears to cause greater increases in ICP on normocapnic patients and in those with intracranial mass lesions. Sevoflurane causes minimal or slight changes in CBF and ICP despite dose-related decreases in $CMRO_2$ and appears to have the most favorable characteristics in patients with raised ICP.

Additionally, all volatile anesthetics appear to exert neuroprotective effects. And although isoflurane has best been described in animal and human studies, sevoflurane appears to have a similar effect at clinical doses (**Table 17.6**).

TABLE 17.6 The Effects of Anesthetic Agents on Cerebral Blood Flow, Metabolism, and Intracranial Pressure

	CBF	$CMRO_2$	ICP
Nitrous oxide	↑↑	↑ or =	↑↑
Halothane (1 MAC)	↑↑↑	↓↓	↑↑
Isoflurane (1 MAC)	↑ or =	↓↓↓	↑ or =
Sevoflurane (1 MAC)	↓ or =	↓↓	↑ or =
Desflurane (1 MAC)	↑	↓↓	↑
Propofol	↓↓↓	↓↓	↓↓
Thiopental	↓↓↓	↓↓↓	↓↓
Ketamine	↑↑	=	↑ or =
Etomidate	↓↓	↓↓	↓
Fentanyl	= or ↓	= or ↓	=
Lidocaine	↓↓	↓↓	
Dexmedetomidine	= or ↓	= or ↓	=

CBF, cerebral blood flow; $CMRO_2$, cerebral metabolic rate of oxygen; ICP, intracranial pressure; MAC, minimum alveolar concentration.

Nitrous Oxide

Despite conflicting studies, N_2O is generally agreed to increase CBF, $CMRO_2$, and ICP. The difficulty with interpreting data on the cerebrovascular effects of N_2O is the heterogeneity of

existing literature, with large variations in the anesthetic regimens. When given as a sole agent or with minimal adjuvant anesthesia, N_2O markedly increases global CBF, $CMRO_2$, and ICP. This effect is preserved when N_2O is given together with volatile anesthetics, but attenuated with intravenous anesthetics are administered. As an *N*-methyl-D-aspartic acid (NMDA) antagonist, both neuroprotective and neurotoxic effects have been attributed to N_2O through its modulation of glutamate excitotoxicity. N_2O has also been shown to induce neuronal apoptosis via its effects on homocysteine and the formation of reactive oxygen species. At best, N_2O offers no neuroprotection, and at worst, its effects might be neurotoxic and counterproductive to surgical exposure. When considered together with its other detrimental effects, including the increased risk of vascular thrombosis, postoperative nausea and vomiting, and the potential expansion of air in the cranium and vasculature, the use of N_2O should be limited in craniotomies.

Intravenous Anesthetics

The intravenous anesthetics that act through GABAergic mechanisms (e.g., barbiturates, propofol, etomidate) cause a dose-dependent reduction in $CMRO_2$, CBF, CBV, and ICP. In contrast to volatile anesthetics, CBF–$CMRO_2$ coupling is preserved in the basal state, with no added vasodilatory effect. Thus, the direct effect of a drug such as propofol is to cause a reduction in $CMRO_2$, and the decreases in CBF, CBV, and ICP follow from intact normal physiologic responses. CO_2 reactivity is preserved. $CMRO_2$ can be reduced to as low as 40% of resting values in the presence of an isoelectric EEG. The preservation of CBF–$CMRO_2$ coupling affords many benefits but also carries an underappreciated risk: If hyperventilation is instituted, it will have an additive effect on the decreases in CBF caused by an

intravenous anesthetic. The result is an appreciable risk of inadequate CBF and hypoperfusion ischemia. It must be remembered that the mantra of "craniotomy → hyperventilation" owes its legacy to a time when most neuroanesthetics involved the use of MAC equivalents of vasodilating volatile agents. Etomidate impairs collateral perfusion of ischemic brain in animal experiments through inhibition of nitric oxide synthase and is thus relatively contraindicated in cerebral ischemia.

The NMDA-antagonist ketamine can increase $CMRO_2$, CBF, and ICP, although in small doses concerns about these effects are probably overstated. Indeed, although ketamine may change the oxygen supply–demand relationship in an adverse way, recent studies suggest that ketamine possesses direct neuroprotective effects, especially when combined with GABAergic agents. There is no definitive evaluation of its clinical use; nevertheless, judicious use of ketamine can probably be justified where there are appropriate indications.

Opioids

Broadly speaking, synthetic opioids such as fentanyl, alfentanil, and remifentanil have minimal effects or slightly decrease $CMRO_2$, CBF, and ICP. In human and animal studies, opioids appear to complement the cerebrovascular effects of the background anesthetic, displaying vasoconstrictor effects in the presence of vasodilating agents and minimal effects when used with vasoconstricting anesthetics. In the spontaneously breathing patient, however, it must be remembered that opioids cause hypoventilation and hypercarbia, leading to increases in CBF, CBV, and ICP.

Many neuroanesthesiologists favor a maintenance strategy of total intravenous anesthesia (TIVA) in an oxygen and air mixture, which is difficult to fault provided that hyperventilation

is not excessive. A TIVA approach maximizes the ability to reduce $CMRO_2$ without impairing surgical exposure through increased CBF or causing cerebral steal, but it incurs the disadvantage of complex pharmacokinetics. Other neuroanesthesiologists (including the authors) favor a mixed volatile-intravenous regimen as a primary strategy in most patients. We typically use 0.3 to 0.5 MAC equivalent of a volatile agent, with propofol titrated to the EEG as an end point. Dexmedetomidine and (usually high-dose) opioids are added to blunt hemodynamic responses and confer hemodynamic stability. This strategy causes a reduction in $CMRO_2$ but with minimal impairment of surgical exposure. Unless precluded by monitoring, a nondepolarizing muscle relaxant is added to ensure that the patient does not move while the head is fixed. We revert to TIVA if there is inadequate brain relaxation or if monitoring dictates.

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C.7. How would you manage ventilation and maintain arterial carbon dioxide (CO_2)?

A reduction of $Paco_2$ decreases CBF and CBV within minutes. Therefore, hyperventilation is a rapidly effective measure that can be instituted to decrease ICP and undoubtedly can improve surgical exposure. Nevertheless, hyperventilation has substantial limitations. At $Paco_2$ values less than 25 mmHg, cerebral ischemia can result from a critical reduction in CBF combined with impaired oxygen unloading caused by a large left shift of the oxyhemoglobin dissociation curve due to respiratory alkalosis. Prolonged hyperventilation results in a compensatory loss of serum bicarbonate and can result in rebound acidosis if hyperventilation is rapidly terminated. Furthermore, hyperventilation-induced alkalosis decreases in ionized Ca^{2+}, leading to hemodynamic difficulties and prolonged emergence from effects on synaptic function.

It is important to remember that the difference between $Paco_2$ and $Etco_2$ can vary greatly. Therefore, arterial blood gas analysis should be performed as soon as possible after induction to establish the arterial–end-tidal gradient in CO_2 partial pressure. A $Paco_2$ of approximately 35 mmHg is reasonable unless ICP is elevated. If, once the bone plate is removed, the surgeons determine that exposure is suboptimal,

hyperventilation to a $Paco_2$ of 30 mmHg for a limited period is helpful for temporizing while other methods to improve brain relaxation are implemented. Further hyperventilation is reserved for situations in which establishing adequate exposure is extremely difficult. To avoid postoperative acid–base instability, hyperventilation can be gradually reduced throughout the closure, permitting reestablishment of bicarbonate and Ca^{2+} equilibrium.

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C.8. How would you approach diuretic therapy?

The purpose of diuretic therapy in intracranial procedures is to dehydrate the brain, thereby leading to a reduction in the volume of the fluid compartment. This facilitates surgical exposure and reduces the requirement for brain retraction. Through the same principle, mannitol is used as therapy for elevated ICP states when the cranium is closed.

Mannitol is an osmotic diuretic that is usually prepared in a 20% solution (20 g per 100 mL). It should initially be given in a dose of 0.5 to 1 g per kg; the total dose can be increased to 1.5 g per kg if initial efforts are ineffective. Higher doses have been reported to lead to cardiac arrest from disruption of cardiac cellular function. Because mannitol initially draws water into the vascular space before it is excreted, rapid dosing can cause a transient increase in ICP, so it should be infused over 20 to 30

minutes. If there is very little intracranial compliance reserve, aggressive dosing should be synchronized with the removal of the bone plate.

If mannitol does not provide adequate surgical conditions, the loop diuretic furosemide can be used. In a naive adult patient, a dose as low as 5 mg might be adequate. Furosemide does not have the problem of an initial increase in vascular volume and so is preferred in patients with marginal cardiac function who can develop congestive heart failure with a large mannitol load. The combination of mannitol and furosemide can cause electrolyte abnormalities and severe systemic dehydration, placing the patient at risk for hemodynamic instability and cardiac arrhythmias. The use of point of care testing for electrolyte derangements is extremely useful in correcting acute changes in serum sodium and potassium. Because mannitol therapy alone is often adequate, we do not administer furosemide routinely, instead reserving its use for situations when surgical exposure is suboptimal. There is evidence in the neurocritical care setting that substituting loop diuretics with an aldosterone antagonist (which is potassium-sparing) may reduce the severity of potassium flux and arrhythmias; however, this is infrequently used in the perioperative arena.

In cases of extreme cerebral edema, hypertonic saline in concentrations of up to 20% can be used—although the most common concentrations used are 2% or 3%. This can be effective in refractory intracranial hypertension and might even be superior to mannitol for routine diuresis, particularly in patients with preexisting hypovolemia. Its use requires caution because of the risk of severe hypernatremia, and central access is required. Patients who are already receiving hypertonic saline should usually have the infusion maintained during the operative period.

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C.9. How would you manage serum glucose?

Serum glucose control and its impact on critical care outcomes have been exhaustively studied in the last decade. There is, however, a paucity of literature specific to neurosurgical patients, and fewer yet focus on the influence of intraoperative glucose control on morbidity and mortality. To date, no study has definitively recommended one strategy over another for neurosurgical patients—much of the neuroanesthesiologist's practice is guided by the medical and general surgical critical care experience.

The relationship between glucose control and morbidity can be described as a U-shaped curve, with worsened outcomes seen with both hypo- and hyperglycemia. Hyperglycemia in neuroanesthesia is common, due to the surgical stress response and perioperative administration of steroids. It is associated with increased rates of infection and sepsis, renal insufficiency, and longer duration of intensive care admission. Conversely,

hypoglycemia is particularly detrimental to the brain, which is reliant on glucose as a major metabolic substrate.

The two dominant treatment strategies are intensive insulin therapy (IIT) to maintain serum glucose between 80 and 100 mg per dL, and standard therapy (ST) to maintain serum glucose below 180 mg per dL. Neurologic subgroup analyses of the landmark study by Van Den Berghe et al. suggested that IIT was associated with a reduction in ICP, seizures, critical illness polyneuropathy, and diabetes insipidus. More recent data from the Normoglycemia in Intensive Care Evaluation-Surviving Using Glucose Algorithm Regulation (NICE-SUGAR) study investigators, however, did not demonstrate benefit in IIT over ST and actually suggested IIT might be harmful due to higher rates of severe hypoglycemia. This is supported by microdialysis studies in traumatic brain injury patients showing that IIT can cause precipitous neuroglycopenia and increase neuronal injury. For these reasons, it would be prudent to aim for serum glucose levels between 110 and 180 mg per dL in the intraoperative setting while taking meticulous care to avoid hypoglycemia.

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C.10. How would you approach fluid management?

If the BBB is intact, the principal determinant of brain tissue water is the osmotic gradient across the BBB. It is this importance of osmotic gradient that guides the use of hypertonic solutions such as mannitol or hypertonic saline to reduce interstitial water and reduce ICP or to optimize surgical exposure. By the same principle, hypotonic solutions are rarely used because they favor the transport of water into the brain interstitium, thereby promoting the development of edema.

In regions where the BBB is not intact because of pathology and surgical tissue injury, osmotic particles can cross from the capillaries into the interstitial tissue. Therefore, the benefits of hypertonic solutions are lost in these areas. It follows that the benefit obtained from the use of hypertonic solutions is because of an *overall* effect on the brain, not from a *specific* effect in localized regions of brain injury.

These considerations favor the use of isotonic fluids as maintenance fluid in craniotomies. Conventionally, normal saline has been the preferred crystalloid solution; however, concerns over the risk of developing a non–anion gap, hyperchloremic metabolic acidosis has led to the use of other isotonic crystalloids such as Plasma-Lyte (**Table 17.7**). More controversial is the approach to volume management. Historically, craniotomy patients have been kept deliberately hypovolemic in the belief that this will increase the passage of free water from the brain in situations involving a disrupted BBB. Relatively recent evidence suggests that there is in fact

very little reduction in interstitial water and that it comes at the price of significant systemic hypoperfusion and hypotension. Therefore, the favored approach to fluid management is now maintenance of isovolemia with isotonic fluids. Dextrose-containing solutions should never be used except to treat hypoglycemia. Colloids such as 5% albumin can be used when volume expansion is a requirement. Albumin has a plasma half-life of 16 hours, and little is known about how the passage of albumin across a damaged BBB influences interstitial water movement over this time period. Therefore, its routine use is not recommended.

TABLE 17.7 The Osmolarity and Composition of Commonly Used Crystalloid Solutions

	Osmolarity (mOsm/L)	Sodium Concentration (mmol/L)	Chloride Concentration (mmol/L)
Plasma	280–300	140	100
0.9% Saline	308	154	154
Lactated Ringer's	273	130	109
Plasma-Lyte	294	140	98
5% Albumin	290	145	0

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1868–1910.

Tommasino C. Fluids and the neurosurgical patient. *Anesthesiol Clin North America*. 2002;20:329–346.

C.11. Once the bone plate is removed and the dura retracted, the surgeon reports that the brain is still "tight." What would be your response?

In almost all cases, the most effective initial response is to transiently increase hyperventilation to a $Paco_2$ of approximately 27 to 30 mmHg. If mannitol 1 g per kg has already been administered, small doses of intravenous

furosemide can be given until a diuresis is established. If a volatile agent is being used, this should be discontinued and the maintenance strategy converted to TIVA. If the patient has a CSF drain, this can be opened and CSF removed in no greater than 10- to 20-mL aliquots, with reassessment in between. Hypertension should be addressed and treated, and the patient should be well anesthetized to attenuate CBF responses to surgical stimulation. Positioning should be reassessed to eliminate any obstruction to jugular venous outflow. Deliberate hypotension can reduce swelling but incurs the risk of inadequate CPP and hypoperfusion ischemia and is thus instituted sparingly.

C.12. If deliberate hypotension is indicated, how will you achieve it?

Although sodium nitroprusside and volatile anesthetics are historically the most commonly used drugs to achieve sustained decreases in blood pressure, both are very far from ideal. Nitroprusside is highly effective and titratable over extremely short periods, but because it causes cerebral vasodilation, it can actually increase vascular engorgement. Nitroglycerin is also a potent cerebral venous vasodilator, and so it has the same limitation. Similarly, high levels of volatile anesthetic have direct cerebral vasodilatory effects. Furthermore, the uncoupled cerebral vasodilation caused by nitrates and volatile anesthetics can theoretically produce cerebral steal.

In most cases, the required level of blood pressure reduction can be achieved with the use of high-dose remifentanil (or other opioid) and propofol, possibly with the addition of a β-adrenergic blocker. Remifentanil enables a profound but rapidly reversible opioid level without unfavorable effects on CBF or vasodilation. Similarly, propofol can produce hypotension through systemic vasodilation but does not cause cerebral

vasodilation and is rapidly reversible. The mixed adrenergic receptor blocker labetalol is often effective as an adjunctive agent. However, the calcium channel blocker nicardipine is probably the most versatile drug for blood pressure control: It is titratable over relatively short periods and is an excellent choice if hypotension is required in situations in which opioids and anesthetic agents are not appropriate—such as during emergence or in the ICU—although it might impair autoregulation. Esmolol infusions can be utilized for a rapidly titratable β_1-adrenergic blockade but are not especially effective if the problem is refractory hypertension.

Degoute CS. Controlled hypotension: a guide to drug choice. *Drugs*. 2007;67:1053–1076.

Hoffman WE, Edelman G, Ripper R, et al. Sodium nitroprusside compared with isoflurane-induced hypotension: the effects on brain oxygenation and arteriovenous shunting. *Anesth Analg*. 2001;93:166–170.

Narotam PK, Puri V, Roberts JM, et al. Management of hypertensive emergencies in acute brain disease: evaluation of the treatment effects of intravenous nicardipine on cerebral oxygenation. *J Neurosurg*. 2008;109:1065–1074.

C.13. While the surgeon is resecting tumor from near the brainstem, the patient's heart rate suddenly drops to 20 beats per minute. What is your assessment and management?

Surgery near the brainstem nuclei can result in dramatic autonomic disturbances. Profound vagal reflexes can be alarming, sometimes resulting in asystole. These are often followed by a compensatory parasympatholytic-sympathetic reflex. Under such circumstances, the hemodynamics can shift from extreme bradycardia and hypotension to tachycardia and hypertension in a matter of seconds.

The first step is to alert the surgeon to stop operating, which almost always alleviates the problem. Once the hemodynamic

status has stabilized, an "autonomic blunting" prophylactic regimen can be given. Glycopyrrolate should be titrated until a 15% to 20% increase in heart rate is observed; if sympathetic reflexes are also involved, β-adrenergic blockade can be added. This approach is usually effective in attenuating the reflexes. In surgery in which an elevated risk of autonomic instability is present, the institution of parasympatholytic prophylaxis should be strongly considered from the outset.

The sudden development of bradycardia should always alert the anesthesiologist to the possibility of a sudden increase in ICP, leading to the Cushing reflex. In this case, hypertension would also be seen, and the surgeon should be immediately notified.

Koerbel A, Gharabaghi A, Samii A, et al. Trigeminocardiac reflex during skull base surgery: mechanism and management. *Acta Neurochir (Wien)*. 2005;147:727–733.

Schaller B, Probst R, Strebel S, et al. Trigeminocardiac reflex during surgery in the cerebellopontine angle. *J Neurosurg*. 1999;90:215–220.

C.14. Are there any measures you can take to prevent VAE?

Prevention is the cornerstone to the management of VAE because current treatment methods of established VAE are limited in their efficacy. The best prevention of VAE is the neurosurgeon's meticulous control of venous bleeding and the tolerance of lower head positions. Extra vigilance on the part of the neuroanesthesiologist also plays an important role—observing a lack of bleeding on the cut edge of bone during removal of the craniotomy bone flap is an early sign of negative venous pressure and an increased likelihood of VAE. Active measures to reduce VAE include raising the venous fluid column by ensuring adequate hydration, and minimizing venous capacitance through the use of pneumatic calf compression

devices and avoidance of venodilators such as nitroglycerin. The use of positive end-expiratory pressure (PEEP) is controversial: PEEP increases cerebral venous pressure and can reduce the risk of entrainment, but it also increases surgical bleeding and can potentially impede CPP. It promotes right-to-left intracardiac shunting, which increases the risk of PAE in susceptible patients, and sudden releases of PEEP (such a ventilator adjustment, or a recruitment maneuver performed during craniotomy) can increase air entrainment as well as the propagation of PAE. We recommend a limitation of PEEP to <5 cm H_2O and only as a means to optimize patient oxygenation. The use of N_2O has clear theoretical disadvantages in posterior fossa craniotomy, not only in the risk of expanding subclinical intravascular air but also in postoperative tension pneumocephalus. Although there is no clear clinical data to demonstrate these associations, its additional adverse effects on CBF and metabolism, ICP and neurotoxicity makes it difficult to justify its use, particularly with the easy availability of excellent alternatives in neuroanesthesia.

Giebler R, Kollenberg B, Pohlen G, et al. Effect of positive end-expiratory pressure on the incidence of venous air embolism and on the cardiovascular response to the sitting position during neurosurgery. *Br J Anaesth*. 1998;80:30–35.

Pasternak JJ, Lanier WL. Is nitrous oxide use appropriate in neurosurgical and neurologically at-risk patients? *Curr Opin Anaesthesiol*. 2010;23:544–550.

Schmitt HJ, Hemmerling TM. Venous air emboli occur during release of positive end-expiratory pressure and repositioning after sitting position surgery. *Anesth Analg*. 2002;94:400–403.

C.15. During the procedure, the precordial Doppler becomes loud and turbulent. The end-tidal CO_2 ($EtCO_2$) drops from 31 to 13 mmHg, and the systemic pressure from 121/63 to 64/32 mmHg. What is your

assessment and management plan?

This is a classic presentation of VAE. Immediately inform the surgeon, institute 100% oxygen, and call for skilled assistance. The surgeon should flood the field with saline and urgently prepare the field for lowering the head (e.g., placement of a protective drape over the operative site, adjusting the head fixation device to allow for position change). Where possible, an assistant should reach under the drapes and apply pressure to the jugular veins to prevent further entrainment (but not enough to occlude carotid flow), although this should be only a transient measure. If a right atrial catheter is in place, an attempt should be made to aspirate air with a large syringe (enough to accommodate 15 to 20 mL air). Intravenous fluids should be opened to full flow, and inotropes and vasopressors should be titrated to support the altered hemodynamics. The head should then be lowered to a level below the heart, or as much as possible. The left lateral decubitus position has been advocated but is probably of little benefit.

If the VAE is detected early, the episode will usually resolve. It is almost always appropriate to resume and complete the surgery, although placement of additional monitors before resumption might be warranted. Undetected, massive, or prolonged entrainment of air can lead to cardiac arrest. If cardiac arrest is present or imminent, and the patient is in a prone or semiprone position, the anesthesiologist must prepare the surgeon and others in the room for an emergent move to the supine position to enable resuscitation. For this reason, a stretcher must always be available outside the operating room when patients are in the prone position.

Kerr RH, Applegate RL II. Accurate placement of the right atrial air aspiration catheter: a descriptive study and prospective trial of intravascular electrocardiography. *Anesth Analg*. 2006;103:435–438.

Mirski MA, Lele AV, Fitzsimmons L, et al. Diagnosis and treatment of

vascular air embolism. *Anesthesiology*. 2007;106:164–177.

C.16. What is your approach to emergence? What if the patient does not regain consciousness?

Providing an early neurologic assessment is one of the most valuable contributions of the anesthesiologist to outcome in neurosurgical patients. Therefore, it is imperative to have patients emerge quickly, even when surgery has been prolonged. At the same time, the emergence from anesthesia incurs substantial changes in pressure, $Paco_2$, CBF, and autonomic activity and therefore must be carefully planned. Transitioning from hyperventilation should be gradual in order to prevent rebound acidosis. Adrenergic blocking agents should be administered to attenuate the sympathetic effects often seen during and following emergence in these patients. Nicardipine or labetalol can be considered if the patient exhibits refractory hypertension or hyperreactivity. Reversal of neuromuscular block should be carefully titrated to avoid autonomic instability, with care taken to ensure that the patient does not move while the head is fixed in pins. Antiemetic therapy should be aggressive because the elevation in ICP caused by retching and vomiting are particularly undesirable in craniotomy patients.

Coughing or "bucking" during emergence causes dramatic spikes in ICP and must be avoided. Several approaches can be used to avoid this, including the use of intravenous lidocaine, an opioid-based anesthetic, or a deep extubation. In the case of a deep extubation, it must be kept in mind that there is always a risk that an intraoperative neurologic event might cause delayed or failed emergence. A strategy of converting the final phase of the anesthetic to a high-dose remifentanil 0.3 to 0.4 μg/kg/min infusion can be highly effective and enables the volatile agent to be eliminated without the patient reacting. After return of ventilation and cognition, remifentanil infusion is stopped and

the patient's trachea is extubated.

A failure to emerge can represent a neurologic event resulting from the surgery (such as an intracranial bleed, vessel occlusion, embolic event, or seizure), metabolic derangements, or a pharmacologic effect. In such cases, the time to diagnosis is a critical determinant of outcome. The anesthesiologist must be able to state with confidence that the delayed emergence is unlikely to be pharmacologic. A rapid assessment can be made in the operating room to exclude nonneurologic causes of failure to emerge (**Table 17.8**); unless there is a clear cause found, a computed tomography (CT) scan should immediately be performed. Should this be necessary, the operating room should be left available in the event that an emergent return is required.

TABLE 17.8 Rapid Assessment of Persistent Coma Immediately Postcraniotomy

Intervention	Assess Cause of Coma
Pupillary exam	• New anisocoria suggesting herniation • Pinpoint pupils suggesting narcotic overdose • Dilated reactive pupils suggesting central anticholinergic syndrome
Arterial blood gas with electrolyte and glucose analysis	• Hypoxia • Hypercarbia • Acidosis • Hypoglycemia/hyperglycemia • Hyponatremia/hypernatremia
Processed electroencephalogram (e.g., BIS monitor, IOM)	• Assess depth of anesthesia • Seizure activity
Nerve stimulator	• Deep neuromuscular blockade
Core temperature	• Hypothermia
Review medication syringes, infusions, vaporizer	• Inadvertent overdose • Medication swap • Consider reversal agents: – Naloxone in 40 μg aliquots, up to 400 μg – Flumazenil 200 μg aliquots, up to 1 μg – Physostigmine 1.25 mg, if centrally acting anticholinergics administered
CT scan	• Hemorrhage

	• Thrombosis (consider basilar artery thrombosis) • Pneumocephalus • Cerebral edema
Other considerations	• Hypothyroidism • Addisonian crisis

BIS, bispectral index; CT, computed tomography; IOM, intraoperative neurophysiologic monitoring.

In some posterior fossa procedures—especially when near the brainstem—postoperative edema can lead to an anticipated worsening of neurologic status before subsequent improvement on the first or second postoperative day, thereby necessitating prolonged intubation. In these cases, the patient can be awakened at the conclusion of the surgery and once a neurologic assessment is obtained, resedated for transport to the ICU. A remifentanil infusion of approximately 0.1 μg/kg/min usually enables an intubated patient to perform a cognitive examination and tolerate the presence of the endotracheal tube.

Bilotta F, Lam AM, Doronzio A, et al. Esmolol blunts postoperative hemodynamic changes after propofol-remifentanil total intravenous fast-track neuroanesthesia for intracranial surgery. *J Clin Anesth*. 2008;20:426–430.

Lauta E, Abbinante C, Del Gaudio A, et al. Emergence times are similar with sevoflurane and total intravenous anesthesia: results of a multicenter RCT of patients scheduled for elective supratentorial craniotomy. *J Neurosurg Anesthesiol*. 2010;22:110–118.

D. Postoperative Management

D.1. What postoperative complications are of greatest concern? What level of monitoring is required?

Part of the neurologic assessment conducted immediately on emergence should be an evaluation of the lower cranial nerves. Damage to the nerves or to nuclei can result in difficulty swallowing and protecting the airway. The principal concern is the development of edema or hematoma causing compression of the brainstem or midbrain structures. The brainstem sits in an

anatomic location with very low compliance; even small degrees of edema that would be well tolerated following supratentorial procedures can lead to catastrophic neurologic compromise. It is critical to appreciate that edema and hematoma can develop over the course of several hours following the procedure; a patient who had a satisfactory emergence might deteriorate neurologically in the middle of the night. In certain circumstances, the risk of postoperative edema is so high that the patient is left intubated prophylactically, as discussed earlier. Deterioration cannot always be anticipated, and these patients should be initially monitored in an intensive care setting in all cases.

Dubey A, Sung WS, Shaya M, et al. Complications of posterior cranial fossa surgery: an institutional experience of 500 patients. *Surg Neurol*. 2009;72:369–375.

Sughrue ME, Rutkowski MJ, Shangari G, et al. Risk factors for the development of serious medical complications after resection of meningiomas. Clinical article. *J Neurosurg*. 2011;114(3):697–704.

Wong JM, Panchmatia JR, Ziewacz JE, et al. Patterns in neurosurgical adverse events: intracranial neoplasm surgery. *Neurosurg Focus*. 2012;33(5):E16.

D.2. What is your approach to postoperative pain control?

Optimal pain control after craniotomy has traditionally been hampered by several challenges. First is the misconception that craniotomy and tumor resection causes minimal pain, despite the rich nociceptive afferents to the meninges, dura, falx, and calvarial periosteum. Using traditional analgesic approaches, nearly 70% of postcraniotomy patients experience moderate to severe pain on the first postoperative day, and just under half continue to do so on the second postoperative day.

Another dogma that persists to this day is that most analgesics are dangerous for the postcraniotomy patient and should be dosed sparingly. Concern remains that opioids have the potential

to cause sedation and respiratory depression in the neurologically vulnerable patient. Despite this, patient-controlled analgesia (PCA) opioid regimens have been used safely in supra- and infratentorial postcraniotomy patients, improving both pain control and patient satisfaction.

In addition to opioid PCAs, we suggest a multimodal approach to minimize opioid use and their side effects. Acetaminophen is nonsedating and safe in recommended doses in the absence of liver disease. Neurosurgeons have traditionally avoided nonsteroidal anti-inflammatory drugs (NSAIDs) in the perioperative period due to risk of postoperative hematoma, although what little evidence exists is not robust. Nonetheless, it behooves the neuroanesthesiologist to discuss the use of NSAIDs with the surgeon before prescribing. Scalp blocks or scalp infiltration performed at the end of surgery have little morbidity and improve pain control in the early postoperative period. Although this effect is not sustained beyond the first postoperative day, there is evidence to suggest this technique reduces the development of chronic postcraniotomy pain. An alternative option would involve regional blockade of the lesser and greater occipital nerves by the anesthesiologist. Preferably, these would be done immediately prior to surgery as anatomy may be altered by the surgical procedure. These have proven to be an effective alternative to scalp block for craniotomy and have longer duration of analgesia. Preinduction gabapentin, in addition to its beneficial effects on minimizing the hemodynamic response to laryngoscopy and head pinning, also decreases postoperative pain and opioid requirements, although it may result in greater sedation and slow emergence. Tramadol has been used successfully for postcraniotomy pain; however, due to its increased risk of nausea and vomiting, and the lowering of the seizure threshold, we do not recommend it as part of a first-line analgesic regimen.

Dunn LK, Naik BI, Nemergut EC, et al. Post-craniotomy pain management: beyond opioids. *Curr Neurol Neurosci Rep*. 2016;16(10):93. doi:10.1007/s11910-016-0693-y.

Gottschalk A, Berkow LC, Stevens RD, et al. Prospective evaluation of pain and analgesic use following major elective intracranial surgery. *J Neurosurg*. 2007;106:210–216.

Hansen MS, Brennum J, Moltke FB, et al. Pain treatment after craniotomy: where is the (procedure-specific) evidence? A qualitative systematic review. *Eur J Anaesthesiol*. 2011;28:821–829.

Jayaram K, Srilata M, Kulkarni D, et al. Regional anesthesia to scalp for craniotomy: innovation with innervation. *J Neurosurg Anesthesiol*. 2016;28(1):32–37. doi:10.1097/ANA.0000000000000184.

Morad A, Winters B, Stevens R, et al. The efficacy of intravenous patient-controlled analgesia after intracranial surgery of the posterior fossa: a prospective, randomized controlled trial. *Anesth Analg*. 2012;114:416–423.

Rahimi SY, Alleyne CH, Vernier E, et al. Postoperative pain management with tramadol after craniotomy: evaluation and cost analysis. *J Neurosurg*. 2010;112(2):268–272.

Tsaousi GG, Logan SW, Bilotta F. Postoperative pain control following craniotomy: a systematic review of recent clinical literature. *Pain Pract*. 2017;17(7):968–981. doi:10.1111/papr.12548.

Türe H, Sayin M, Karlikaya G, et al. The analgesic effect of gabapentin as a prophylactic anticonvulsant drug on postcraniotomy pain: a prospective randomized study. *Anesth Analg*. 2009;109(5):1625–1631.

Umamaheswara Rao GSU, Gelb AW. To use or not to use: the dilemma of NSAIDs and craniotomy. *Eur J Anaesthesiol*. 2009;26(8):625–626.

Williams DL, Pemberton E, Leslie K. Effect of intravenous parecoxib on post-craniotomy pain. *Br J Anaesth*. 2011;107:398–403.

D.3. In the ICU, the patient's neurologic status deteriorates and ICP monitoring is instituted. What are the different methods of monitoring ICP, and what are their limitations?

ICP monitoring is commonly used in neurosurgical critical care as a marker of intracranial compliance and to allow a more objective calculation of CPP. Typically, an ICP monitor is placed at a discrete anatomic point of measurement, and data from this monitor is extrapolated to the whole brain. It is

important to remember, however, that significant differences in regional ICP can exist, particularly in patients where there is a pathologic disruption of normal CSF circulation. In the case of this patient, for instance, an ICP monitor positioned in the supratentorial region may not accurately represent the pressure in the posterior fossa.

There are many methods of ICP monitoring available, differing on the basis of invasiveness, site of measurement, and degree of validation. An external ventricular drain (EVD) is considered the gold standard and allows for both ICP measurement and CSF drainage to treat intracranial hypertension (although not simultaneously). The catheter tip is introduced into one of the lateral ventricles via a blind technique or with imaging guidance and connected to a fluid column with a pressure transducer and drainage system. It is the most invasive method of ICP monitoring and is associated with significant rates of intracranial infection and bleeding during placement. Other limitations of the EVD include difficult placement in patients with midline shift, catheter malfunction, and potential CSF overdrainage. An alternate method of measuring ICP is through the use of microtransducers. These devices transduce an external force (e.g., applied by edematous brain tissue) to an alteration in electrical or light signal. Fiberoptic devices transmit light to a flexible reflective tip that is displaced by an external force, and the change in light reflection is extrapolated into a change in ICP. Similarly, electronic strain gauge devices are deformed by external pressure thereby inducing a change in electrical resistance. These devices are miniaturized to the extent that their placement into brain parenchyma would cause little damage and are typically secured to the skull with a bone bolt. Depending on manufacturer, microtransducers may also be introduced into the subarachnoid, epidural, or subdural spaces, with some attrition in accuracy.

The primary advantages of microtransducers are the decreased rate of intracranial infection, the absence of catheter-related malfunction, and the stability of the fixation bolt. However, these devices are prone to zero drift over time (between 1 mmHg per 1 to 5 days) and cannot be re-zeroed without removing the device entirely. Further limitations include local sampling of parenchymal pressure and significantly higher cost compared to catheter systems.

More recently, the use of transcranial Doppler (TCD) has been proposed as an alternate, noninvasive method of ICP and CPP measurement. This method analyzes middle cerebral artery flow characteristics for degree of pulsatility. This pulsatility index (PI) has been used as a surrogate measurement of a variety of neurovascular parameters, including cerebrovascular resistance, vasospasm, and CPP. Although initial reports showed good correlation between TCD-PI and ICP, subsequent studies have revealed wide discrepancies in predicted ICP and measured ICP with a catheter-based system. Further investigations are needed before TCD can be considered an acceptable alternative to invasive methods of ICP measurement.

Raboel PH, Bartek J Jr, Andresen M, et al. Intracranial pressure monitoring: invasive versus non-invasive methods—a review. *Crit Care Res Pract*. 2012;2012:950393.

Steiner LA, Andrews PJD. Monitoring the injured brain: ICP and CBF. *Br J Anaesth*. 2006;97(1):26–38.

Zweifel C, Czosnyka M, Carrera E, et al. Reliability of the blood flow velocity pulsatility index for assessment of intracranial and cerebral perfusion pressures in head-injured patients. *Neurosurgery*. 2012;7:853–861.

18 Carotid Artery Disease

Priscilla Nelson and Hugh C. Hemmings Jr.

An 85-year-old woman is scheduled for a left carotid endarterectomy (CEA) for asymptomatic left carotid stenosis. She has 90% occlusion of her left carotid artery and 60% occlusion of the right carotid artery. Her past medical history is remarkable for hypertension, insulin-dependent diabetes mellitus, and coronary artery disease. She had coronary artery bypass surgery 4 years ago. Her blood pressure is 170/80 mmHg, and her pulse is 59 beats per minute and regular.

A. Medical Disease and Differential Diagnosis

1. What are the presenting symptoms of carotid stenosis?
2. What is the prevalence of carotid artery disease?
3. What is the natural course of carotid artery disease as it relates to stroke?
4. What in the patient's history puts them at higher risk for having carotid atherosclerosis?
5. Do we screen patients for asymptomatic carotid stenosis?
6. What is the risk of stroke and cardiovascular events in asymptomatic carotid atherosclerosis?
7. What are the current medical options that the patient has for treating carotid atherosclerosis?
8. What are the indications for CEA and carotid artery stenting

(CAS) in asymptomatic carotid atherosclerotic disease?

9. What are the indications for performing a CEA in symptomatic carotid stenosis?
10. Is there any role for CAS in symptomatic patients?
11. Discuss the anatomy of the cerebral vasculature, including the carotid artery and the circle of Willis.
12. Discuss cerebral blood flow (CBF) in the presence of carotid artery disease.
13. Discuss the different surgical approaches to carotid revascularization.
14. Discuss the endovascular approaches to carotid stenting.
15. What is normal CBF?
16. What is critically low CBF as measured by the electroencephalogram (EEG)?
17. What is cerebral autoregulation?
18. How does $Paco_2$ affect CBF?
19. What are the principal determinants of CBF?
20. What is meant by the term *luxury perfusion*?
21. What is meant by the term *intracerebral steal*?

B. Preoperative Evaluation and Preparation

1. What will you look for in your preoperative evaluation of this patient?
2. Is this patient's blood pressure too high for elective surgery?
3. What laboratory data are required preoperatively?
4. Will you treat this patients' blood glucose?
5. Will you premedicate this patient?

C. Intraoperative Management

1. How will you monitor this patient?
2. How will you know that the patient's cerebral perfusion is adequate during surgery?
3. Discuss the differences and relative advantages and disadvantages of unprocessed EEG and processed EEG

monitoring.

4. How will you measure CBF intraoperatively? What are the relative advantages and disadvantages of each technique?
5. Describe the use of stump pressure and its limitations.
6. Describe the use of transcranial Doppler (TCD) and its limitations.
7. Describe the use of jugular venous oxygen saturation ($SjvO_2$) and its limitations.
8. Describe the use of cerebral oximetry and its limitations.
9. Discuss somatosensory evoked potentials (SSEPs) as a monitor of CBF during CEA.
10. What type of anesthesia will you choose for this patient if she chose to have an endarterectomy?
11. What type of anesthesia will you choose for this patient if she chose to have a carotid stent?
12. How will you induce and maintain general anesthesia in this patient for CEA?
13. How would you proceed if the patient were to receive regional anesthesia?
14. Discuss the effects of anesthetics on CBF.
15. Discuss the protective effects of anesthetic agents on cerebral function.
16. How will you manage this patient's ventilation under general anesthesia?
17. How will you manage this patient's blood pressure intraoperatively?
18. Discuss reperfusion injury following CEA and CAS.
19. What intravenous fluids will you give this patient intraoperatively?

D. Postoperative Management

1. The patient does not "wake up" from general anesthesia. Why?
2. Postoperatively, the patient's blood pressure is 170/96 mmHg.

Will you treat this?

3. What immediate postoperative complications might you expect after a CEA?
4. What postoperative complications might you expect after a CAS?
5. Discuss postoperative neurocognitive dysfunction following uncomplicated carotid intervention.

A. Medical Disease and Differential Diagnosis

A.1. What are the presenting symptoms of carotid stenosis?

Carotid stenosis is often asymptomatic, only to be discovered on physical exam as a carotid bruit or incidentally on imaging.

- Symptomatic carotid stenosis presents with focal neurologic deficits in the corresponding carotid artery territory. These focal neurologic deficits can be characterized as a transient ischemic attack (TIA) or ischemic stroke. A TIA is a transient focal neurologic deficit attributable to a vascular cause **without** corresponding appropriate lesions on imaging.
- An ischemic stroke is characterized by an acute onset of focal neurologic symptoms that leaves permanent injury either seen clinically, or by appropriate corresponding lesions on imaging. Ischemic symptoms from carotid stenosis originate from the vascular distribution supplied by the internal or external carotid artery. The symptoms can be from artery-to-artery embolization of the plaque or from cerebral hypoperfusion caused by the stenotic lesion.
- Ischemic symptoms can be divided into three main categories: (1) Ocular ischemia or infarction, (2) ipsilateral hemispheric signs, and (3) atypical symptoms. Ocular ischemia or infarction symptoms include partial or complete blindness in one eye. Ipsilateral hemispheric signs include

contralateral homonymous hemianopsia, hemiparesis, or hemisensory loss. Specific ischemic signs associated most commonly with left-side lesions include aphasia, whereas right hemispheric symptoms can include visuospatial neglect. Atypical symptoms include unilateral limb shaking and transient monocular vision loss when exposed to bright light, which can also occur from ischemia downstream to the embolus.

Javaid A, Alfishawy M. Internal carotid artery stenosis presenting with limb shaking TIA. *Case Rep Neurol Med*. 2016;2016:3656859.

Kernan WN, Ovbiagele B, Black HR, et al. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2014;45:2160–2236.

Liberman AL, Zandieh A, Loomis C, et al. Symptomatic carotid occlusion is frequently associated with microembolization. *Stroke*. 2017;48:394–399.

Pickett CA, Jackson JL, Hemann BA, et al. Carotid bruits and cerebrovascular disease risk: a meta-analysis. *Stroke*. 2010;41:2295–2302.

A.2. What is the prevalence of carotid artery disease?

Carotid artery disease is a marker of generalized arteriosclerosis. The prevalence of asymptomatic carotid disease, which is defined as stenosis greater than 50%, ranges from 4% to 8%. In a meta-analysis of 40 studies, the prevalence of moderate stenosis increased with age in both men and women. Men at all ages have the highest prevalence estimates. Approximately 10% to 15% of strokes (approximately 200,000 strokes per year) in the United States are attributable to carotid stenosis.

Adams HP Jr, Bendixen BH, Kappelle LJ, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in acute stroke treatment. *Stroke*. 1993;24:35–41.

de Weerd M, Greving JP, de Jong AW, et al. Prevalence of asymptomatic carotid artery stenosis according to age and sex: systematic review and metaregression analysis. *Stroke*. 2009;40:1105–1113.

Pujia A, Rubba P, Spencer MP. Prevalence of extracranial carotid artery

disease detectable by echo-Doppler in an elderly population. *Stroke*. 1992;23:818–822.

Safian RD. Carotid artery revascularization: the known knowns and the known unknowns. *J Am Coll Cardiol*. 2017;69:2276–2278.

A.3. What is the natural course of carotid artery disease as it relates to stroke?

Carotid artery disease carries a typical natural course of plaque development, which is cumulative. Continued development leads to possible stenosis or the possibility of plaque rupture. Atherosclerosis in the extracranial carotid arteries is usually most severe within 2 cm of the bifurcation of the common carotid artery. Atherosclerotic lesions are predominantly found in the posterior wall of the internal carotid artery. Over time, the plaque extends proximally into the common carotid artery and the stenotic lesion takes on an hourglass shape. Extracranial carotid atherosclerotic disease can lead to stroke by embolism of cholesterol crystals or debris, artery-to-artery embolism, dissection or disintegration of arterial wall, and decreased cerebral perfusion because of the stenosis causes by plaque buildup. Although the risk of stroke has historically been correlated to the degree of carotid stenosis, new markers for plaque vulnerability as it relates to disease severity are emerging. They include plaque progression, ulcerations seen on plaques, echo-lucency, intraplaque hemorrhage, and high lipid content of the stenotic lesion. The risk factors for the development of carotid artery disease are similar to those causing atherosclerotic occlusive disease in other vascular beds, namely, increasing age, male gender, hypertension, tobacco smoking, diabetes mellitus, homocysteinemia, and hyperlipidemia.

Barash PG, Cullen BC, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1112–1143.

Fisher M, Paganini-Hill A, Martin A, et al. Carotid plaque pathology:

thrombosis, ulceration, and stroke pathogenesis. *Stroke*. 2005;36:253–257.

Furie KL. Pathophysiology of symptoms from carotid atherosclerosis. https://www.uptodate.com/contents/pathophysiology-of-symptoms-from-carotid-atherosclerosis. Accessed October 19, 2018.

Ooi YC, Gonzalez NR. Management of extracranial carotid artery disease. *Cardiol Clin*. 2015;33:1–35.

A.4. What in the patient's history puts them at higher risk for having carotid atherosclerosis?

Hypertension, hyperlipidemia, obesity, smoking, diabetes and physical inactivity puts one at high risk for carotid atherosclerosis.

Conrad MF, Boulom V, Mukhopadhyay S, et al. Progression of asymptomatic carotid stenosis despite optimal medical therapy. *J Vasc Surg*. 2013;58:128–135.e121.

Mathiesen EB, Joakimsen O, Bønaa KH. Prevalence of and risk factors associated with carotid artery stenosis: the Tromso Study. *Cerebrovasc Dis*. 2001;12:44–51.

A.5. Do we screen patients for asymptomatic carotid stenosis?

The prevalence of asymptomatic carotid atherosclerosis in the general population is approximately 3%. The U.S. Preventive Services Task Force (USPSTF), American College of Cardiology and American Heart Association (AHA) and American Stroke Association (ASA) recommends against routine screening.

Brott TG, Halperin JL, Abbara S, et al. 2011 ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SV guideline on the management of patients with extracranial carotid and vertebral artery disease: executive summary. *Circulation*. 2011;124:489–532.

de Weerd M, Greving JP, de Jong AW, et al. Prevalence of asymptomatic carotid artery stenosis according to age and sex: systematic review and metaregression analysis. *Stroke*. 2009;40:1105–1113.

de Weerd M, Greving JP, Hedblad B, et al. Prevalence of asymptomatic carotid artery stenosis in the general population: an individual participant data

meta-analysis. *Stroke*. 2010;41:1294–1297.

Meschia JF, Bushnell C, Boden-Albala B, et al. Guidelines for the primary prevention of stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2014;45:3754–3832.

Wolff T, Guirguis-Blake J, Miller T, et al. Screening for carotid artery stenosis: an update of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2007;147:860–870.

A.6. What is the risk of stroke and cardiovascular events in asymptomatic carotid atherosclerosis?

Although ischemic stroke is the most feared event with carotid atherosclerosis, the estimated risk is approximately 0.5% to 1% per year ipsilaterally in patients with >50% stenosis. Asymptomatic carotid stenosis is considered a risk equivalent for coronary artery disease and is a marker for increased risk of myocardial infarction (MI) and death.

Goessens BM, Visseren FL, Kappelle LJ, et al. Asymptomatic carotid artery stenosis and the risk of new vascular events in patients with manifest arterial disease: the SMART study. *Stroke*. 2007;38:1470–1475.

Spence JD. Management of asymptomatic carotid stenosis. *Neurol Clin*. 2015;33:443–457.

A.7. What are the current medical options that the patient has for treating carotid atherosclerosis?

Best medical therapy was outlined by the Asymptomatic Carotid Surgery Trial (ACST) and includes the use of a 3-hydroxy-3-methylglutaryl-coenzyme (HMG-CoA) reductase inhibitors, aggressive blood pressure control with antihypertensive drugs, strict glycemic control for patients with diabetes mellitus, smoking cessation, and the use of antiplatelet drugs.

Meschia JF, Bushnell C, Boden-Albala B, et al. Guidelines for the primary prevention of stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2014;45:3754–3832.

A.8. What are the indications for CEA and carotid artery stenting (CAS) in asymptomatic carotid atherosclerotic disease?

The recommendation for surgical treatment by many societies are based on three major trails that took place in patients with asymptomatic carotid stenosis: the Veterans Administration (VA) trial, the Asymptomatic Carotid Atherosclerosis Study (ACAS) trial, and the ACST trial.

The indications differ by society. The AHA and the ASA note the following with respect to CEA: If the risk of perioperative stroke, MI, and death are low (<3%), it may be reasonable to consider CEA in asymptomatic patients with >70% stenosis. AHA/ASA with respect to CAS: In asymptomatic patients with >60% stenosis by angiography or >70% by duplex ultrasound, prophylactic CAS might be considered but its effectiveness compared to medical therapy is not well established.

The Society for Vascular Surgery notes the following: Asymptomatic patients with >60% diameter stenosis CEA should be considered if the patient has a 3- to 5-year life expectancy and the perioperative and death rates are less than 3%. They do not recommend CAS for asymptomatic patients because there are insufficient data.

There are three main trials that examined carotid stenting *versus* endarterectomy for asymptomatic stenosis. They include the Asymptomatic Carotid Trial (ACT) 1 trial, the Carotid Revascularization Endarterectomy Versus Stenting (CREST) trial, and the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial. A meta-analysis of these trials indicated that both endarterectomy and CAS are viable long-term options for patients with carotid atherosclerosis. The evidence suggests that the 30-day risk of stroke or death is higher with CAS compared to CEA, but after

30 days the risk of stroke and death are similar. Patients older than 70 years of age had poorer outcomes with stenting than endarterectomy.

Significant progress has been made since the late 1980s and early 1990s when the major CEA trials were underway. At that time, the best medical treatment was antiplatelet therapy with aspirin. Since then, the utility of statins, antihypertensive drugs, smoking cessation, and lifestyle modification has been shown. This change in medical therapy and its effect on carotid stenosis became apparent from the ACST. Over the 10-year course, statin usage became more prevalent from 17% in 1993 to 1996 to 58% from 2000 to 2003. With this modern multimodal approach to medical therapy, many experts argue that the gap between medical and surgical treatment of carotid disease has narrowed for reducing the risk of stroke.

If a surgical option is chosen, keep in mind that it is a long-term investment and that the benefit may not be apparent until 2 years or more. Also, trials show that there was a trend toward CEA being less effective in women and older individuals and that these procedures should be performed at institutions where the perioperative stroke and death rates are less than 3%. Contralateral stenosis also matters when considering a surgical option. When a subgroup analysis was performed, CEA with contralateral total occlusion provided no long-term benefit.

Baker WH, Howard VJ, Howard G, et al. Effect of contralateral occlusion on long-term efficacy of endarterectomy in the Asymptomatic Carotid atherosclerosis Study (ACAS). ACAS Investigators. *Stroke*. 2000;31:2330–2334.

Brett AS, Levine JD. The case against identifying carotid stenosis in asymptomatic patients. *JAMA Intern Med*. 2014;174:2004–2008.

Brott TG, Hobson RW II, Howard G, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. *N Engl J Med*. 2010;363:11–23.

Brott TG, Howard G, Roubin GS, et al. Long-term results of stenting versus endarterectomy for carotid-artery stenosis. *N Engl J Med*. 2016;374:1021–

1031.

Halliday A, Harrison M, Hayter E, et al. 10-Year stroke prevention after successful carotid endarterectomy for asymptomatic stenosis (ACST-1): a multicenter randomized trial. *Lancet*. 2010;376(9746):1074–1084.

Hobson RW II, Weiss DG, Fields WS, et al. Efficacy of carotid endarterectomy for asymptomatic carotid stenosis. The Veterans Affairs Cooperative Study Group. *N Engl J Med*. 1993;328:221–227.

Moresoli P, Habib B, Reynier P, et al. Carotid stenting versus endarterectomy for asymptomatic carotid artery stenosis: a systematic review and meta-analysis. *Stroke*. 2017;48:2150–2157.

Raman G, Moorthy D, Hadar N, et al. Management strategies for asymptomatic carotid stenosis: a systematic review and meta-analysis. *Ann Intern Med*. 2013;158:676–685.

Ricotta JJ, Aburahma A, Ascher E, et al. Updated Society for Vascular Surgery guidelines for management of extracranial carotid disease. *J Vasc Surg*. 2011;54:e1–31.

Rosenfield K, Matsumura JS, Chaturvedi S, et al. Randomized trial of stent versus surgery for asymptomatic carotid stenosis. *N Engl J Med*. 2016;374:1011–1020.

Sardar P, Chatterjee S, Aronow HD, et al. Carotid artery stenting versus endarterectomy for stroke prevention: a meta-analysis of clinical trials. *J Am Coll Cardiol*. 2017;69:2266–2275.

Spence JD. Asymptomatic carotid stenosis. *Circulation*. 2013;127(6):739–742.

Voeks JH, Howard G, Roubin GS, et al. Age and outcomes after carotid stenting and endarterectomy: the carotid revascularization endarterectomy versus stenting trial. *Stroke*. 2011;42:3484–3490.

Walker MD, Marler JR, Goldstein M. Endarterectomy for asymptomatic carotid artery stenosis. *JAMA*. 1995;273:1421–1428.

Yadav JS, Wholey MH, Kuntz RE, et al. Protected carotid-artery stenting versus endarterectomy in high-risk patients. *N Engl J Med*. 2004;351:1493–1501.

A.9. What are the indications for performing a CEA in symptomatic carotid stenosis?

Symptomatic carotid stenosis is defined as focal neurologic symptoms, attributable to the appropriate carotid distribution, that have occurred within the past 6 months. Decisions for care in symptomatic disease come from three main trials, which

include the North American Symptomatic Carotid Endarterectomy (NASCET) trial, the European Carotid Surgery Trial (ECST), and the VA trials.

Guidelines issued in 2014 by the AHA/ASA make the following recommendations with respect to CEA:

- CEA is recommended for severe symptomatic stenosis (70% to 99%) as long as the perioperative morbidity and mortality risk is estimated to be less than 6%. The number needed to treat (NNT) to prevent one stroke at 5 years is 6.3.
- CEA is also recommended for moderate symptomatic patients (50% to 69% stenosis) depending on patient characteristics if the perioperative morbidity and mortality risk is estimated to be less than 6%. The NNT to prevent one stroke over 5 years is 22 in moderate symptomatic stenosis.
- CEA or stenting (CAS) is not recommended for less than 50% stenosis. Carotid revascularization was found to be harmful for symptomatic patients with less than 30% stenosis.

In studies leading to these recommendations, surgeries were performed at high-volume centers where the combined morbidity and mortality did not exceed 6%. Although it may be difficult to decipher one surgeon or institution morbidity or mortality rate, a rate over 6% can negate the benefit gained from a CEA. Other factors that may impact the benefit gained from CEA include timing of surgery, age, sex, presenting symptoms, and plaque morphology. There is evidence that performing CEA within 2 weeks of a nondisabling TIA or stroke improves outcomes compared with later surgery, but that performing it within 48 hours of a stroke or TIA leads to an elevated risk of stroke. This decline in benefit with time was more rapid with women than men. It was also noted that women who did not have their CEA within 2 weeks did not gain any benefit from the procedure irrespective of degree of stenosis. Best medical therapy has also improved significantly from when the first CEA

trials in the 1980s were started. As such, the NNT may be higher to prevent one stroke today with current medical therapy.

Meschia JF, Bushnell C, Boden-Albala B, et al. Guidelines for the primary prevention of stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2014;45:3754–3832.

MRC European Carotid Surgery Trial: interim results for symptomatic patients with severe (70-99%) or with mild (0-29%) carotid stenosis. European Carotid Surgery Trialists' Collaborative Group. *Lancet*. 1991;337:1235–1243.

Rerkasem K, Rothwell PM. Carotid endarterectomy for symptomatic carotid stenosis. *Cochrane Database Syst Rev*. 2011;(4):CD001081.

Rothwell PM, Eliasziw M, Gutnikov SA, et al. Analysis of pooled data from the randomised controlled trials of endarterectomy for symptomatic carotid stenosis. *Lancet*. 2003;361:107–116.

A.10. Is there any role for CAS in symptomatic patients?

CAS and CEA achieve similar long-term outcomes for symptomatic disease, but the periprocedural stroke or death rate was greater with CAS than CEA. The increased risk of stroke was only found in patients over 70 years of age. Although old age was originally proposed to be high risk for surgery and therefore an indication for stenting, studies have shown that older adults have worse outcomes with CAS. Age above 70 years linearly correlated with the risk of stroke during CAS. The CAS group had a lower rate of MI, cranial nerve palsy, or access site hematoma.

The guidelines issued in 2014 by the AHA/ASA make the following recommendations with respect to CAS.

CAS is indicated as an alternative to CEA for symptomatic patients at average or low risk of complications associated with endovascular intervention for stenosis >70% by noninvasive imaging or >50% with angiography as long as the anticipated perioperative morbidity and mortality is less than 6%.

Consider patients age when choosing between CEA and CAS as patients older than 70 years may have improved outcomes

with CEA. For patients younger than 70 years, CAS is equivalent to CEA with respect to periprocedural complications namely stroke, MI, and death.

CAS is reasonable for patients with symptomatic severe stenosis who have anatomic or medical conditions that greatly increase the risk of surgery.

Carotid revascularization is not recommended for patients with severe disability caused by cerebral infarction that precludes useful function or for patients with chronic total occlusion of the targeted artery. Conditions thought to increase the risk for surgery include radiation-induced stenosis, contralateral vocal cord paralysis, and tracheostomy.

Bonati LH, Lyrer P, Ederle J, et al. Percutaneous transluminal balloon angioplasty and stenting for carotid artery stenosis. *Cochrane Database Syst Rev*. 2012;(9):CD000515.

Brott TG, Hobson RW II, Howard G, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. *N Engl J Med*. 2010;363:11–23.

Meschia JF, Bushnell C, Boden-Albala B, et al. Guidelines for the primary prevention of stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2014;45:3754–3832.

A.11. Discuss the anatomy of the cerebral vasculature, including the carotid artery and the circle of Willis.

The common carotid arteries originate in the thorax. The right common carotid artery originates at the bifurcation of the brachiocephalic trunk, and the left originates from the aortic arch. In the neck, the common carotid arteries travel within the carotid sheath. At the level of the thyroid cartilage, each common carotid artery bifurcates into the internal and external carotid arteries.

Branches of the external carotid artery include the superior thyroid, lingual, facial, ascending pharyngeal, occipital, posterior auricular, maxillary and superficial temporal arteries.

The internal carotid artery passes through the neck without branching to enter the middle cranial fossa. It enters the middle cranial fossa through the carotid canal of the temporal bone, adjacent to the sphenoid bone. It supplies the hypophysis cerebri, the orbit, and the major portion of the supratentorial region of the brain. The cerebral arteries are derived from the internal carotid and vertebral arteries. The anastomosis they form at the base of the brain is known as the *circle of Willis* (**Fig. 18.1**). The two anterior cerebral arteries form the circle anteriorly. They are connected through the anterior communicating artery. The two posterior cerebral arteries form the circle posteriorly, which then ends at the junction of the basilar artery. The posterior cerebral arteries are connected to the internal carotid arteries by the two posterior communicating arteries. The middle cerebral artery primarily supplies the lateral surface of each cerebral hemisphere. The anterior cerebral and posterior cerebral arteries supply the medial and inferior surfaces of the cerebral hemisphere.

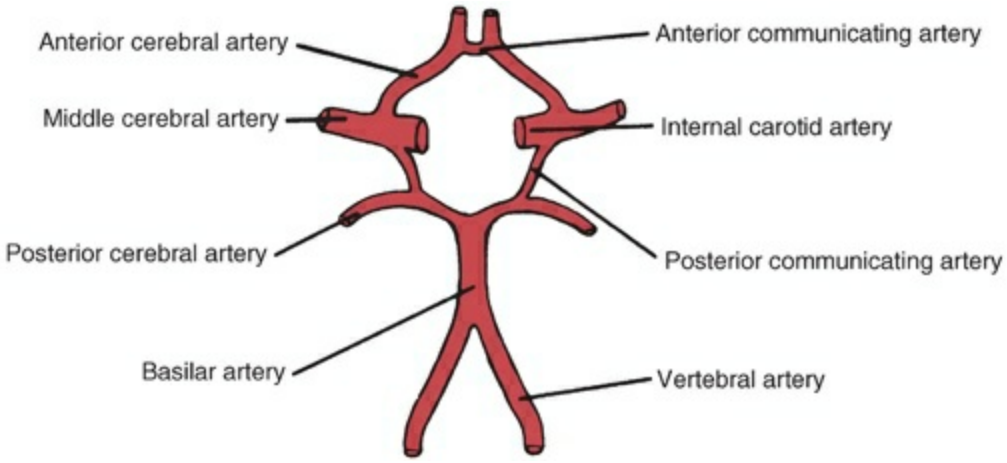

FIGURE 18.1. Arterial circle of Willis.

Moore KL. *Clinically Oriented Anatomy*. 5th ed. Baltimore: Lippincott Williams & Wilkins; 2006:930–931.

A.12. Discuss cerebral blood flow (CBF) in the presence of

carotid artery disease.

Stable CBF is maintained within a given range of systemic blood pressure through autoregulation and collateral flow. Whereas most studies focus on the degree of carotid stenosis and the risk of stroke, emerging evidence indicates that downstream hemodynamic effects distal to the stenosis also play an important role in stroke risk classification.

Cerebrovascular reserve is the capacity of the brain to increase cerebral blood volume through vasodilation to maintain a constant regional CBF in the face of low cerebral perfusion pressure (CPP). When CPP is reduced, the cerebral vasculature autoregulates by dilation of cerebral arterioles to maintain CBF. With severe carotid stenosis, vasodilatory capacity is maximally exhausted, and a further decrease in CPP, such as with induction of anesthesia can also decrease CBF and increase the risk of stroke.

The hemodynamic intracerebral effects of carotid stenosis also depend on collateral flow. The circle of Willis is the primary collateral circulation of cerebral arteries, followed by the ophthalmic artery, leptomeningeal vessels, and anastomoses among the perforating cortical arteries.

Current understanding of CBF is incomplete as most of our knowledge of cerebral hemodynamics comes from changes that occur in the large vessels. Flow in the large cerebral vessels may not correlate to flow in the capillary network, which limits our current knowledge of microvascular perfusion

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Edinburgh, United Kingdom: Elsevier Saunders; 2017.

Edvinsson L, Krause D. *Cerebral Blood Flow and Metabolism*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2002.

Gupta A, Chazen JL, Hartman M, et al. Cerebrovascular reserve and stroke risk in patients with carotid stenosis or occlusion: a systematic review and meta-analysis. *Stroke*. 2012;43:2884–2891.

Gur AY, Bova I, Bornstein NM. Is impaired cerebral vasomotor reactivity a predictive factor of stroke in asymptomatic patients? *Stroke*. 1996;27:2188–2190.

Hedera P, Bujdáková J, Traubner P. Effect of collateral flow patterns on outcome of carotid occlusion. *Eur Neurol*. 1995;35:212–216.

Markus H, Cullinane M. Severely impaired cerebrovascular reactivity predicts stroke and TIA risk in patients with carotid artery stenosis and occlusion. *Brain*. 2001;124:457–467.

Silvestrini M, Vernieri F, Pasqualetti P, et al. Impaired cerebral vasoreactivity and risk of stroke in patients with asymptomatic carotid artery stenosis. *JAMA*. 2000;283:2122–2127.

Tsivgoulis G, Alexandrov AV. Cerebral hemodynamics in acute stroke: pathophysiology and clinical implications. *J Vasc Interv Neurol*. 2008;1:65–69.

Vernieri F, Pasqualetti P, Matteis M, et al. Effect of collateral blood flow and cerebral vasomotor reactivity on the outcome of carotid artery occlusion. *Stroke*. 2001;32:1552–1558.

Zhou H, Sun J, Ji X, et al. Correlation between the integrity of the circle of Willis and the severity of initial noncardiac cerebral infarction and clinical prognosis. *Medicine (Baltimore)*. 2016;95:e2892.

A.13. Discuss the different surgical approaches to carotid revascularization.

CEA is performed through either a transverse incision or an incision bordering the sternocleidomastoid muscle (also known as a carotid incision). The subcutaneous tissue and platysma muscle are divided, and the carotid sheath is exposed. Usually, dissection is performed exposing the common carotid artery to a point distal to the bifurcation of the internal carotid artery and external carotid artery. Next, in this order, the internal, common, and external arteries are sequentially clamped, and the patient is given a heparin bolus. Depending on institution and surgeon preference, carotid stump pressures can be obtained by attaching a transducer into the common carotid artery after clamping the proximal common and external carotid artery. A mean pressure of 40 to 50 mmHg suggests adequate collateralization through the circle of Willis from the contralateral carotid artery. Some

use lower stump pressures as an indication for shunt placement manipulation of the carotid bulb can result in hemodynamic instability (e.g., bradycardia) due to the carotid sinus reflex. Typically, reducing direct surgical pressure will allow for return of normal sinus rhythm. Pharmacologic therapy can involve direct injection of lidocaine into the sinus or intravenous administration of atropine, both of which can lead to cessation of the reflex.

To remove the lesion, a longitudinal arteriotomy is performed below the level of the bifurcation and extended both proximally and distally. At this point, some surgeons routinely place shunts, others choose to do so only if there are signs of cerebral ischemia, and others opt to not place shunts altogether and decrease the cerebral metabolic rate by requesting an increase in anesthetic depth to achieve EEG burst suppression. If a shunt is placed, it is done after the vessel is open but before the plaque is removed. The plaque is dissected and freed from the deep layers of the media after which the arteriotomy is repaired. Some surgeons do a primary repair while others patch the artery with a synthetic or biologic patch. The clamps are sequentially released to back bleed the external and internal carotid arteries and forward flush the common carotid artery. After the suture line is completed, flow is restored in the external then internal carotid artery. A Jackson-Pratt drain can be placed to prevent incisional hematoma. A completion study to assess integrity of the repair is usually performed using a duplex ultrasound or contrast angiogram. Another variation of the conventional CEA is eversion endarterectomy. Here, the carotid is transected horizontally at the carotid bulb, and the artery is turned inside out or everted, although this variation is infrequently performed. There is no evidence indicating one technique is superior to the other; the surgical method is usually chosen because of institution and surgical preference.

Calligaro KD, Dougherty MJ. Correlation of carotid artery stump pressure and neurologic changes during 474 carotid endarterectomies performed in awake patients. *J Vasc Surg*. 2005;42:684–689.

Cao P, Giordano G, De Rango P, et al. A randomized study on eversion versus standard carotid endarterectomy: study design and preliminary results: the Everest Trial. *J Vasc Surg*. 1998;27:595–605.

Jacob T, Hingorani A, Ascher E. Carotid artery stump pressure (CASP) in 1135 consecutive endarterectomies under general anesthesia: an old method that survived the test of times. *J Cardiovasc Surg*. 2007;48:677–681.

Kumar S, Lombardi JV, Alexander JB, et al. Modified eversion carotid endarterectomy. *Ann Vasc Surg*. 2013;27:178–185.

Rerkasem K, Rothwell PM. Routine or selective carotid artery shunting for carotid endarterectomy (and different methods of monitoring in selective shunting). *Cochrane Database Syst Rev*. 2009;(4):CD000190.

A.14. Discuss the endovascular approaches to carotid stenting.

Access to the carotid artery is obtained usually through the common femoral artery. Transcervical (though a cutdown or percutaneously) via the common carotid or transradial approaches have also been used. If the transfemoral approach is chosen, an angiogram is performed to identify the aortic arch anatomy to safely maneuver the catheter, wires, and embolic protection device up to the internal carotid artery. If the transcervical route is chosen, the arch is bypassed. This approach is appealing but currently only a handful of centers are adept with this technique.

The patient is heparinized prior to manipulating guidewires and catheters. The goal is to maintain an activated clotting time (ACT) of 250 to 300 seconds. The common steps for stenting are (1) advancement of a guidewire, (2) sheath placement, (3) embolic protection device placement, (4) carotid lesion predilated (if needed), (5) stent positioning, (6) stent deployment, and (7) stent expansion with post-stent angioplasty to ensure good apposition against the arterial wall. As it can be difficult to get the wire and embolic protection device across a

stenotic lesion, predilation may be needed. Predilation is recognized as a risk factor for perioperative stroke and vasospasm. During dilation, stenting, and angioplasty, bradycardia and hypotension due to baroreceptor activation can occur and are usually treated with vagolytic drugs such as atropine. The carotid baroreceptors are located within the adventitia of the origin of the internal carotid artery and innervated by a branch of the glossopharyngeal nerve called the sinus of Hering. The baroreceptors are stretch-sensitive mechanoreceptors that respond to alterations in blood pressure.

The two main considerations in the stent procedure are the type of stent utilized and the type of embolic protection device that is used. The two types of bare-metal carotid stents that are common placed are open and closed architecture stents. Open stents are typically more flexible and are used for complex angulated carotid lesions. Closed stents cover more surface area and are commonly used in straighter less complex carotid lesions. Randomized clinical trials have failed to show any relationship between the type of stent used and complications that stem from CAS.

Embolic protection device technology is evolving but in general fall into three main types: (1) distal filter, (2) distal occlusion devices, and (3) proximal protection devices. The filter design allows for antegrade flow through the internal carotid artery during stent placement and is commonly used. The main limitation of distal filter devices is that they need to cross the lesion, which in and of itself can lead to embolism. Distal occlusion devices have a low profile and require a short landing zone. This is advantageous for tortuous vessels. The lesion is crossed with a wire, the balloon inflated, and angiography used to confirm that there are no leaks. After the stent is deployed, an aspiration catheter is advanced to the occlusion device to remove all debris after which the balloon is deflated. The main

concerns are intolerance to occlusion of the artery and embolism. Careful preoperative assessment of collaterals (i.e., via the circle of Willis) is important. Retrograde flow devices are the newest advancement in embolic protection devices and are designed to promote flow and debris away from the internal carotid artery. Balloons are deployed in the common carotid and external carotid artery causing flow stasis or reversal. With these devices, there is no interaction with the plaque until reversal or stasis of flow is achieved. Some patients may not tolerate occlusion or flow reversal in the internal carotid artery. Evidence of which embolic protection device to use and whether they decrease the rate of periprocedural stroke and death is conflicting, although the studies trend toward a decrease in the risk of perioperative stroke.

Alvarez B, Matas M, Ribo M, et al. Transcervical carotid stenting with flow reversal is a safe technique for high-risk patients older than 70 years. *J Vasc Surg*. 2012;55:978–984.

Etxegoien N, Rhyne D, Kedev S, et al. The transradial approach for carotid artery stenting. *Catheter Cardiovasc Interv*. 2012;80:1081–1087.

Garg N, Karagiorgos N, Pisimisis GT, et al. Cerebral protection devices reduce periprocedural strokes during carotid angioplasty and stenting: a systematic review of the current literature. *J Endovasc Ther*. 2009;16:412–427.

Giri J, Kennedy KF, Weinberg I, et al. Comparative effectiveness of commonly used devices for carotid artery stenting: an NCDR analysis (National Cardiovascular Data Registry). *JACC Cardiovasc Interv*. 2014;7:171–177.

Knappich C, Kuehnl A, Tsantilas P, et al. The use of embolic protection devices is associated with a lower stroke and death rate after carotid stenting. *JACC Cardiovasc Interv*. 2017;10:1257–1265.

Kwolek CJ, Jaff MR, Leal JI, et al. Results of the ROADSTER multicenter trial of transcarotid stenting with dynamic flow reversal. *J Vasc Surg*. 2015;62:1227–1234.

Lin PH, Zhou W, Kougias P, et al. Factors associated with hypotension and bradycardia after carotid angioplasty and stenting. *J Vasc Surg*. 2007;46:846–853; discussion 853–854.

Macdonald S. New embolic protection devices: a review. *J Cardiovasc Surg (Torino)*. 2011;52:821–827.

Mousa AY, Campbell JE, Aburahma AF, et al. Current update of cerebral embolic protection devices. *J Vasc Surg*. 2012;56:1429–1437.

Mylonas SN, Moulakakis KG, Antonopoulos CN, et al. Carotid artery stenting-induced hemodynamic instability. *J Endovasc Ther*. 2013;20:48–60.

Timaran CH, Rosero EB, Higuera A, et al. Randomized clinical trial of open-cell vs closed-cell stents for carotid stenting and effects of stent design on cerebral embolization. *J Vasc Surg*. 2011;54:1310–1316.e1311; discussion e1316.

White CJ. Carotid artery stenting. *J Am Coll Cardiol*. 2014;64:722–731.

A.15. What is normal CBF?

Normal CBF is approximately 50 mL/100 g/min for the entire brain. Blood flow is about 4 times higher in gray matter than in white matter, or 80 and 20 mL/100 g/min, respectively.

Gropper MA, Eriksson LI, Fleisher LA, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier Saunders; 2019:294–332.

Kety SS, Schmidt CF. The nitrous oxide method for the quantitative determination of cerebral blood flow in man: theory, procedure and normal values. *J Clin Invest*. 1948;27:476–483.

Lassen NA, Munck O. The cerebral blood flow in man determined by the use of radioactive krypton. *Acta Physiol Scand*. 1955;33:30–49.

A.16. What is critically low CBF as measured by the electroencephalogram (EEG)?

Assuming normal temperature and hematocrit, 100 mL of blood contains approximately 20 mL of oxygen. Normal global CBF of 50 mL/100 g/min delivers oxygen to the brain at a rate of 10 mL/100 g/min. This is more than the high metabolic requirements of the brain for oxygen (3 to 5 mL/100 g/min), which affords a relative margin of safety. The CBF at which ischemia becomes apparent in the EEG is approximately 20 mL/100 g/min. Changes on EEG may be delayed for up to 150 seconds following onset of ischemia. It is not currently possible to define the specific changes that represent irreversible

ischemia. In the setting of an isoelectric EEG, oxygen delivery to the brain may be adequate to keep neurons alive but may provide insufficient energy for them to function.

Development of cerebral infarction depends on both the degree and duration of ischemia. Jones et al. showed in an animal model of reversible ischemia that with CBF of 18 to 23 mL/100 g/min, animals recovered from impaired neurologic function when blood flow was returned to normal levels regardless of the duration of the ischemic period. Infarction development at lower flows depends on both the degree of regional CBF reduction and the duration of ischemia. Neurons that are nonfunctional but will recover fully with restoration of adequate flow are said to be in an ischemic penumbra. Neuronal death occurs with CBF less than 10 mL/100 g/min.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1120–1127.

Boysen G, Engell HC, Pitolese GR, et al. On the critical level of cerebral blood flow in man with particular reference to carotid surgery. *Circulation*. 1974;49:1023–1025.

Jones TH, Morawetz RB, Crowell RM, et al. Threshold of focal cerebral ischemia in awake monkeys. *J Neurosurg*. 1981;54:773–782.

A.17. What is cerebral autoregulation?

Cerebral autoregulation is the tendency of the brain to match cerebral oxygen delivery with metabolic oxygen requirements despite variations in blood pressure. In normotensive individuals, CBF is relatively constant between mean arterial pressures of 70 and 150 mmHg. It is generally considered that the lower limit of autoregulation is a mean arterial pressure of 50 mmHg based on animal studies. Above and below the plateau phase, CBF is dependent on pressure and varies linearly with CPP. Note that the limits of autoregulation are a conceptual construct and not an “all-or-none” phenomenon. In addition, autoregulation is affected by the underlying level of vasodilation

or vasoconstriction that depends on the $PaCO_2$ or anesthetic conditions among other things.

In hypertensive patients, the upper and lower limits of the autoregulatory curve are shifted to the right, to higher arterial pressures (**Fig. 18.2**). What this means is that a mean arterial pressure of 60 mmHg, which would be well-tolerated in a normotensive individual, may actually be below the lower limit of autoregulation in the hypertensive individual, resulting in cerebral hypoperfusion. Conversely, hypertensive patients tolerate marked increases in mean arterial pressure better than their normotensive counterparts. In treated hypertensive patients, the limits of autoregulation are shifted with time toward normal.

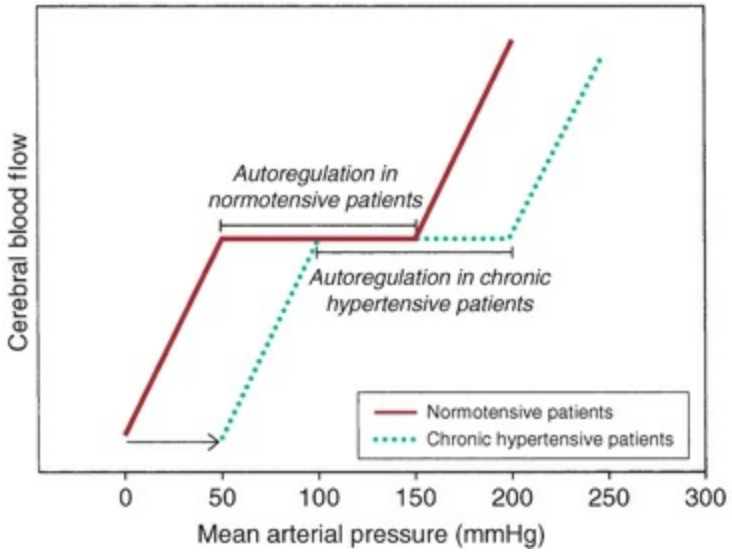

FIGURE 18.2. Cerebral autoregulatory curves in normotensive and chronic hypertensive patients. A shift in the autoregulation curve occurs with chronic hypertension. The curve shifts back to normotensive range once hypertension is well controlled.

Gropper MA, Eriksson LI, Fleisher LA, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier Saunders; 2019:294–332.

Paulson OB, Strandgaard S, Edvinsson L. Cerebral autoregulation. *Cerebrovasc Brain Metab Rev*. 1990;2:161–192.

A.18. How does $PaCO_2$ affect CBF?

Hypercarbia results in cerebral vasodilation, and hypocarbia in

cerebral vasoconstriction. CBF changes about 4% for each mmHg increase or decrease in arterial $Paco_2$ for partial pressures between 20 and 80 mmHg. The appropriate level of $Paco_2$ during carotid revascularization has not been established, and because there are no clear clinical benefits to either hypercapnia or hypocapnia, it is recommended to maintain normocapnia.

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Edinburgh, United Kingdom: Elsevier Saunders; 2017:19–58.

Gropper MA, Eriksson LI, Fleisher LA, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier Saunders; 2019:294–332.

A.19. What are the principal determinants of CBF?

The principal determinants of CBF are nerve cell activity, CPP, blood viscosity, $Paco_2$, pH of brain extracellular fluid, Pao_2, and neurogenic influences.

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Edinburgh, United Kingdom: Elsevier Saunders; 2017:19–58.

Gropper MA, Eriksson LI, Fleisher LA, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier Saunders; 2019:294–332.

A.20. What is meant by the term *luxury perfusion*?

Luxury perfusion is blood flow that is in excess of metabolic need (increased CBF relative to cerebral metabolic rate for oxygen). It is most frequently observed in tissues surrounding tumors or areas of infarction. It has also been described in tissues that have been manipulated during surgery.

Cottrell JE, Patel P, eds. ***Cottrell and Patel's Neuroanesthesia***. 6th ed. Edinburgh, United Kingdom: Elsevier Saunders; 2017:19–58.

A.21. What is meant by the term *intracerebral steal*?

Intracerebral steal is a paradoxical response to carbon dioxide in which hypercapnia decreases blood flow to an ischemic area.

With hypercapnia, normally perfused arterioles vasodilate, and this shunts blood from the ischemic lesion. This occurs because at baseline, hypoperfused regions in the brain are maximally dilated and cannot dilate further to hypercapnia. As a result, it is common practice to maintain normocapnia during carotid surgery.

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Edinburgh, United Kingdom: Elsevier Saunders; 2017:19–58.

Paulson OB. Cerebral apoplexy (stroke): pathogenesis, pathophysiology and therapy as illustrated by regional blood flow measurements in the brain. *Stroke*. 1971;2:327–360.

B. Preoperative Evaluation and Preparation

B.1. What will you look for in your preoperative evaluation of this patient?

Once the presence of a carotid lesion amenable to surgical treatment has been documented by Doppler ultrasonography or angiographic studies, the anesthesiologist will be asked to evaluate the patient regarding readiness for surgery. Because a majority of patients who have carotid disease also have coexisting cardiac atherosclerosis, the main focus of the preoperative evaluation will be to optimize cardiac function. Evidence of medical conditions associated with arteriosclerosis, such as coronary artery disease, hypertension, renal disease, obesity, diabetes mellitus, and pulmonary disease secondary to cigarette smoking, should be sought.

The patient's neurologic status also needs to be evaluated preoperatively. Although it would be preferable to medically optimize the patient with uncontrolled hypertension or untreated metabolic disease, or if possible delay surgery in the patient with a recent MI, the presence of symptomatic carotid disease may not allow that option. This is because there is good evidence that

surgical intervention should take place within 2 weeks of symptoms in order to reap the benefits of surgery.

The patient's airway needs to be assessed for ease of ventilation and intubation. A patient who is difficult to ventilate may become hypercarbic during induction, and the increase in $PaCO_2$ may have adverse effects on regional CBF. As part of the airway evaluation, the range of motion of the patient's neck that is tolerated without evidence of cerebral ischemia needs to be determined so that relative extremes of extension and lateral rotation of the neck during ventilation, intubation, and finally patient positioning can be avoided. Extreme extension and rotation of the neck can occlude the vertebral artery and contribute to postoperative neurologic deficits.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1120–1127.

Fleisher LA, Fleischmann KE, Auerbach AD. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;64(22):e77–e137.

Rerkasem K, Rothwell PM. Carotid endarterectomy for symptomatic carotid stenosis. *Cochrane Database Syst Rev*. 2011;(4):CD001081.

B.2. Is this patient's blood pressure too high for elective surgery?

Although hypertension is present in most patients presenting for CEA, its rapid correction is not recommended because this may exacerbate cerebral ischemia. If this patient had evidence of myocardial ischemia at this blood pressure and was stable from a neurologic standpoint, blood pressure could be gradually decreased with antihypertensive medications.

Normal myocardial and cerebral function need to be preserved. These goals are not necessarily at odds with each other. To decrease myocardial oxygen consumption, one would

want to decrease heart rate, blood pressure, and myocardial contractility. In this patient population, decreasing heart rate can decrease myocardial work, whereas CPP is maintained with adequate mean arterial pressure. If a hypertensive patient presents with an unstable neurologic status, it may be necessary to control blood pressure only once the obstruction to CBF has been relieved.

A single blood pressure measurement is of little use in the preoperative assessment of the patient. It is the range of the blood pressures normally tolerated by the patient that will guide perioperative blood pressure management. For example, if the patient's blood pressure is measured at 80/50 mmHg and at 170/100 mmHg, preoperatively, and at these blood pressures, she does not develop any new neurologic deficits or myocardial ischemia, the clinician will be inclined to treat blood pressures only beyond these two extremes.

Because this patient is hypertensive, one can expect that wide swings in blood pressure will occur while she is receiving anesthesia. Variations in blood pressure should be minimized because these have been related to increased cardiac and neurologic morbidity. The anesthesiologist must be prepared for blood pressure variations by having both vasopressors and vasodilators readily available. Total fluid administration should be limited to no more than 10 mL per kg for a typical 2-hour operation in most patients because fluid overload can contribute to postoperative hypertension.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1120–1127.

Smith JS, Roizen MF, Cahalan MK, et al. Does anesthetic technique make a difference? Augmentation of systolic blood pressure during carotid endarterectomy: effects of phenylephrine versus light anesthesia and of isoflurane versus halothane on the incidence of myocardial ischemia. *Anesthesiology*. 1988;69:846–853.

B.3. What laboratory data are required preoperatively?

Laboratory tests should be ordered based on the patient's cardiac, respiratory, and metabolic status. Hemoglobin and hematocrit should be determined preoperatively because values may be abnormal in a patient with advanced age, renal or pulmonary disease. A type and screen while routinely performed at most institutions is rarely needed as transfusion after CEA or stenting is rare. A baseline basic metabolic panel is useful to determine the electrolyte status. Blood urea nitrogen and creatinine help to determine baseline renal status.

An electrocardiogram (ECG) should be examined preoperatively to look for arrhythmias, evidence of ischemia, previous MIs, or left ventricular hypertrophy. Where appropriate, the preoperative ECG should be compared with earlier studies to determine whether interval changes have occurred.

If present, a chest radiograph should be examined to look for cardiomegaly, evidence of pulmonary edema, chronic obstructive pulmonary disease, or pneumonia. If the patient has a history of chronic obstructive pulmonary disease, a preoperative arterial blood gas reading should be obtained once the arterial line is placed to identify the baseline $PaCO_2$. In patients who are chronically hypercarbic, rapid adjustment to normocarbia intraoperatively will result in relative hypocarbia and CBF will be reduced accordingly. Management of intraoperative ventilation should be aimed at maintaining normal arterial carbon dioxide partial pressure.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1120–1127.

Stangenberg L, Curran T, Shuja F, et al. Development of a risk prediction model for transfusion in carotid endarterectomy and demonstration of cost-saving potential by avoidance of "type and screen." *J Vasc Surg*. 2016;64:1711–1718.

B.4. Will you treat this patients' blood glucose?

Hyperglycemia lowers the ischemic threshold in clinical and experimental models. Poorly controlled diabetes mellitus is a marker for vascular disease, and preoperative optimization if time allows may improve perioperative outcome.

McGirt MJ, Woodworth GF, Brooke BS, et al. Hyperglycemia independently increases the risk of perioperative stroke, myocardial infarction, and death after carotid endarterectomy. *Neurosurgery*. 2006;58:1066–1073.

B.5. Will you premedicate this patient?

Ideally, the patient should present to the operating room calm and awake. Preoperative anxiety should be alleviated in these patients because it can lead to hypertension, which has been associated with adverse neurologic outcome. Increases in heart rate in the anxious patient lead to increased myocardial oxygen consumption and, potentially, ischemia, ventricular dysfunction, and arrhythmias.

Premedication, however, can lead to ventilatory depression, with resultant hypercarbia and alterations in CBF that can exacerbate cerebral ischemia. Sedation can also interfere with the immediate postoperative neurologic assessment of the patient because it may cause delayed awakening from anesthesia. One of the anesthetic goals for CEA under general anesthesia is to have a patient who promptly emerges from anesthesia and is able to cooperate with a basic neurologic evaluation.

To achieve these goals, a thorough and reassuring preoperative visit alone may provide sufficient anxiolysis. The anesthesiologist should explain the preoperative procedure and what can be expected in the postoperative period, answering any questions that the patient has. If an anxiolytic is chosen, a short-acting agent should be used after documentation of the patient's neurologic exam.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1120–1127.

C. Intraoperative Management

C.1. How will you monitor this patient?

Regardless of whether the patient is having an awake CEA or a carotid stent, routine monitoring of cardiovascular, pulmonary, and metabolic function is important. ECG leads II and V_5, noninvasive blood pressure monitor, pulse oximetry, end-tidal capnometry, and temperature are monitored. An intra-arterial catheter should be used to monitor arterial blood pressure closely. Its presence will permit immediate identification of blood pressure changes and allow for repetitive sampling of arterial blood gases.

Rarely is a central venous catheter or a pulmonary artery catheter required to monitor cardiac function. Large fluid shifts or major blood loss is not anticipated, and most anesthesiologists place one 18-gauge or larger bore peripheral intravenous.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1120–1127.

C.2. How will you know that the patient's cerebral perfusion is adequate during surgery?

In the awake patient undergoing CEA or stent under local anesthesia, repeated neurologic examinations can be done to assess the adequacy of cerebral perfusion. This is the most sensitive and specific way to detect intraoperative cerebral ischemia.

If the patient receives general anesthesia, neuromonitoring is generally employed in order to detect and treat ischemia in a timely fashion. Various neuromonitoring modalities exist, which are classified in the categories of brain activity monitoring,

cerebral perfusion monitoring, and brain oxygen saturation monitoring. These include the EEG, SSEPs, TCD, internal carotid stump pressure, $SjvO_2$, and near-infrared spectroscopy (NIRS). No one monitor is routinely used in all operating rooms, and each modality has its own specific indication as well as strengths and weaknesses. Therefore, the simultaneous application of more than one monitoring device is recommended.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1120–1127.

Pennekamp CW, Moll FL, de Borst GJ. The potential benefits and the role of cerebral monitoring in carotid endarterectomy. *Curr Opin Anaesthesiol*. 2011;24(6):693–697.

C.3. Discuss the differences and relative advantages and disadvantages of unprocessed EEG and processed EEG monitoring.

The 16-channel EEG is a sensitive indicator of cerebral ischemia. Intraoperative changes in EEG related to ischemia are classified as mild, moderate, or severe. Severe EEG changes (>50% decrease in waveform amplitude in a generalized or lateralized distribution) suggest a need for blood pressure augmentation by the anesthesiologist or shunt placement by the surgeon. The EEG is neither a measure of CBF nor a way to determine whether irreversible neuronal damage has occurred. Rather, it is an indicator that areas of the brain may be at risk for infarction. Changes that occur in the EEG with hypothermia, hypocarbia, hypoxemia, and deep anesthesia mimic those of ischemia. In patients who have had a cerebrovascular accident, the processed EEG does not predict cerebral ischemia.

Problems associated with intraoperative monitoring of the 16-lead EEG have detracted from its popularity. These include difficulty in obtaining a meaningful recording in the electrically

noisy environment of the operating room, the bulk of the equipment required, and the need for specially trained personnel for interpretation.

The processed EEG has eliminated many of the problems associated with the 16-channel EEG. The equipment is generally compact, and the data display allows for ease of interpretation. One commonly used processed encephalogram is power spectrum analysis. For this analysis, the EEG is studied in short time intervals of 2 to 16 minutes, called *epochs*. Each epoch then is subjected to a fast Fourier transform analysis during which the complex waveform of the unprocessed EEG is broken down into its component sine waves of varying amplitudes and frequencies. The power spectrum is calculated by squaring the amplitude of the individual frequency components. The power spectrum can then be displayed in various forms, two of which are the compressed spectral array and the density-modulated spectral array. Data are displayed in these two forms as relative power versus frequency (**Fig. 18.3**).

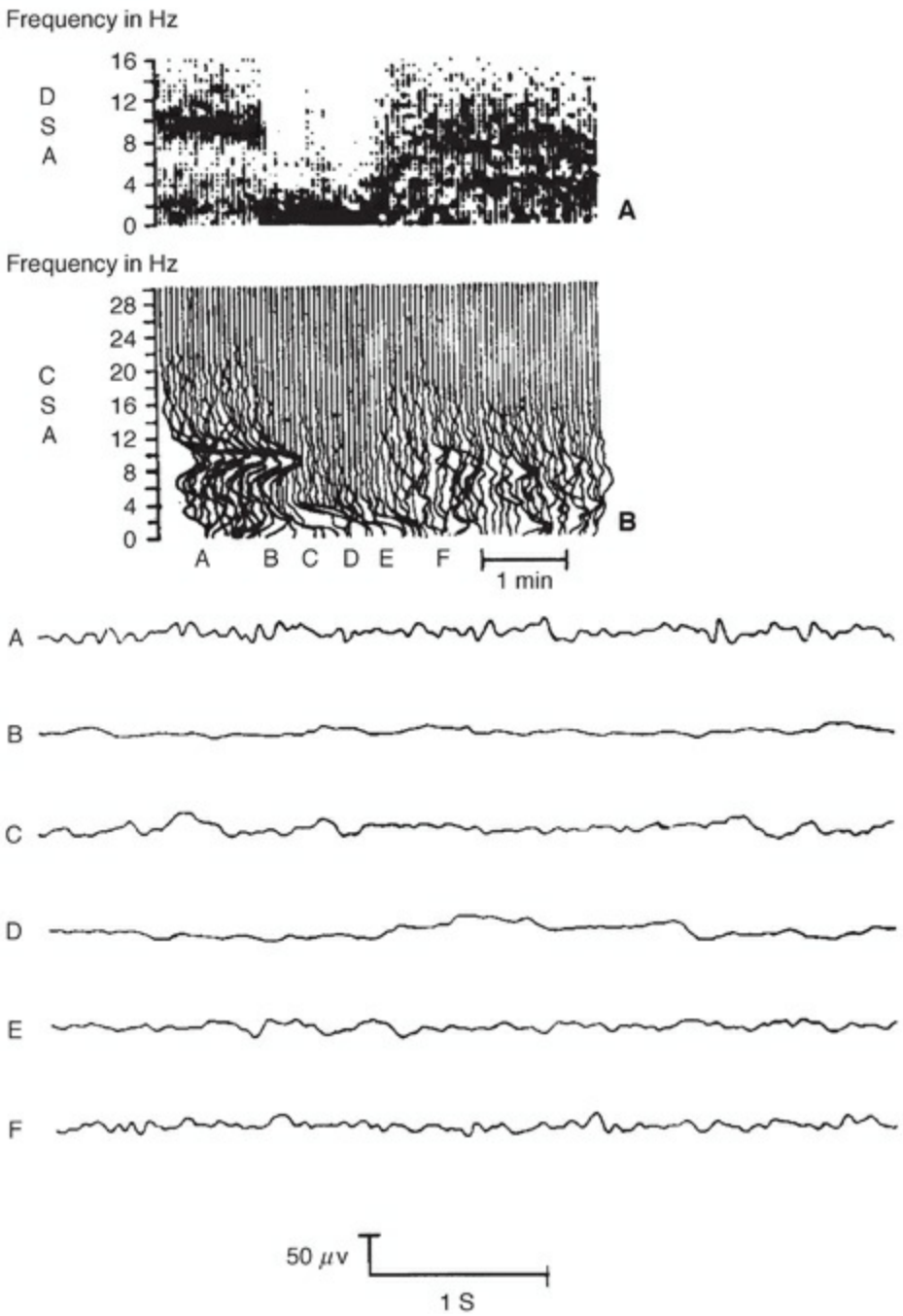

FIGURE 18.3. An example of density spectral array (A) and compressed spectral array (B) during a period of marked hypotension during initiation of bypass. Slowing waveform activity in the unprocessed EEG (B to E) is also evident in the density-modulated spectral array (DSA) and compressed spectral array (CSA). (*Reprinted with permission from Levy WJ, Shapiro HM, Maruchak G, et al. Automated EEG processing for intraoperative monitoring*. Anesthesiology. *1980;53:223*.)

The processed EEG is only as good as the original from which it was obtained. Therefore, meticulous recording

techniques are required even when monitoring a processed EEG. During CEA, generally two or four channels of the EEG are monitored to determine right and left symmetry in neuronal activity during interruption of CBF.

The bispectral index (BIS) monitor is another commonly used processed EEG parameter that uses a proprietary methodology to calculate indices of the EEG power spectrum, burst synchronization, and phase coupling. It is primarily used as a monitor to assess depth of anesthesia. Although the BIS may have some utility as a marker of global cerebral ischemia, it is unreliable as an indicator of hemispheric cerebral ischemia during carotid cross-clamping.

Deogaonkar A, Vivar R, Bullock RE, et al. Bispectral index monitoring may not reliably indicate cerebral ischaemia during awake carotid endarterectomy. *Br J Anaesth*. 2005;94:800–804.

Gropper MA, Eriksson LI, Fleisher LA, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier Saunders; 2019:1825–1867.

Kearse LA, Martin D, McPeck K, et al. Computer-derived density spectral array in detection of mild analog electroencephalographic ischemic pattern changes during carotid endarterectomy. *J Neurosurg*. 1993;78:884–890.

Rampil IJ, Holzer JA, Quest DO, et al. Prognostic value of computerized EEG analysis during carotid endarterectomy. *Anesth Analg*. 1983;62:186–192.

Sundt TM Jr, Sharbrough FW, Piepgras DG, et al. Correlation of cerebral blood flow and electroencephalographic changes during carotid endarterectomy: with results of surgery and hemodynamics of cerebral ischemia. *Mayo Clin Proc*. 1981;56:533–543.

C.4. How will you measure CBF intraoperatively? What are the relative advantages and disadvantages of each technique?

CBF can be indirectly measured by neurophysiologic monitoring. Monitoring techniques can be broken down into techniques that assess the overall integrity of cerebral function, cerebral flow, and cerebral metabolism. EEG, SSEPs, and motor evoked potentials (MEP) assess the integrity of cerebral

function. Cerebral perfusion monitoring can be done indirectly with internal carotid artery stump pressures or directly with TCD, which assesses flow in large intracranial vessels. Brain oxygen saturation monitoring can be done with jugular venous bulb monitoring ($SjvO_2$) or cerebral oximetry by NIRS, and they assess overall cerebral metabolism.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1120–1127.

C.5. Describe the use of stump pressure and its limitations.

Internal carotid artery stump pressure is one way to assess cerebral perfusion; however, this is indirect because it measures perfusion pressure and not flow per se. Typically, the stump pressure is obtained after the initial clamping of the internal carotid artery. The stump pressure presumably reflects pressure transmitted through collateral vessels. Maintaining stump pressures from 25 to 70 mmHg has been described as necessary to avoid neurologic injury. Nevertheless, this range of stump pressures may not reliably represent the adequacy of collateral CBF because it does not correlate consistently with changes in the EEG, regional CBF, or changes in the neurologic status of the awake patient. Furthermore, anesthetic agents can alter carotid stump pressure without changing regional CBF. Inadequate stump pressures have been shown when measured regional CBF was adequate. If shunting during CEA were to be done only on the basis of stump pressures, some patients would unnecessarily receive shunts. Finally, because stump pressure is not continuously monitored, it only gives a snapshot in time of cerebral perfusion and therefore this technique is less commonly used.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed.

Philadelphia, PA: Wolters Kluwer; 2017:1120–1127.

Harada RN, Comerota AJ, Good GM, et al. Stump pressure, electroencephalographic changes, and the contralateral carotid artery: another look at selective shunting. *Am J Surg*. 1995;170:148–153.

C.6. Describe the use of transcranial Doppler (TCD) and its limitations.

Another technique that can be used to assess CBF is TCD ultrasonography, which uses pulse wave Doppler ultrasound to measure flow in the ipsilateral middle cerebral artery. It can aid in determining the need for a shunt by detecting a decrease in the middle cerebral artery blood flow velocity with placement of the carotid cross-clamp. It allows for continuous assessment of shunt function. It can be used to assess the adequacy of pharmacologically induced intraoperative hypertensive therapy. TCD also allows detection of air or particulate embolization with endarterectomy or stenting. A higher embolic burden has been associated with stroke. The disadvantage of TCD is that it is technically demanding and not obtainable in approximately 20% of patients. As changes in flow velocities can be due to changes in arterial diameter or low perfusion, it is not very sensitive or specific for assessing cerebral perfusion.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1120–1127.

C.7. Describe the use of jugular venous oxygen saturation ($SjvO_2$) and its limitations.

$SjvO_2$ follows oxygen saturation obtained from a catheter that is inserted into the internal jugular vein of the carotid surgical site. The major disadvantage of $SjvO_2$ monitoring is that it is a global and not regional monitor for ischemia. $SjvO_2$ also has a wide range of normal values, and there is a possibility of extracranial blood sampling. This technique has not shown to improve

outcomes with CAS or CEA.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1120–1127.

C.8. Describe the use of cerebral oximetry and its limitations.

Cerebral oximetry uses NIRS to detect regional cerebral oxygen saturation. This is done by applying small adhesive monitoring pads to the forehead. The major limitations to NIRS is that there are wide variations in baseline readings in a single individual, and the lack of agreement as to what constitutes ischemic changes to warrant interventions like shunt placement. The ability to detect ischemia is limited to the region in the frontal cortex and limited by the sampling window.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1120–1127.

Grubhofer G, Plöchl W, Skolka M, et al. Comparing Doppler ultrasonography and cerebral oximetry as indicators for shunting in carotid endarterectomy. *Anesth Analg*. 2000;91:1339–1344.

C.9. Discuss somatosensory evoked potentials (SSEPs) as a monitor of CBF during CEA.

SSEPs are a specialized form of electrophysiologic monitoring that reflects the presence of intact sensory pathways from a stimulated peripheral nerve to the cortex, where electrical activity is monitored. Evidence exists that distortion of certain waveforms is associated with ischemia. These SSEP changes are not consistently associated with changes in the EEG. Questions have been raised regarding whether SSEPs can overpredict the presence of ischemia and the need for shunting. If SSEPs are a useful indicator of ischemia, they may be used when ischemia cannot be detected on an EEG tracing, such as during barbiturate anesthesia. During barbiturate anesthesia, the isoelectric EEG

can only indicate that neurons are quiet. It cannot indicate whether these same neurons are ischemic. The SSEP tracing remains intact with barbiturate anesthesia and, therefore, would potentially be more useful as a clinical monitor. Patients who have had strokes have some asymmetry in baseline SSEP waveforms. This asymmetry does not appear to affect the SSEP as an effective clinical monitor, which may also be a relative advantage over the EEG in patients with prior stroke.

Gropper MA, Eriksson LI, Fleisher LA, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier Saunders; 2019:1825–1867.

Manninen PH, Tan TK, Sarjeant RM. Somatosensory evoked potential monitoring during carotid endarterectomy in patients with a stroke. *Anesth Analg*. 2001;93:39–44.

C.10. What type of anesthesia will you choose for this patient if she chose to have an endarterectomy?

Regional or general anesthesia can be used for patients undergoing CEA. Each type of anesthesia has advantages and disadvantages that must be considered when choosing the optimal anesthetic for each patient. Benefits of general anesthesia include a still patient and a quiet operative field; early control of the airway and ventilation; and the ability to "protect" the brain should ischemia, which cannot be eliminated, develop. A disadvantage of general anesthesia is the inability to perform repeated neurologic evaluations during surgery. Therefore, patients receiving general anesthesia should have their CBF or neurologic function monitored as previously discussed.

The primary advantage of a regional anesthetic is that the patient remains awake allowing for repeated neurologic evaluations. Although anecdotal reports support that regional anesthesia allows for greater stability of blood pressure, decreased requirement for vasoactive medications to support blood pressure, and decreased incidence of perioperative MI,

further outcome studies are warranted. Potential complications associated with regional anesthesia include seizures, alteration of mental status with cerebral ischemia, and loss of patient cooperation associated with cerebral hypoperfusion, inadequate ventilation, and sedation.

Early analyses of mainly nonrandomized trials comparing regional and general anesthesia for CEA initially suggested a reduced risk of morbidity and mortality with regional anesthesia. However, subsequent analyses of larger, randomized trials have generally refuted this finding. The general anesthesia versus local anesthesia for carotid surgery (GALA) trial was a multicenter, randomized controlled trial that included 3,526 patients with symptomatic or asymptomatic carotid stenosis who were randomly assigned to surgery under general anesthesia or regional anesthesia. This study showed no definite differences in the primary study outcome (stroke, MI, or death within 30 days), quality of life, or length of hospital stay. However, there was a nonsignificant trend toward a higher rate of MI in the regional anesthesia group as well as a nonsignificant trend toward a higher rate of stroke among patients with bilateral carotid disease in the general anesthesia group.

A meta-analysis of 14 randomized trials involving 4,596 procedures (the majority of which came from the GALA study) found that there was no statistically significant difference between general and regional anesthesia groups in the proportion of patients who had a stroke or died within 30 days of surgery. In this meta-analysis, there was a nonsignificant trend toward lower operative mortality with regional anesthetic; however, none of the individual studies or the meta-analysis were adequately powered to reliably detect an effect on mortality. Therefore, evidence suggests that patients and surgeons may choose either anesthetic technique, depending on the clinical situation and individual preference.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1120–1127.

Unic-Stojanovic D, Babic S, Neskovic V. General versus regional anesthesia for carotid endarterectomy. *J Cardiothorac Vasc Anesth*. 2013;27(6):1379–1383.

Vaniyapong T, Chongruksut W, Rerkasem K. Local versus general anaesthesia for carotid endarterectomy. *Cochrane Database Syst Rev*. 2013; (12):CD000126.

C.11. What type of anesthesia will you choose for this patient if she chose to have a carotid stent?

Carotid stents are usually performed under local anesthesia. Patients get minimal to no sedation so that a continuous neurologic assessment can be performed. An arterial line is placed in addition to standard monitoring as hemodynamic instability is common during and after stenting is performed. During the angioplasty and stent placement, studies have reported bradycardia, hypotension, and asystole. Bradycardia and hypotension are seen more often when angioplasty is performed prior to stenting. The interventionalist will usually ask for prophylactic atropine or glycopyrrolate before balloon angioplasty and stent deployment. Satya et al. reported an approximately 5% incidence of asystole after stenting and found a higher association with right-sided stents in patients with reduced left ventricular ejection fraction and significant contralateral stenosis.

Bussière M, Lownie SP, Lee D, et al. Hemodynamic instability during carotid artery stenting: the relative contribution of stent deployment versus balloon dilation. *J Neurosurg*. 2009;110:905–912.

Cayne NS, Faries PL, Trocciola SM, et al. Carotid angioplasty and stent-induced bradycardia and hypotension: impact of prophylactic atropine administration and prior carotid endarterectomy. *J Vasc Surg*. 2005;41:956–961.

Gropper MA, Eriksson LI, Fleisher LA, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier Saunders; 2019:1825–1867.

Satya K, Dougherty K, Lee W. Determinants and outcomes of asystole during

carotid artery stenting. *J Endovasc Ther*. 2011;18:513–517.

C.12. How will you induce and maintain general anesthesia in this patient for CEA?

Any anesthetic regimen is suitable if it provides hemodynamic stability, does not exacerbate cerebral ischemia, and allows for prompt emergence from anesthesia at the end of surgery. Premedication with midazolam has the potential to compromise early neurologic assessment and is usually avoided. Following preoxygenation, anesthetics should be titrated slowly with special attention to their effect on blood pressure. Control of the airway should be taken as soon as the patient is no longer able to breathe adequately to maintain normocarbia. While breathing oxygen, short-acting opioids are administered until the patient is comfortably sedated. Lidocaine 1 mg per kg is administered intravenously at least 2 minutes before laryngoscopy and intubation to blunt the hemodynamic response to airway manipulation. Following administration of propofol or etomidate, controlled ventilation is instituted with 100% oxygen to avoid hypoxia and hypercarbia. A muscle relaxant is administered to facilitate tracheal intubation. Succinylcholine should be avoided in hemiparetic patients because of the possibility of a hyperkalemic response. Nondepolarizing muscle relaxants with significant hemodynamic effects such as sympathomimetic activity, vagolysis, or histamine release should be avoided. Once the patient is relaxed, expeditious laryngoscopy and intubation are performed. Atomized lidocaine can be used prior to intubation to minimize stimulation by the endotracheal tube during surgery and prevent coughing on emergence.

During the induction and intubation sequence, blood pressure is kept in the patient's normal range using vasopressors or vasodilators as indicated. Short-acting and easily titratable

vasoactive medications should be chosen to facilitate blood pressure control.

Anesthesia can be maintained with volatile anesthetics or intravenous agents. The addition of short-acting opioids to a volatile or intravenous anesthetic will decrease heart rate and when properly dosed, allow for a prompt, smooth emergence from general anesthesia. Maintenance of a light anesthetic appears to have several advantages over deep anesthesia. It allows ischemic patterns on the EEG to be recognized easily. It also facilitates maintenance of blood pressure. In addition, administration of a light anesthetic, compared to a deep anesthetic using phenylephrine to maintain blood pressure, results in a lower incidence of perioperative MI. Arterial blood pressure should be maintained in the high normal range throughout the procedure. When the carotid artery is clamped, induced hypertension (10% to 20% above baseline) is often requested by the surgeon to increase contralateral flow and prevent ischemia. During surgical manipulation of the carotid sinus, sudden bradycardia and hypotension can occur. Alerting the surgeon and asking them to stop manipulating the area usually restores hemodynamics.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1120–1127.

Gropper MA, Eriksson LI, Fleisher LA, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier Saunders; 2019:1825–1867.

Jellish WS, Sheikh T, Baker WH, et al. Hemodynamic stability, myocardial ischemia, and perioperative outcome after carotid surgery with remifentanil/propofol or isoflurane/fentanyl anesthesia. *J Neurosurg Anesthesiol*. 2003;15(3):176–184.

Mutch WA, White IW, Donen N, et al. Haemodynamic instability and myocardial ischaemia during carotid endarterectomy: a comparison of propofol and isoflurane. *Can J Anaesth*. 1995;42(7):577–587.

Umbrain V, Keeris J, D'Haese J, et al. Isoflurane, desflurane and sevoflurane for carotid endarterectomy. *Anaesthesia*. 2000;55(11):1052–1057.

C.13. How would you proceed if the patient were to receive regional anesthesia?

Patient cooperation is essential for a regional anesthetic to proceed successfully. For a patient to be adequately anesthetized, a sensory blockade is required in the C2–C4 dermatomes. This can be accomplished with either deep or superficial cervical plexus blocks. In doing the blocks, care must be taken not to excessively palpate the neck because part of the plaque in the carotid artery may dislodge and embolize.

Superficial cervical plexus blocks are performed by infiltrating along with middle third of the posterior border of the sternocleidomastoid muscle with local anesthesia. Deep cervical plexus blocks are performed with three injections along a line drawn from Chassaignac tubercle (C6) to the mastoid process. The C4 nerve root is located at the intersection of that line with one drawn horizontally from the lower border of the mandible. C2 and C3 are located by dividing the distance between the mastoid process and the horizontal line into thirds. Alternatively, a single injection of local anesthetic can be made on the line between the mastoid process and Chassaignac tubercle at the level of C4 with the needle directed medially and slightly caudad.

Patients receiving regional anesthesia must be both cooperative and not overly sedated with intravenous medications. If they are unable to cooperate and become obtunded, the primary advantage of regional anesthesia (which is continuous neurologic evaluation) is lost. Intravenous sedation, therefore, must be given judiciously, if at all, to these patients.

Gropper MA, Eriksson LI, Fleisher LA, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier Saunders; 2019:1825–1867.

Unic-Stojanovic D, Babic S, Neskovic V. General versus regional anesthesia

for carotid endarterectomy. *J Cardiothorac Vasc Anesth*. 2013;27(6):1379–1383.

C.14. Discuss the effects of anesthetics on CBF.

It is important to remember that all general anesthetics affect CBF and cerebral metabolic oxygen consumption. This can be used to the anesthesiologist's advantage when the decrease in oxygen consumption is greater than the decrease in CBF.

In general, volatile anesthetics are cerebral vasodilators and intravenous anesthetics are cerebral vasoconstrictors. Ketamine is an exception because it can increase in both CBF and cerebral metabolic rate. Volatile anesthetics produce a dose-dependent increase in CBF. The magnitude of vasodilation depends on the balance between the anesthetic's intrinsic vasodilatory property and vasoconstriction secondary to its reduction in cerebral metabolic rate.

Studies suggest that anesthetic agents only affect the blood flow in normally perfused areas of the brain. If this is the case, volatile anesthetics could cause a steal phenomenon, in which the blood vessels in normal brain dilate and steal blood flow away from ischemic areas of the brain that are both already maximally vasodilated and unresponsive to further vasodilating effects of the anesthetics.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1120–1127.

Gropper MA, Eriksson LI, Fleisher LA, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier Saunders; 2019:1825–1867.

C.15. Discuss the protective effects of anesthetic agents on cerebral function.

Although it has not been proven that general anesthetics afford brain protection, agents that cause the greatest decrease in cerebral metabolic oxygen consumption should lessen the risk of cerebral ischemia. Whether a particular anesthetic is optimal for

these patients is an area of discussion. Obviously, avoiding or eliminating ischemia is preferable to protecting against it.

Messick et al. examined the effects of volatile anesthetics on critical regional CBF, that is, the regional CBF at which EEG evidence of cerebral ischemia became apparent. They found that critical regional CBF in patients receiving isoflurane was less than 10 mL/100 g/min, and in patients receiving halothane was 18 to 20 mL/100 g/min. This decrease in critical CBF suggests that isoflurane may offer some protective effect. Because of the potential to cause a decrease in blood pressure and reflex increase in heart rate, it probably should not be used at high concentrations as the sole anesthetic. A significant proportion of patients with carotid artery disease also have coronary artery disease and may not tolerate the hypotension and tachycardia associated with the use of high-dose isoflurane. By using this anesthetic in low concentrations in combination with other anesthetic agents, one can better maintain hemodynamic stability while perhaps providing for an increased tolerance of cerebral hypoperfusion. Other evidence suggests that isoflurane may not offer protection during regional cerebral ischemia.

The newer agents sevoflurane and desflurane have been investigated for their possible role in neuroanesthesia. Compared to isoflurane, desflurane has no significant difference in its effects on decreasing cerebral glucose utilization, increasing blood flow, and maintaining coupling between local CBF and local cerebral glucose utilization. Although sevoflurane showed no significant difference in its effects on decreasing cerebral glucose utilization and coupling between local CBF and local cerebral glucose utilization at one minimum alveolar concentration, it did show less of an increase in CBF. This difference between isoflurane and sevoflurane was independent of their effects on systemic blood flow and cardiac output. Hence, desflurane and sevoflurane may have similar

neuroprotective effects as isoflurane and, with their lower blood gas solubility coefficients, may promote a more rapid recovery from anesthesia, allowing faster evaluation of neurologic status.

Thiopental affords cerebral protection against focal or incomplete global cerebral ischemia. It is a cerebral vasoconstrictor, as are most other intravenous anesthetics. It will also transiently decrease cerebral metabolism from 40% to 50% of baseline. The combined effect is that cerebral metabolic oxygen consumption is decreased more than oxygen delivery. The reduction in oxygen demand is the result of inhibition of functioning neurons, which can be observed as a quiet or isoelectric EEG. When dosing barbiturates for cerebral protection, the EEG should be monitored and repeated doses given to achieve and then maintain a burst suppression pattern. Once the EEG is isoelectric, indicating lack of neuronal function, further doses of thiopental do not provide additional protection. It is generally not recommended that thiopental be used for cerebral protection during CEA. As mentioned previously, avoidance of ischemia is preferable to its treatment. If thiopental is used, the EEG, because of its isoelectricity, becomes useless as a monitor of cerebral ischemia. This is especially problematic if selective shunting is to be done. Furthermore, the doses of thiopental required to suppress the EEG may cause hypotension and a delayed emergence from anesthesia. Barbiturate use to minimize the possibility of cerebral ischemia has been advocated for the patient undergoing carotid bypass procedures in which temporary occlusion of the recipient vessel is required. Whether treatment of patients with a 3 to 5 mg per kg dose of thiopental affects their outcome in terms of neurologic deficit is not known, although it has been shown to be efficacious in animal models.

Like barbiturates, the intravenous anesthetics propofol and etomidate also decrease brain electrical activity and cellular

oxygen requirements while preserving cerebral autoregulation of blood flow. Although the available evidence for the protective effects of etomidate and propofol during CEA is inconclusive, these agents reduce brain infarction and prolong tolerable ischemia time in patients undergoing temporary ischemia for intracranial aneurysm clipping. Additionally, animal studies have suggested a degree of neuroprotection with propofol.

Dexmedetomidine is a selective α_2-adrenergic agonist with sedative, analgesic, and anxiolytic properties. It does not cause respiratory depression. In animal studies, dexmedetomidine reduces ischemic damage after transient and permanent ischemia. Its mechanism of neuroprotection is unclear. One hypothesis suggests that with the onset of cerebral ischemia, one of the initial responses in the central nervous system is the excessive release of norepinephrine and glutamate during energy failure. If the increase in norepinephrine release is a causative component of injury, an α_2-adrenergic agonist may decrease the damage afforded by cerebral ischemia. Dexmedetomidine has been shown to reduce arousal and decrease CBF in volunteers.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1120–1127.

Hicks RG, Kerr DR, Horton DA. Thiopentone cerebral protection under EEG control during carotid endarterectomy. *Anaesth Intensive Care*. 1986;14:22–28.

Holzer A, Greher M, Hetz H, et al. Influence of aortic blood flow velocity on changes of middle cerebral artery blood flow velocity during isoflurane and sevoflurane anaesthesia. *Eur J Anaesthesiol*. 2001;18:238–244.

Kuhmonen J, Pokorný J, Miettinen R, et al. Neuroprotective effects of dexmedetomidine in the gerbil hippocampus after transient global ischemia. *Anesthesiology*. 1997;87:371–377.

Matta BF, Heath KJ, Tipping K, et al. Direct cerebral vasodilatory effects of sevoflurane and isoflurane. *Anesthesiology*. 1999;91:677–680.

Messick JM Jr, Casement B, Sharbrough FW, et al. Correlation of regional cerebral blood flow (rCBF) with EEG changes during isoflurane anesthesia for carotid endarterectomy: critical rCBF. *Anesthesiology*. 1987;66:344–349.

Michenfelder JD, Sundt TM, Fode N, et al. Isoflurane when compared to enflurane and halothane decreases the frequency of cerebral ischemia during carotid endarterectomy. *Anesthesiology*. 1987;67:336–340.

Nehls DG, Todd MM, Spetzler RF, et al. A comparison of the cerebral protective effects of isoflurane and barbiturates during temporary focal ischemia in primates. *Anesthesiology*. 1987;66:453–464.

C.16. How will you manage this patient's ventilation under general anesthesia?

Because carbon dioxide is a potent cerebral vasodilator, patients undergoing CEA historically were hypoventilated intraoperatively to achieve hypercarbia and cerebral vasodilation. However, it is now accepted that hypercapnia should be avoided in patients with carotid artery disease. Carbon dioxide causes vasodilation in normally reactive, nonischemic, vascular beds. In patients with carotid artery disease, this means that blood flow is diverted away from the already maximally dilated vessels in the territory of the occluded carotid and toward normal areas of the brain. This decrease in regional CBF in ischemic areas of the brain with increased CBF in normal areas of the brain is known as *intracerebral steal*.

Other authors have recommended extreme hypocapnia during CEA, reasoning that this would result in an "inverse steal" or "Robin Hood" phenomenon. Hypocapnia will cause constriction of cerebral vessels in normally perfused areas of the brain, possibly diverting blood flow into the maximally vasodilated, unreactive, hypoperfused regions of the brain. Clinical trials have been unable to demonstrate any benefit from hypocapnia, and animal studies have shown that it may, in fact, exacerbate ischemia. This most likely happens not only because of intense vasoconstriction but also because of a leftward shift of the oxyhemoglobin dissociation curve so that hemoglobin is less able to give its oxygen to tissues.

The general recommendation for patients with

cerebrovascular disease is that normocarbia or mild hypocarbia be maintained. After repair of their carotid stenosis, some patients will have a marked hyperemia with CBF of 100 mL/100 g/min. In these patients, decreasing both blood pressure and arterial carbon dioxide tension to decrease their CBF is indicated. Without a decrease in CBF, these patients are at risk for postoperative intracerebral hemorrhage.

Baker WH, Rodman JA, Barnes RW, et al. An evaluation of hypocarbia and hypercarbia during carotid endarterectomy. *Stroke*. 1976;7:451–454.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1120–1127.

Gropper MA, Eriksson LI, Fleisher LA, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier Saunders; 2019:1825–1867.

C.17. How will you manage this patient's blood pressure intraoperatively?

Various factors need to be considered in the blood pressure management of patients undergoing CEA. In the patient with carotid artery disease, a loss of autoregulation occurs in ischemic areas of the brain. In areas of chronic hypoperfusion, vessels are maximally vasodilated and unresponsive to vasomotor stimuli. Perfusion in these ischemic areas is pressure dependent.

During cerebral arterial occlusion, systemic blood pressure may need to be increased to augment collateral blood flow. The primary collateral pathways include the Willisian channels. If Willisian channels are not available, either because of the patient's anatomy or a therapeutic intervention, secondary collateral channels are available that bridge adjacent major vascular territories. These pathways are known as the *pial-to-pial collateral* or *leptomeningeal* pathways.

Because of the adjustment of the autoregulatory limits in hypertensive patients and because of a lack of autoregulation in

ischemic areas of the brain, hypotension should be avoided. Blood pressure should be maintained in its high normal range. During arterial occlusion, the only practical way to increase collateral blood flow may be by increasing the collateral perfusion pressure by raising the systemic blood pressure. The extent to which the blood pressure should be raised depends on the nature of the disease. During deliberate hypertension, the systemic blood pressure is raised by 30% to 40% above the baseline or until ischemic symptoms resolve. Both maintenance of and increases in blood pressure can be accomplished with light anesthesia and, when necessary, infusion of the α-agonist phenylephrine. Phenylephrine has no direct effect on the cerebral vasculature; therefore, cerebral perfusion is increased by an elevation in the CPP. Phenylephrine increases blood pressure, CPP, stump pressure, and regional CBF. It also increases myocardial oxygen consumption. Because it increases afterload, care must be taken when it is used in patients with coronary artery disease, and it can exacerbate myocardial ischemia and congestive heart failure. In patients with coronary artery disease, blood pressure should not be increased above baseline unless evidence of cerebral ischemia develops. Extreme increases in blood pressure can and should be managed with easily titratable intravenous vasodilators.

Once the stenosis has been relieved and the carotid cross-clamp removed, the patient's blood pressure should be maintained in its low normal range. This lowering of blood pressure offers several advantages. It decreases myocardial oxygen consumption by decreasing the work of the heart, it decreases the amount of stress on the suture line in the carotid artery, and finally, it minimizes the possibility of reperfusion hemorrhage.

Aaslid R, Lindegaard KF, Sorteberg W, et al. Cerebral autoregulation

dynamics in humans. *Stroke*. 1989;20:45–52.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1120–1127.

Gropper MA, Eriksson LI, Fleisher LA, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier Saunders; 2019:1825–1867.

Smith JS, Roizen MF, Cahalan MK, et al. Does anesthetic technique make a difference? Augmentation of systolic blood pressure during carotid endarterectomy: effects of phenylephrine versus light anesthesia and of isoflurane versus halothane on the incidence of myocardial ischemia. *Anesthesiology*. 1988;69:846–853.

C.18. Discuss reperfusion injury following CEA and CAS.

Reperfusion injury involves cerebral hemorrhage or the development of cerebral edema after obstruction to flow through the carotid artery has been relieved. Although rare, it is an often fatal complication of CEA. Patients present with headache, seizure, focal neurologic signs, brain edema, and intracerebral bleeds. The incidence of intracerebral hemorrhage after CEA ranges from 0.4% to 2.0%, and it usually occurs 1 to 5 days after surgery. Patients with a previous stroke are most likely to suffer reperfusion hemorrhage, but it can occur in otherwise normal brain tissue. Poorly controlled blood pressure after the carotid cross-clamp has been removed contributes to this complication. One proposed mechanism for this injury is that once flow is returned to normal, vascular beds in previously hypoperfused areas of the brain are unable to respond properly with vasoconstriction. They are unable to maintain normal flow with increased perfusion. Because hypoperfusion distal to the carotid stenosis has been long-standing, these vessels have lost their ability to autoregulate. Once the carotid stenosis is eliminated, the perfusion pressure distal to the former site of the stenosis is markedly increased. Because of the lack of autoregulation in this area, CBF increases with increasing perfusion pressure. The patients at highest risk for reperfusion injury have the greatest degree of stenosis and the greatest pressure drop across the

carotid lesion. Again, maintaining blood pressure control with antihypertensive medications once the carotid obstruction is eliminated decreases the incidence of reperfusion injury.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1120–1127.

Breen JC, Caplan LF, DeWitt LD, et al. Brain edema after carotid surgery. *Neurology*. 1996;46:175–181.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2106–2157.

Solomon RA, Loftus CM, Quest DO, et al. Incidence and etiology of intracerebral hemorrhage following carotid endarterectomy. *J Neurosurg*. 1986;64:29–34.

C.19. What intravenous fluids will you give this patient intraoperatively?

Because moderate hyperglycemia has been shown to worsen neurologic outcome after ischemia, care must be taken to avoid increasing glucose by exogenous administration. Balanced intravenous fluids such as PlasmaLyte, lactated Ringer's solution, or another buffered crystalloid solution would be appropriate choices for patients undergoing CEA.

These patients should not be vigorously hydrated intraoperatively. It is best to limit their intraoperative fluids to what is required for maintenance, with additional colloid and blood replacement being given as needed. Intraoperative overhydration may lead to some of the frequently observed postoperative hypertension and in patients with myocardial disease may exacerbate congestive heart failure.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1120–1127.

Gropper MA, Eriksson LI, Fleisher LA, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier Saunders; 2019:1825–1867.

Li PA, Siesjö BK. Role of hyperglycaemia-related acidosis in ischaemic brain damage. *Acta Physiol Scand*. 1997;161:567–580.

McGrit MJ, Woodworth GF, Brooke BS, et al. Hyperglycemia independently increases the risk of perioperative stroke, myocardial infarction, and death after carotid endarterectomy. *Neurosurgery*. 2006;58:1066–1073.

D. Postoperative Management

D.1. The patient does not "wake up" from general anesthesia. Why?

Once other causes of slow emergence from general anesthesia (e.g., hyperglycemia or hypoglycemia, hypothermia, anesthetic overdose, hypercarbia, and hypoxemia) have been ruled out, the possibility of an adverse intraoperative event having occurred needs to be considered. Patency of the carotid artery should be evaluated. This can be done by Doppler studies while the patient is still in the operating room. If no blood flow is seen in the carotid artery, the incision can be reexplored immediately. If Doppler studies are normal, the possibility of a cerebral infarction from prolonged hypoperfusion or from emboli must be considered. The patient should remain intubated while further studies, including a computed tomography (CT) scan and cerebral angiography, are done as expeditiously as possible. The incidence of new perioperative neurologic deficits is 3% or less in centers where the operation is done commonly.

Graber JN, Vollman RW, Johnson WC, et al. Stroke after carotid endarterectomy: risk as predicted by preoperative computerized tomography. *Am J Surg*. 1984;147:492–497.

Gropper MA, Eriksson LI, Fleisher LA, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier Saunders; 2019:1825–1867.

Paciaroni M, Eliasziw M, Kappelle LJ, et al. Medical complications associated with carotid endarterectomy. *Stroke*. 1999;30:1759–1763.

D.2. Postoperatively, the patient's blood pressure is 170/96 mmHg. Will you treat this?

This patient's blood pressure needs to be carefully controlled

because postoperative hypertension is associated with bleeding at the operative site, myocardial ischemia, arrhythmias, intracerebral hemorrhage, and cerebral edema.

Hypertension is observed more commonly than hypotension after CEA. Causes of hypertension include hypoxemia, hypercarbia, pain, and a full bladder. Obviously, if any or all of these causes are present, they need to be dealt with promptly. Another common cause of postoperative hypertension and tachycardia is blunting of the carotid baroreceptor mechanism secondary to carotid sinus dysfunction caused by surgical trauma. If this is the cause of hypertension, therapy with antihypertensive agents should be started.

This patient's blood pressure should be maintained in her low normal range postoperatively. Elevated blood pressure can be treated with hydralazine in 5-mg increments or, if the patient is not bradycardic, labetalol in 5- to 10-mg increments. Alternatively, infusions of nicardipine, sodium nitroprusside, or nitroglycerin can be used. β-Blockade with metoprolol or an infusion of esmolol may be added to this regimen.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1120–1127.

Gropper MA, Eriksson LI, Fleisher LA, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier Saunders; 2019:1825–1867.

D.3. What immediate postoperative complications might you expect after a CEA?

Immediate postoperative complications include neurologic deficits, hemodynamic instability, and respiratory insufficiency. Evaluation of the NASCET showed that 8.1% of patients had medical complications: 1% with MIs, 7.1% with other cardiovascular disorders such as arrhythmias and congestive heart failure, 0.8% with respiratory complications, 0.4% with transient confusion, and 0.7% with other complications. CEA is

1.5 times more likely to be associated with complications in patients with a history of cardiac disease or hypertension.

Postoperative neurologic complications are usually embolic in nature, occurring during surgery. Other neurologic complications result from reperfusion injury and intracranial hemorrhage.

Circulatory instability is common after CEA, with either hypotension or hypertension observed. Hypotension can have any of several causes, as does hypertension, as noted previously. These include hypovolemia, depression of the circulation by residual anesthetics, prolonged effect of intraoperatively administered antihypertensives, dysrhythmias, and myocardial ischemia. Each of these causes needs to be sought and, if present, treated. Another possible cause of hypotension is an excessive reflex response because of increased sensitivity of the carotid sinus after exposure of the baroreceptor mechanism to a higher pressure with removal of the plaque. If this is the cause, therapy needs to be instituted with fluids and vasopressors.

Postoperative respiratory insufficiency is a rare but potentially life-threatening complication. This can be due to vocal cord paralysis from intraoperative traction on the laryngeal nerves. Should this present with inability to protect the airway, the patient should be reintubated immediately. A prospective trial found that 12.5% of patients had nerve injuries after CEA, but all were transient, lasting from 1 week to 37 months. No patient had life-threatening respiratory insufficiency from the nerve injuries. The most commonly injured nerves were the hypoglossal, recurrent laryngeal, superior laryngeal, and greater auricular nerves.

Airway obstruction can also occur from hematoma formation at the operative site, from either arterial or venous bleeding. The hematoma needs to be evacuated as quickly as possible, and depending on ventilatory status, the patient may need to be

intubated. This is most easily done after evacuation of the hematoma if the clinical condition allows. Supraglottic edema may also be a rare cause of postoperative upper airway obstruction after CEA. CT analysis of airways postoperatively showed reduction in the volume of the airway in all patients, with a greater reduction seen in intubated patients (63% ± 9%) than in nonintubated patients (32% ± 7%).

Tension pneumothorax can result from air dissecting through the wound and the mediastinum to the pleura. This diagnosis should be considered in all patients after CEA who seem to have respiratory distress and no evidence of upper airway obstruction. Absence of breath sounds over half of the chest and hemodynamic instability would support this diagnosis.

Chemoreceptor function is irreversibly suspended in most patients after CEA for up to 10 months. Lack of chemoreceptor function means that there is a loss of circulatory response to hypoxia and an increase in resting Pa_{CO_2} of approximately 6 mmHg. This complication is potentially very serious, and one needs to be most concerned about its development in patients who have had a previous contralateral CEA, where function may be lost bilaterally. In all patients after CEA, supplemental oxygen should be provided and opioids administered cautiously.

Ballotta E, Da Giau G, Renon L, et al. Cranial and cervical nerve injuries after carotid endarterectomy: a prospective study. *Surgery*. 1999;125:85–91.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1120–1127.

Carmichael FJ, McGuire GP, Wong DT, et al. Computed tomographic analysis of airway dimensions after carotid endarterectomy. *Anesth Analg*. 1996;83:12–17.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1855–1864.

Paciaroni M, Eliasziw M, Kappelle LJ, et al. Medical complications associated with carotid endarterectomy. *Stroke*. 1999;30:1759–1763.

Wade JG, Larson CP Jr, Hickey RF, et al. Effects of carotid endarterectomy

on carotid chemoreceptor and baroreceptor function in man. *N Engl J Med*. 1970;282:823–829.

D.4. What postoperative complications might you expect after a CAS?

Complications after CAS include hemodynamic instability, stroke, MI, renal failure, and access-related problems. In a pooled analysis of 27 studies, Mylonas et al. found that approximately 39% of patients experienced some degree of hemodynamic instability (bradycardia/hypotension) after CAS, but in a majority of patients it resolved in 8 to 10 hours. Stroke following CAS could be secondary to thromboembolism, hypoperfusion, stent thrombosis, intracranial hemorrhage, or cerebral hyperperfusion. In several pooled meta-analysis studies, the periprocedural risk of stroke following stenting appears to be higher than CEA, but this is debated as stroke rates have improved since the introduction of CAS. The risk of MI in CAS ranges from 1% to 4%. Renal dysfunction following CAS is attributed to contrast-induced nephropathy, atheroembolism from instrumentation of the aorta or hypoperfusion from hemodynamic instability. Access-related problems are related to pseudoaneurysm formation, bleeding, and atheroembolism to the lower extremities.

Economopoulos KP, Sergentanis TN, Tsivgoulis G, et al. Carotid artery stenting versus carotid endarterectomy: a comprehensive meta-analysis of short-term and long-term outcomes. *Stroke*. 2011;42:687–692.

Kim LK, Yang DC, Swaminathan RV, et al. Comparison of trends and outcomes of carotid artery stenting and endarterectomy in the United States, 2001 to 2010. *Circ Cardiovasc Interv*. 2014;7:692–700.

Moulakakis KG, Mylonas SN, Lazaris A, et al. Acute carotid stent thrombosis: a comprehensive review. *Vasc Endovascular Surg*. 2016;50:511–521.

Mylonas SN, Moulakakis KG, Antonopoulos CN, et al. Carotid artery stenting-induced hemodynamic instability. *J Endovasc Ther*. 2013;20:48–60.

Qureshi AI, Luft AR, Sharma M, et al. Frequency and determinants of postprocedural hemodynamic instability after carotid angioplasty and stenting.

Stroke. 1999;30:2086–2093.

Vincent S, Eberg M, Eisenberg MJ, et al. Meta-analysis of randomized controlled trials comparing the long-term outcomes of carotid artery stenting versus endarterectomy. *Circ Cardiovasc Qual Outcomes*. 2015;8:S99–S108.

D.5. Discuss postoperative neurocognitive dysfunction following uncomplicated carotid intervention.

CEA can reduce the incidence of stroke in patients with high-grade carotid artery stenosis. Increasing evidence suggests that as many as 28% of surgical patients have significant neuropsychological dysfunction 1 day after carotid artery surgery. Between 9% and 23% of these patients continue to exhibit cognitive decline 1 month after surgery.

The apolipoprotein E (APOE)-ε4 allele has been associated with worse outcome following stroke. In a prospective trial, 75 patients undergoing CEA were studied. Of 75 patients, 12 (16%) possessed the APOE-ε4 allele. Of the 75 patients, 8 (11%) experienced cognitive dysfunction on postoperative day 30. One month after CEA, APOE-ε4-positive patients were more likely to have suffered a neurocognitive injury (42%) than APOE-ε4-negative patients (5%). The presence of the APOE-ε4 allele increases the risk of neurocognitive dysfunction 62-fold 1 month after surgery. Diabetes mellitus and obesity also predisposed to injury.

Evidence also indicates increased cognitive dysfunction in patients with carotid stenosis treated with stenting performed under cerebral embolic protection. In a prospective case control study, 41% of patients undergoing carotid stenting developed moderate-to-severe cognitive dysfunction compared to a matched control group. The average deficit score was significantly higher in the CAS group at 1 day. These differences were independent of age and history of stroke or TIA. The absence of oral statin medication may increase the probability of cognitive dysfunction.

The influence of regional versus general anesthesia in postoperative subclinical cognitive dysfunction remains unclear, although a study by Heyer et. al showed no difference in the incidence if cognitive dysfunction in patients who underwent CEA under general or regional anesthesia. Most concur that multiple factors, including surgical technique, anesthetic technique, and patient status, influence postoperative outcome.

Gaudet JG, Meyers PM, McKinsey JF, et al. Incidence of moderate to severe cognitive dysfunction in patients treated with carotid artery stenting. *Neurosurgery*. 2009;65:325–329.

Heyer EJ, Gold MI, Kirby EW, et al. A study of cognitive dysfunction in patients having carotid endarterectomy performed with regional anesthesia. *Anesth Analg*. 2008;107:636–642.

Heyer EJ, Wilson DA, Sahlein DH, et al. APOE-epsilon4 predisposes to cognitive dysfunction following uncomplicated carotid endarterectomy. *Neurology*. 2005;65:1759–1763.

Mazul-Sunko B, Hromatko I, Tadinac M, et al. Subclinical neurocognitive dysfunction after carotid endarterectomy—the impact of shunting. *J Neurosurg Anesthesiol*. 2010;22:195–201.

19 Awake Craniotomy for Mapping and Surgery in the Eloquent Cortex

Thomas A. Moore II and
Kenneth G. Smithson

A 30-year-old right-handed male presented with increased seizure frequency and tumor progression following two prior awake craniotomies. The initial pathology was reported as a World Health Organization (WHO) grade II oligodendroglioma. Following the second awake craniotomy, the tumor had undergone malignant transformation to a WHO grade IV glioblastoma multiforme (isocitrate dehydrogenase [IDH]-mutated). Magnetic resonance imaging (MRI) revealed a 5.6 × 2.9 × 3.6 cm heterogeneously enhancing lesion with associated marked vasogenic edema in the right frontoparietal and temporoparietal white matter, with effacement of the right lateral ventricle (**Fig. 19.1A**). His anticonvulsant medications were increased, and he was given a short course of a corticosteroid with symptom improvement. He underwent functional MRI (fMRI) that revealed asymmetric cortical activation in the right motor cortex when compared to the left side. The primary descending fibers of the corticospinal tract (CST) were intimately associated with the medial enhancing margin of the tumor (**Fig. 19.1B**). He underwent a third uncomplicated awake craniotomy with motor and sensory mapping. He was discharged to home on postoperative day 2. Final pathology

revealed a WHO grade IV glioblastoma multiforme (IDH-mutated).

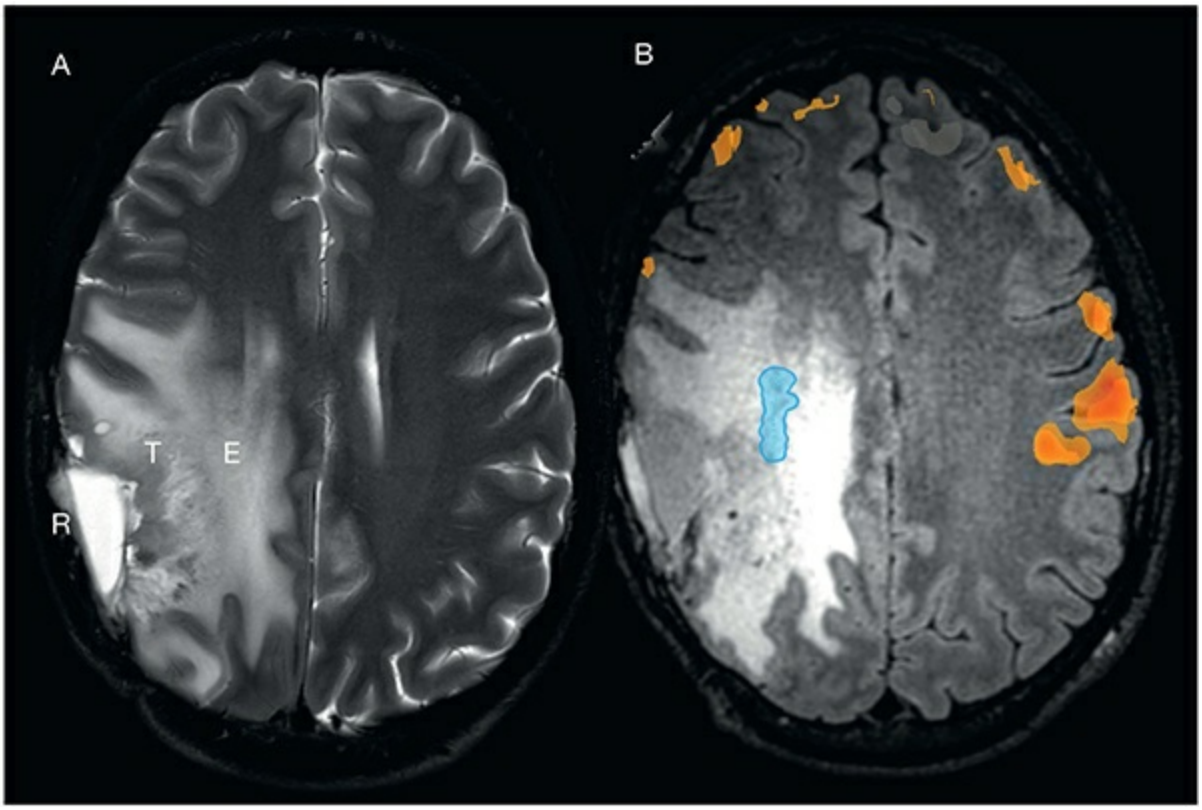

FIGURE 19.1. A. A 30-year-old male with a known glioblastoma presents with increasing seizure frequency and tumor progression on follow-up studies. Note the remarkable level of vasogenic edema (E) surrounding the tumor (T) and extensive effacement of the right lateral ventricle. This patient underwent an uncomplicated redo-awake craniotomy with motor and sensory mapping. Final pathology was a WHO grade IV glioblastoma multiforme. R, prior resection cavity. **B.** A 30-year-old male with recurrent glioblastoma undergoing a repeat awake craniotomy. fMRI demonstrates asymmetric cortical activity from bilateral and right-hand tapping in orange color. The intimate proximity of the CST, in blue, to the medial enhancing margin of the tumor is evident. Juxtaposition of new tumor growth, pervasive edema, and more important, the cortical spinal tract proximity made simple resection via stereotactic methods virtually impossible. Only an awake patient who is actively involved in cortical mapping via task performance could minimize damage to the CST.

A. Medical Disease and Differential Diagnosis

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2. What is the underlying pathology?
3. What determines intracranial pressure (ICP)?
4. How does a space-occupying mass alter ICP?

5. What is autoregulation, and why is it important?
6. How is cerebral blood flow (CBF) regulated?
7. What drug therapies may be associated with this pathology?

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1. What are the major concerns following craniotomy?

A. Medical Disease and Differential Diagnosis

A.1. What is the eloquent cortex?

Eloquent cortex is a term usually used to describe functional areas of the cerebral cortex associated with motor, language, and sensory activity. Traditionally, tumors or epileptic foci within or near these areas have been termed *inoperable* because of the devastation caused to the patient by injury to these critical brain regions.

De Benedictis A, Moritz-Gasser S, Duffau H. Awake mapping optimizes the extent of resection for low-grade gliomas in eloquent areas. *Neurosurgery*. 2010;66(6):1074–1084.

A.2. What is the underlying pathology?

The underlying pathology requiring an awake craniotomy for mapping and resection within the eloquent cortex can be either a space-occupying lesion or epileptic foci. In either case, mapping of the cortical and subcortical structures with an awake and cooperative patient is necessary to minimize neurologic injury and maximize lesion resection. Mapping of the motor cortex is often done under general anesthesia, and more specifically a total intravenous (IV) anesthetic typically with a propofol and remifentanil infusions, after reversal of any residual muscle relaxant because the stimulated area(s) can usually be seen by an observer. Additionally, motor responses are directly measured electrophysiologically as muscle motor evoked potentials (mMEPs). These same techniques can also be done in the awake patient. Nevertheless, there are several potential problems. In the case of a space-occupying lesion, the neuronal pathways can become distorted secondary to the expanding mass and mislead the surgeon who is searching not only for the functional area but also a “quiet” area of cortex through which to do the resection. In addition, these patients are frequently in a lateral decubitus position, with the side to be observed in the down position, obscuring small motor responses. Visualization of the patient

can be further obstructed with sheets, blankets, forced warm-air blankets, and other patient-positioning devices. Hence, we tend to map the motor cortex in an awake craniotomy whenever possible and monitor mMEPs simultaneously. Furthermore, in cases involving complex sensory or motor activities such as language comprehension or speech production, our current electrophysiologic and imaging techniques remain limited as compared to the awake and interactive patient.

Supratentorial brain tumors are about 31% gliomas, 15% meningiomas, 12% metastatic lesions, and 8% pituitary tumors (**Fig. 19.1**). Metastatic lesions are most frequently lung, breast, and gastrointestinal tract tumors. Additional space-occupying lesions include blood and blood vessels, infections, hydrocephalus, cerebral infarctions, radiation necrosis, arachnoid cysts, and cerebral edema. Several of these often coexist depending on the primary pathology of the lesion.

These space-occupying lesions can present in various manners. The most common presentation of brain tumors is a progressive neurologic deficit (68%), usually motor weakness (45%), headache (54%), and seizures (26%). Others may present from progressive focal deficits resulting from infiltration of tumor cells and destruction of normal brain cytoarchitecture or compression or displacement of normal brain structures by the mass itself or peritumoral edema. Additional presentations include nausea or vomiting, vertigo, lethargy, apathy, and changes in mental status as several examples.

In addition to these various presenting signs and symptoms, asymmetric supratentorial tumors can enlarge to the point of causing a midline shift of the intracranial contents, possibly leading to herniation. The brain can be displaced across the midline beneath the falx or compressed through the tentorial incisura into the posterior fossa. As these various areas of the brain are compressed against these dense fibrous structures,

stretching and shearing of the penetrating arteries can result in devastating neurologic injuries.

An area of cerebral edema surrounds most intracranial masses; secondary to the disruption of the blood–brain barrier (BBB) usually associated with a localized acidosis. Vasogenic edema reflects a shift of fluid from the intravascular to the extravascular space; the interstitial space of the brain. Cytotoxic edema represents a shift of fluid from the extracellular to the intracellular space. Vasogenic edema responds very well to corticosteroid treatment. Dexamethasone is frequently prescribed for this problem. This area of cerebral edema is known as the penumbral area and represents areas of autoregulatory dysfunction as well as BBB breakdown. The vasculature in this area of the brain is usually maximally vasodilated. Hypercapnia in surrounding normal brain causes vasodilation in the normal vasculature and may result in decreased flow to the ischemic area. Hypocapnia, on the other hand, causes vasoconstriction of the normal adjacent vascular beds, with the resultant redistribution of blood to the ischemic area. This has been referred to as the "Robin Hood" phenomenon. The formation of peritumoral edema increases the overall size of the tumor, which can lead to or exacerbate the same signs and symptoms as noted earlier. Such was the case in our patient (**Fig. 19.1**), a tumor with much vasogenic edema, who had a dramatic improvement in symptoms after initiation of dexamethasone.

Patients presenting for an awake craniotomy for excision of an epileptic foci have usually had a seizure disorder for many years and have been on numerous antiepileptic drugs (AEDs) in an attempt to control their disorder. Unfortunately, many of these patients develop adverse reactions or cannot tolerate the side effects of the AEDs and become, for practical purposes, medication failures. **Table 19.1** lists the more common AEDs

and the types of seizure disorder they treat.

TABLE 19.1 Commonly Used Drugs in Seizure Control

Type of Seizure	First-Line Drug	Second-Line Drug
Generalized tonic–clonic	Carbamazepine Phenytoin Valproate	Clobazam Clonazepam Lamotrigine Phenobarbital Vigabatrin Felbamate Acetazolamide
Generalized absence	Valproate Ethosuximide	Clonazepam Lamotrigine Acetazolamide
Tonic, atonic, atypical absences	Valproate Clobazam Clonazepam Lamotrigine Phenytoin	Carbamazepine Phenobarbital Felbamate Acetazolamide
Myoclonic seizures	Valproate Clonazepam	Phenobarbital Acetazolamide
Simple partial, complex partial, secondarily generalized	Carbamazepine Valproate Phenytoin	Clobazam Lamotrigine Gabapentin Vigabatrin Phenobarbital Felbamate Acetazolamide

Reprinted with permission from Frost EAM, LaFleur JL. Awake craniotomy for deep brain stimulation. In: Yao FF, Fontes ML, Malhotra V, eds. *Yao and Artusio's Anesthesiology: Problem-Oriented Patient Management*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:585.

Only patients with seizures in whom the foci are localized in an area of eloquent cortex require an awake craniotomy. Temporal lobe, hippocampal-localized foci are usually resected under general endotracheal anesthesia with intraoperative electrocorticography. Most of these patients have had preceding intracranial strips, grids, or electrodes placed to help localize the seizure foci.

Fishman RA. Brain edema. *N Engl J Med*. 1975;293:706–711.

Greenberg MS, ed. *Handbook of Neurosurgery*. 8th ed. New York: Thieme; 2016:443–460.

O'Rourke DK, Oldfield EH. Supratentorial masses: surgical considerations. In: Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2017:298–316.

A.3. What determines intracranial pressure (ICP)?

The adult skull is a rigid, bony box with a fixed volume. Neonatal and infant skulls have several noncalcified portions, called fontanels, which allow the skull to deform during passage through the birth canal. These noncalcified areas also allow the volume of the skull to increase in the presence of increased ICP such as congenital hydrocephalus. Once these areas have calcified, the pediatric skull is also a rigid, fixed-volume box.

The intracranial constituents are intravascular blood, CSF, and the brain. As liquids, the blood and CSF are noncompressible and can be physiologically redistributed outside of the intracranial space. Although water can be extracted from the brain by use of osmotic diuretics and other hypertonic fluids, this does not result in much change in brain volume, and its gel-like consistency also makes it virtually noncompressible, yet both movable and deformable, often resulting in irreversible damage. This can also be redistributed pathologically outside the intracranial vault with uncal herniation.

ICP is a relationship of the homeostatic balance of the noncompressible contents within a fixed-volume container, the skull. The normal value is 10 to 15 mmHg. In the early 19th century, the Monro-Kellie hypothesis was the first attempt to describe this relationship. Although several modifications of this doctrine have been made over the years as more has been learned, the basic principle still holds true: Because the intact skull is unyielding, an increase in volume of any one of the

normal contents or the addition of a space-occupying lesion must be accompanied by a reduction in one or more of the normal constituents to maintain normal ICP (also see Chapter 17, section A.2).

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2017:59–73.

Mokri B. The Monro-Kellie hypothesis: applications in CSF volume depletion. *Neurology*. 2001;56:1746–1748.

A.4. How does a space-occupying mass alter ICP?

There are limits to the balanced relationship described by the Monro-Kellie hypothesis. **Figure 19.2** represents an idealized ICP–volume curve and diagrams these limitations.

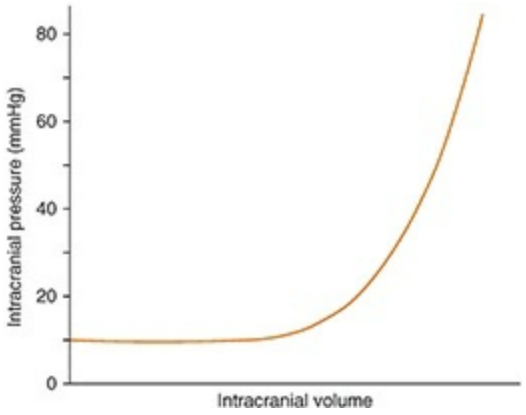

FIGURE 19.2. Idealized ICP volume curve. (*Reprinted with permission from Hou YJ, Kass IS. Physiology and metabolism of the brain and spinal cord. In: Newfield P, Cottrell JE, eds.* Handbook of Neuroanesthesia*. 5th ed. Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2012:16.*)

The flat portion of the curve represents increasing volume with no increase in ICP. Several compensatory mechanisms are at work to keep the ICP steady. The most effective of these mechanisms is the dynamic nature of CSF. The rate of absorption increases or the rate of production decreases in light of an increase in ICP. Cerebral blood volume (CBV) is decreased by a redistribution primarily of the intracranial venous blood volume. These mechanisms work to keep the ICP at its

normal value of 10 to 15 mmHg. As the volume continues to increase, these compensatory mechanisms become exhausted and ICP starts to rise as represented by the “knee” of the graph. It is important to note that at this area of the curve, small increases in volume give rise to a much larger increase in ICP. The sharp rise in the graph demonstrates rapidly increasing ICP with even smaller increases in volume. It is vitally important to understand that as the volume continues to rise and ICP continues to increase, the risk of cerebral herniation also increases. The acute rise in ICP is often a localized increase in intracranial volume associated with the underlying pathologic process with a corresponding localized increase in ICP producing a vectorial force and resulting in movement of the brain. Cerebral perfusion pressure (CPP) is also adversely affected with a rise in ICP. CPP is defined as: CPP = MAP − ICP or CVP (depending on which is higher), where MAP = mean arterial pressure and CVP = central venous pressure. MAP, for the purposes of calculating CPP, is measured at the tragus. Implicit in this measurement is that position of the head relative to the heart can dramatically affect these estimates. This equation also shows that an increase in ICP will lead to a decrease in CPP, if MAP does not increase to maintain CPP. However, an increase in MAP is one of the normal physiologic compensatory mechanisms to maintain CPP and hence brain perfusion. Yet, there are many common clinical situations where this compensatory response has been blunted by preexisting comorbid conditions, acute injury, or drugs (e.g., large doses of propofol).

Figure 19.3 shows that CBF is *independent* of MAP over a wide range of pressures from 50 to 150 mmHg. The magnitude of the CBF is determined by the metabolic demands of the brain. Here, the CBF is dynamically increased or decreased to accommodate the changing electrical activity of the brain and

the associated metabolic processes. Some have advocated that the lower threshold for autoregulation should be shifted toward 70 mmHg and the upper threshold shifted toward 180 mmHg. In the supine position, ICP is effectively zero when the dura is opened, making CPP directly related to MAP (at least for structures adjacent to the open dura).

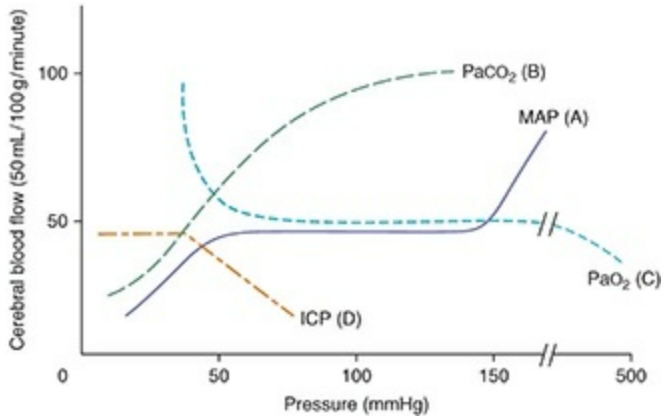

FIGURE 19.3. Pressure–CBF relationships. A, CBF autoregulation. CBF is maintained at 50 mL/100 g/min for mean arterial pressure (MAP) / cerebral perfusion pressure (CPP) = 50 to 150 mmHg; **B,** linear relationship between $PaCO_2$ and CBF for $PaCO_2$ = 20 to 80 mmHg; **C,** PaO_2 and CBF; **D,** intracranial pressure (ICP) and CBF. (*Reprinted with permission from Hou YJ, Ravussin PA. Anesthesia for supratentorial tumors. In: Newfield P, Cottrell JE, eds.* Handbook of Neuroanesthesia. *5th ed. Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2012:118.*)

A.5. What is autoregulation, and why is it important?

In its simplest form, autoregulation is a myogenic response of the vascular smooth muscle of the intracranial cerebral arterioles to dynamically maintain a nearly constant CBF in the face of changing CPP. Not all of the mechanisms controlling this action are fully understood.

When MAP becomes less than 50 mmHg or greater than 150 mmHg, CBF becomes pressure passive. This response is important to keep in mind when considering the use of deliberate hypotension. A MAP of less than 50 mmHg could theoretically cause a decrease in CPP and thereby decrease CBF to the point of causing cerebral ischemia. On the other side of the spectrum, MAPs greater than 150 mmHg can cause

disruption of the BBB and vasogenic edema throughout the brain, not only in the area of vasogenic edema surrounding the tumor.

The autoregulation curve is shifted to the right in the presence of chronic uncontrolled hypertension, as shown in **Figure 19.4**.

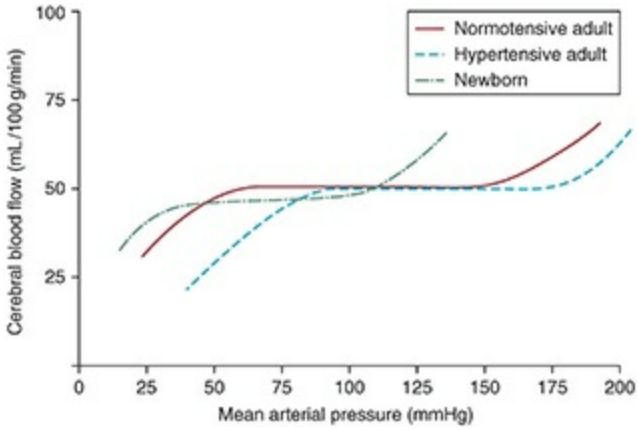

FIGURE 19.4. Autoregulatory curve of the cerebral vasculature in the normotensive adult, the hypertensive adult, and the newborn. (*Reprinted with permission from Hou YJ, Ravussin PA. Anesthesia for supratentorial tumors. In: Newfield P, Cottrell JE, eds.* Handbook of Neuroanesthesia. *5th ed. Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2012:15.*)

This is important because now the lower threshold for cerebral ischemia is higher than in the normal state. Although there is not a direct correlation between degree of hypertension and rightward shift of the autoregulatory curve, it is possible that where signs of cerebral ischemia might not have become obvious until the CPP was 30 to 40 mmHg in the normotensive person, these signs may now occur with the CPP at 80 to 90 mmHg, a usually normal CPP. Therefore, great care must be taken to keep MAP near the patient's usual levels in the uncontrolled or poorly controlled hypertensive patient. On the other end of the curve, it is possible that the rightward shift adds some form of cerebral protection against perfusion breakthrough at the higher CPPs. Chronic treatment with antihypertensive drugs modifies this rightward shift back toward the normal range. The degree to which this occurs depends both on the

length of time the hypertension has been treated and the resultant decrease in blood pressure.

The type of drug used to treat hypertension may also determine the effect on autoregulation. Systemic direct-acting vasodilators without action on cerebrovascular smooth muscle and α-adrenergic and ganglionic blocking drugs should have no effect on cerebrovascular autoregulation. Systemic direct-acting vasodilators that do have an action on the cerebrovascular smooth muscle, such as hydralazine, sodium nitroprusside, nitroglycerin, and calcium channel blockers may influence autoregulation. Treating congestive heart failure may also improve CPP by lowering CVP and thereby decreasing cerebral venous outflow pressure.

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2017:19–58.

Drummond JC. The lower limit of autoregulation: time to revise our thinking? *Anesthesiology*. 1997;86:1431–1433.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1868–1910.

Paulson OB, Strandgaard S, Edvinsson L. Cerebral autoregulation. *Cerebrovasc Brain Metab Rev*. 1990;2:161–192.

A.6. How is cerebral blood flow (CBF) regulated?

In addition to metabolic demand, CBF also responds to modulation by dissolved gases. **Figure 19.3** demonstrates these relationships in the arterial carbon dioxide partial pressure ($PaCO_2$) and arterial oxygen partial pressure (PaO_2) curves. Carbon dioxide (CO_2) concentration is the most potent modulator of CBF. Insonating the middle cerebral artery of a volunteer by means of transcranial Doppler device and asking the subject to hyperventilate will show an increase in cerebral blood velocity reflecting a decrease in CBF secondary to cerebral vascular constriction, usually within 3 to 4 breaths, a

very rapid response. This principle is utilized to treat increased ICP by decreasing CBV secondary to the hyperventilation. However, this mechanism is self-limited after approximately 6 to 10 hours and will no longer provide the decreased ICP.

As shown in **Figure 19.3**, there is a near-linear response in CBF at a $Paco_2$ between 20 and 80 mmHg, with CBF increasing about 2% to 4% for each millimeter of mercury change in $Paco_2$. In general, doubling $Paco_2$ from 40 to 80 mmHg doubles CBF and likewise halving $Paco_2$ from 40 to 20 mmHg halves CBF. This represents maximal vasodilation at extreme hypercapnia and maximal vasoconstriction at extreme hypocapnia, respectively.

CBF also responds to the oxygen partial pressure. As shown in **Figure 19.3**, when the Pao_2 reaches approximately 50 mmHg, a steep increase in CBF occurs, as the Pao_2 continues to fall. At normal Pao_2 levels, CBF is not affected. Hyperoxia can actually cause a 10% to 15% decrease in CBF at 1 atm. Temperature can also affect CBF: For each 1°C decrease in body temperature, the cerebral metabolic rate for oxygen consumption ($CMRO_2$) decreases by approximately 7%. The regulation of CBF is closely coupled to the cerebral metabolism and is reflected by a parallel decrease. These changes are not homogeneous, with more changes seen in the cerebral and cerebellar cortices; less so in the thalamus and no difference in the hypothalamus and brainstem. During hypothermic cardiopulmonary bypass, lowering the body temperature to 26°C results in a 56% calculated reduction in $CMRO_2$ and a 55% reduction in CBF.

The potent inhalational anesthetics can also increase CBF in the presence of decreasing $CMRO_2$, thus uncoupling their relationship. Increasing doses can also blunt the CO_2 response or render CBF pressure passive. CO_2 reactivity is preserved during

intraoperative use of opioids such as fentanyl and remifentanil.

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2017:19–58.

Govier AV, Reves JG, McKay RD, et al. Factors and their influence on regional cerebral blood flow during nonpulsatile cardiopulmonary bypass. *Ann Thorac Surg*. 1984;38:592–600.

A.7. What drug therapies may be associated with this pathology?

Patients can present with intracranial pathology at any age. Patients with comorbidities may be taking medications for hypertension, diabetes mellitus, congestive heart failure, atrial fibrillation, prior myocardial infarction (MI), and reactive airway disease with and without frank chronic obstructive pulmonary disease (COPD) as examples. It is not uncommon today for many patients with cardiac comorbidities to be on anticoagulation and also some form of antiplatelet drug whether they have suffered an MI or not. These chronic comorbid conditions should be well treated and relatively stable, with the coagulation system reconstituted prior to undertaking any awake procedure. The success of the procedure is critically dependent on a compensated and stable cardiopulmonary system and an expectation of relatively small blood loss (<500 ml). The effects of some of these drugs can be reversed with fresh frozen plasma, whereas others are not immediately reversible and need 7 to 10 days before their effect is gone.

Patients with epilepsy may be on several medications in an attempt to control their seizures. These drugs are listed in **Table 19.1**. Presenting signs and symptoms have been described earlier. AEDs are indicated in 26% of patients presenting with seizures who are later diagnosed with a brain tumor.

Another 20% to 45% of patients with brain tumors will eventually develop a seizure after diagnosis. The current

standard (2016) is that prophylactic AEDs should not be started in this group of patients. As a guideline, in patients with brain tumors undergoing craniotomy, prophylactic AEDs may be used, and if there is no seizure activity, they may be tapered, starting 1 week postoperatively. If initiated at the time of surgery, they should be administered early in the procedure because they often have sedating properties and can delay awakening.

As previously discussed, most intracranial mass lesions are surrounded by an area of vasogenic edema to varying extents. The use of steroids, in particular dexamethasone, is commonly employed to help alleviate the problems associated with this. Dexamethasone is more beneficial, and the effect of reducing the area of edema often much more dramatic in metastatic tumors than primary tumors. The usual dosage in the corticosteroid-naive patient is a loading dose of 10 mg IV and then 4 to 6 mg by mouth or IV every 6 hours. Doses of up to 10 mg every 4 hours have been given for severe vasogenic edema. For the patient previously diagnosed and on corticosteroids, the current dose is doubled for acute deterioration.

Greenberg MS. General information, classification and tumor markers. In: Greenberg MS, ed. *Handbook of Neurosurgery*. 8th ed. New York: Thieme; 2016:584–602.

B. Preoperative Evaluation and Preparation

B.1. Why is the craniotomy performed awake?

An awake craniotomy is performed when the pathologic lesion, be it a tumor or an epileptic focus, is in or near an area of eloquent cortex, as defined earlier, in an effort to preserve neurologic function.

The extent of the craniotomy is variable. Some neurosurgeons advocate a carefully planned, limited-exposure craniotomy

defined with neuronavigational devices to encompass primarily the area of the lesion and immediate surrounding brain. Others advocate a large craniotomy exposing a wide cortical area for mapping. In either case, the primary goal of the surgical procedure is to obtain the greatest degree of tumor resection with as little damage to the eloquent cortex as possible and hence the least postoperative neurologic deficit.

Even with the cortex exposed, there are many challenges in identifying these areas of eloquent cortex that demand an awake and cooperative patient. As a tumor within or near the eloquent cortex grows and expands, the various neuronal pathways can become distorted from their normal anatomic locations. Ultrasonography may assist the neurosurgeon in identifying the lesion borders so testing can proceed in the surrounding areas of the cortex. Areas that do not elicit a response, respective of the area being tested, are also identified as areas of negative mapping and may serve as an entrance site for both cortical and subcortical resection as needed. Several studies have indicated that surgery through these areas of absolute negative mapping have a significantly lower incidence of both intraoperative and postoperative neurologic deficits. There is also increasing realization that there are more cortical areas that relate to an acceptable quality of life other than the areas of eloquent cortex. Nonlanguage areas that have to do with visual and/or vestibular functions, spatial awareness, cognitive function, understanding and judgment, memory, calculation, and emotion can be mapped both cortically and subcortically to help prevent postoperative complications that are usually not discussed or described.

De Benedictis A, Moritz-Gasser S, Duffau H. Awake mapping optimizes the extent of resection for low-grade gliomas in eloquent areas. *Neurosurgery*. 2010;66(6):1074–1084.

Duffau H. Awake surgery for nonlanguage mapping. *Neurosurgery*. 2010;66:523–529.

Kim SS, McCutcheon IE, Suki D, et al. Awake craniotomy for brain tumors near eloquent cortex: correlation of intraoperative cortical mapping with neurological outcomes in 309 consecutive patients. *Neurosurgery*. 2009;64:836–846.

B.2. What neurologic symptoms of the patient are important?

In order to successfully complete an awake craniotomy, the patient must be motivated to undergo the demanding procedure and able to effectively communicate with the neurosurgeon, the neurologist or the speech pathologist and the neuroanesthesiologist. The patient's ability to understand and execute a myriad of tasks, depending on the tumor's location, remains of paramount importance. In many cases, the patient must also be able to read short phrases, identify various objects, and describe pictures.

A patient who presents with some form of dysphasia may not be able to participate at all. Expressive dysphasia and global dysphasia are extreme examples but not uncommon presentations. At times, a short course of corticosteroids will decrease the penumbral area enough that verbal testing is practical. Some patients will present greatly agitated. Although this is usually their presenting symptom, they cannot cooperate in any fashion, even with minimal commands, and other means are necessary to care for these patients.

Areas of muscular weakness or paralysis, either from the current problem or past injury, must be identified preoperatively to differentiate between postoperative worsening and new neurologic deficits. Rarely will the patient show improvement in the immediate postoperative period; however, preexisting problems can actually be accentuated in the postoperative period.

Overall, patients who cannot communicate effectively or cooperate do not make good candidates for an awake

craniotomy.

In those patients with an ongoing seizure disorder associated with their tumor or epilepsy, the frequency and character of their ictal and postictal periods should be well understood. Limited seizures during mapping procedures are usually well tolerated if treated promptly. Patients with worsening seizures or generalized tonic–clonic seizures that are frequent are not ideal candidates for an awake procedure. The movements of the body while fixed in a rigid Mayfield frame, hemodynamic derangements, and altered control of the upper airway and ventilation associated with tonic–clonic seizures are potentially life-threatening. In fact, retrospective analysis of failed awake procedure was associated with increased postoperative morbidity and reduction of gross-total resection. Thus, the success of these procedures is critically dependent of good patient selection and the experience of the anesthesia and surgical teams with the nuances of these procedures.

B.3. What is the status of their other comorbid conditions?

Aside from the symptoms associated with their neurologic condition, those associated with the patient's other comorbid conditions can significantly limit the potential success of, and are a relative contraindication to, an awake procedure. This procedure requires the patient to lie in one position with little ability to move and "get-comfortable" for a period of wakefulness of 2 to 4 hours and to remain "motionless" for the remainder of the procedure, typically requiring about 6 to 8 hours of stable hemodynamics and adequate ventilation with an unsecured airway. This represents both a psychological and physiologic stress of significance. There are five common areas of comorbidity to consider when evaluating the relative fitness of the patient for this procedure: morbid obesity, pulmonary,

cardiac, chronic pain, and psychiatric disorders. The morbidly obese patient, body mass index (BMI) >40, presents significant challenges in positioning without incurring skin breakdown and maintenance of upper airway patency in a patient with functional obstructive sleep apnea or hypoventilation syndromes. Poor upper airway control, rocking-shaking ventilatory effort and inability to maintain normocarbia all pose significant challenges. Much of this can be ameliorated with judicious use of airway adjuncts while sedated, in particular, a nasal trumpet. Similarly, COPD particularly with CO_2 retention also complicates CO_2 management. Together, these conditions lead to cerebral vasodilatation and increased CBV. Elevations of CO_2 are particularly detrimental for patients with pulmonary hypertension, especially those with right heart strain. Thus, monitoring of end-tidal CO_2 to help ensure adequacy of ventilation and to minimize CO_2 rebreathing during the initial stages of the procedure is important.

Cardiac arrhythmias such as atrial fibrillation with poor ventricular rate control and poorly or uncontrolled hypertension both place the patient at increased risk for untoward hypotension and hypertension, respectively. Exacerbations of congestive heart failure or ischemic heart disease require further treatment prior to the procedure. Patients with chronic pain pose a special dilemma, especially those on chronic opioid therapy. The short-term management of their chronic pain during the procedure remains problematic because opioids are usually spared to avoid oversedation and hypoventilation. However, this can be addressed with low-dose remifentanil infusion. Paramount to the success of the procedure is the awake and communicative patient; preexisting psychiatric conditions that impair calm and focused attention will most assuredly not improve under the conditions of this procedure and should not be attempted unless

the conditions have been well controlled.

B.4. Are there anesthetic implications from current treatment drugs?

Many of the AEDs currently available for treating patients with seizure disorders or those secondary to a brain tumor are listed in **Table 19.1**. Many of these drugs, such as the benzodiazepines, hydantoin analogs, and phenytoins, can interfere with drug metabolism in the liver, requiring increased dosages of IV anesthetic agents and opioids.

Potential side effects associated with corticosteroid use include, but are not limited to, increased white blood cell (WBC) count, glucose intolerance, corticosteroid "stress ulcers," corticosteroid-induced psychosis, hypertension, water and electrolyte imbalance, suppression of the hypothalamic–pituitary–adrenal axis, weight gain, infection, and impaired wound healing.

B.5. What laboratory data are required?

Although the current practice is to minimize the number of preoperative laboratory tests obtained, several are necessary in the patient undergoing a craniotomy, awake or under general anesthesia, for tumor or epileptic foci resection.

Coagulation studies are a must. Although some tumors can have a significant amount of blood loss associated with their resection (meningioma), bleeding from an abnormal coagulation system into a tumor bed can pose very serious and at times life-threatening problems. Partial thromboplastin time, prothrombin time, international normalized ratio, and fibrinogen and platelet counts are routinely obtained. If patients have been on novel oral anticoagulation (e.g., dabigatran, rivaroxaban, apixaban), there are no routine standardized laboratory studies to quantify drug levels. Institution-specific approaches to monitoring anticoagulation with these drugs should be available in

consultation with a hematologist. In patients who are or have recently taken clopidogrel or other antiplatelet, adenosine diphosphate inhibitors, a platelet activity test is beneficial. This test requires specialized equipment and may be done only at certain times of the day; it may require some form of prenotification to the laboratory to ensure that pretesting preparation is completed before the blood sample arrives. Some AEDs may cause thrombocytopenia, but leukopenia is more common.

Electrolyte studies are necessary. This patient population can have imbalances from substances secreted by the tumor, such as atrial natriuretic factor, or secondary to drug effects, such as hyponatremia or hypokalemia. Blood glucose levels are also included and should be controlled to 120 to 180 mg per dL or less, but hypoglycemia (less than 55 mg per dL) should be avoided. Complete blood count with differential will give information about the hematocrit and WBC count. The differential will be normal if the WBC count is elevated from degranulation of WBCs caused by preoperative corticosteroids. If not, an infection may be present and must be addressed. A routine urinalysis will rule out an asymptomatic urinary tract infection.

Blood type, antibody screen, and crossmatch are also required. In the case of a positive antibody screen, at least 4 units of crossmatched blood are recommended to be available before starting the procedure. Imagine a worst case scenario: a patient with several major antibodies, compatible with 1 in 10,000 blood donors per the blood bank. It could take several days to find acceptable blood. Transfusion during an awake craniotomy is uncommon because these lesions are usually small. Nevertheless, if it does become necessary, the need will be immediate. For a negative antibody screen, 2 units of blood readily available is acceptable.

Depending on comorbidities, an electrocardiogram (ECG) can be obtained.

B.6. What radiology data should be reviewed?

Reviewing the most recently obtained MRI or computed tomography (CT) scans can provide a great deal of insight about the intracranial pathology. Characteristics of the tumor such as ring enhancement, cystic or lobulated nature, or variously weighted CT studies may give the neuroradiologist and neurosurgeon some insight regarding the diagnosis of the tumor as well as the location of the lesion. The location of the lesion may confirm the presenting symptoms. Vasogenic edema is readily seen, and the progress of resolution with corticosteroids is possible by reviewing a series of CT scans since presentation. Additional information can be gained but is not always present for the smaller lesions usually associated with the awake craniotomy. A midline shift would be evidence of increased ICP, as would loss of sulci and gyri, not to mention the presence of uncal or falcine herniation (**Fig. 19.5**). The presence of hydrocephalous from blockage of CSF pathways is also readily seen and could be a source of increased ICP. Previous areas of stroke are usually easily visualized and need to be noted. This is a very rapidly changing field, so there should be no hesitation in calling on the neuroradiologist or neurosurgeon to point out the pathology and their major concerns. Important considerations are how big is the lesion, and how much work needs to be done to provide for safe and effective brain relaxation. A neuroanesthesiologist can never overcommunicate with the neurosurgeon.

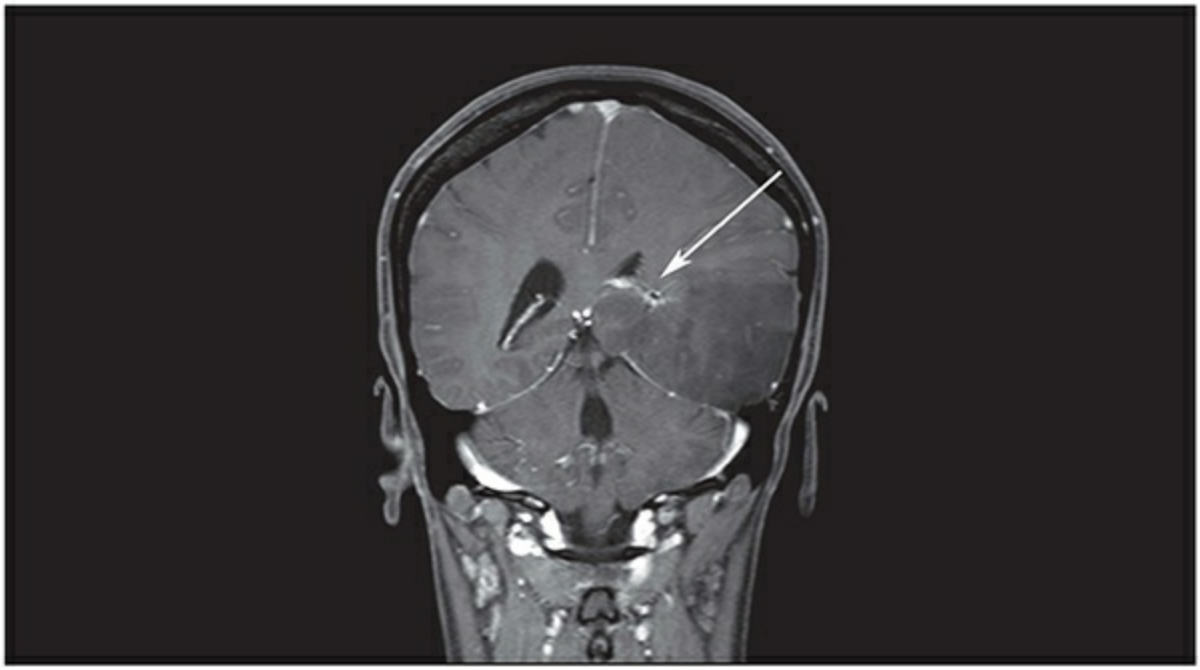

FIGURE 19.5. MRI scan of a 29-year-old female with a 2-week history of word-finding difficulty and no other symptoms. Note the rather significant uncal herniation (*arrow*). The patient underwent an uneventful left, awake craniotomy with language area mapping and was discharged to home the next day. Final pathology revealed a WHO grade III anaplastic oligoastrocytoma.

B.7. How do you prepare the patient for an awake craniotomy?

The most important preparation is proper patient selection, as alluded to earlier. A patient who cannot effectively communicate and cooperate will not do well with this procedure regardless of how well everything else is done.

The need for an awake craniotomy is usually first broached by the neurosurgeon during the workup. It is not unusual then to have a rather concerned and anxious patient arrive in the preanesthetic clinic. Ideally, the neuroanesthesiologist who will handle the case will conduct the interview, although this is not frequent. If not, the neuroanesthesiologist must make every effort to see the patient well before the patient arrives in the operating room. In either case, a direct and detailed explanation of what will happen should be provided. Assure the patient that adequate means will be taken to control any pain, that he or she

can ask for more medications if needed given the limitations secondary to needing the patient awake and cooperative. Discuss additional IV lines, invasive monitors if deemed necessary and why they are used, and when they will be placed.

A discussion about the anesthetic itself is essential. Usually, if patients have a good understanding of the sequence of the procedure and that they may not be exactly fully awake for the entire time they are in the operating room, they are more at ease. Describe everything in detail. This may be the first surgical procedure they have had.

B.8. Should this patient receive premedications?

Any premedications that might affect the intraoperative ability to adequately map the cortex are contraindicated. This includes medications that might not only cause prolonged sedation but, in the case of epilepsy surgery, interfere with intraoperative intracranial electrocorticography to define epileptic foci; benzodiazepines and barbiturates should be avoided for these reasons. A calm and reassuring neuroanesthesiologist is usually the best "premedication."

The *other* premedications are those taken for preexisting comorbidities. Typically, patients should receive medications for their chronic conditions, including (but not limited to) antihypertensive, antiarrhythmics, bronchodilators, as would be the standard practice of the institution, with the exception of anxiolytics, short- and long-acting opioids, aspirin, and nonsteroidal anti-inflammatory drugs. Patients on AEDs for tumor-related seizures should take their AED prior to the procedure. Patients with epilepsy as their primary diagnosis should follow the neurosurgeon's instruction on taking their AED. Often, these medications are held prior to surgery to help with intraoperative electrocorticography.

B.9. What precautions should be made for airway

management?

Airway evaluation is extremely important in this patient population. The head will most likely be fixed in a three-pronged device, making the ability to intubate the patient via direct laryngoscopy virtually impossible. Further limitations include the surgical drapes and the instrument table, which often extend over the patient completely. The patient is often positioned in the lateral decubitus position, making moving the patient to a flat position time-consuming, if possible at all. Patient body habitus can also make tracheal intubation challenging in the nonsupine position. Obese and morbidly obese patients present exceptionally difficult challenges; edentulous patients have bone erosion of both the maxilla and mandible that could make mask ventilation difficult in any position. Patients on phenytoin can have rather impressive gingival hypertrophy and associated bleeding that can interfere with intubation if required; teeth can be loose and easily displaced. These problems can make placement of an airway or laryngeal mask airway (LMA) difficult at best, impossible at worst. The next section suggests that use of an LMA or even endotracheal intubation for these cases is for some the preferred method.

Having an airway cart immediately available and prepared for a fiberoptic intubation with an assorted and readily available selection of LMAs is recommended. At baseline, a nasal cannula for oxygen delivery and CO_2 measurement should be placed before starting sedation. The maintenance of a patent airway is often facilitated by placement of a nasal trumpet. This is placed after sedation has started and may be removed while the patient is awake for testing.

C. Intraoperative Management

C.1. How should this patient be monitored?

Monitoring should be in accordance with the guidelines of the American Society of Anesthesiologists. These include pulse oximetry, electrocardiography, noninvasive blood pressure monitor, capnography, and temperature measurement as a minimum.

American Society of Anesthesiologists. Standards for basic anesthetic monitoring. https://www.asahq.org/standards-and-guidelines/standards-for-basic-anesthetic-monitoring. Accessed November 12, 2019.

C.2. Does this patient require invasive monitoring?

In general, for awake craniotomy, invasive blood pressure monitoring is not a requirement but should be placed in patients with comorbid conditions who would regularly receive invasive arterial monitoring. Nevertheless, many circumstances might be better served with an arterial line. Blood pressure measurement with an oscillometric device can be problematic in patients with atrial fibrillation; it also overestimates both systolic and diastolic blood pressure readings in patients with stiff arteries, such as diabetics. The diabetic patient may also require frequent blood glucose measurements, and the presence of an arterial line facilitates this and avoids multiple venous blood draws in the operating room. In several of the comorbid diseases of particular concern (e.g., obesity, COPD, pulmonary hypertension), the objective data of interest is the $PaCO_2$ and arterial sampling offers the most reliable method, although this could be accomplished with measurement of venous CO_2. Lastly, an arterial line may be placed for comfort as a regular inflation of a blood pressure cuff can be very distracting to some patients. In this, we try to place a radial arterial line in an arm that will not be involved in testing. A central venous line (CVL) for pressure measurement is not required in the awake patient. Nevertheless, at times, venous access is so poor that one needs to be placed

merely for that purpose. The best monitoring system for this case is the awake, cooperative patient.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1868–1910.

van Popele NM, Bos WJ, de Beer NA, et al. Arterial stiffness as underlying mechanism of disagreement between an oscillometric blood pressure monitor and a sphygmomanometer. *Hypertension*. 2000;36:484–488.

C.3. Can current drug therapy alter eloquent cortex mapping?

For mapping of the language areas, any drug that would cause long-lasting, deep sedation, as discussed earlier, would be contraindicated. Patients presenting with new onset of seizures associated with the new diagnosis of brain tumor may have been started on any one or several of the AEDs listed in **Table 19.1**. These drugs may interfere with mapping of the eloquent cortex. In patients undergoing epilepsy surgery, the surgeon has usually stopped these drugs several days in advance so as not to interfere with intraoperative electrocorticography or placing of electrodes directly on the surface of the exposed brain. Corticosteroids and opioids do not interfere, but propofol can produce a pattern of high-frequency, high-amplitude β activity on the electroencephalogram for at least 20 minutes, which can cloud the abnormal activity being sought and should be stopped appropriately.

C.4. Why use hypertonic fluids during a craniotomy?

The intact brain, primarily the BBB, acts as an osmometer. Water can freely cross this semipermeable membrane in response to osmotic pressures created by dissolved solutes until there is an equal water pressure across the membrane. This is a function of the number of osmotically active, dissolved solutes (osmoles) present in a solution: The greater the number of osmoles, the greater is the osmolarity or osmotic activity of the

solution. At times, this is also called the *osmolality*. This term describes the same principle but does have several differences. *Osmolarity* is defined as osmoles per liter of fluid and is a calculated value. Osmolality is one of the four colligative properties of a solution. It is defined as osmoles per kilogram of fluid and is a measured value, usually by a freezing point depression method.

Table 19.2 lists several commonly used IV fluids and compares their osmolarity and osmolality. The osmolality is lower secondary to the presence of undissociated solutes in the solution. When solutes are given intravenously, the intact BBB prevents polar solutes from crossing into the brain, thus sequestering them to the intracranial intravascular space and creating a high vascular osmotic pressure, with resultant movement of water from the brain into the vascular space. This reduces brain bulk, which may provide better visualization of the tumor by the surgeon and hopefully decreases the need to apply retractors to the brain surface to enhance visualization. This in turn may help decrease ischemic injury to the brain directly under the retractors. It also decreases ICP in the intact brain. Intravascular proteins create a much smaller oncotic pressure in the intracranial vasculature than do the dissolved solutes, secondary to the intact BBB, and play a lesser role than they do in the peripheral circulation, where they are the primary determinant of fluid moving extravascular to intravascular.

TABLE 19.2 Osmotic Values of Common Intravenous Fluids

Fluid	Osmolarity (mOsm/L)	Osmolality (mOsm/kg)
Water	0	0
5% dextrose (D_5W)	252	259
Normal saline	308	282
Lactated Ringer's	273	250
3% Saline	1,027	921
6% Hetastarch	310	307

20% Mannitol	1,098	1,280
5% Albumin	290	283
Normosol–R	294	281
D_5W/0.2 NaCl	325	321

D_5W, 5% dextrose in water; D_5W/0.2 NaCl, 5% dextrose and 0.2% sodium chloride.

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2017:152–165.

Hall JE, ed. *Guyton and Hall Textbook of Medical Physiology*. 13th ed. Philadelphia, PA: Saunders; 2016:787–794.

C.5. What intravenous fluids (IVFs) are recommended?

Commonly used IVFs during craniotomy, awake or under general anesthesia, include 0.9% saline, 3% saline, 20% mannitol, and 5% albumin.

Normal plasma osmolality is 285 to 295 mOsm per kg. Therefore, any solution with a higher osmolality could act to extract water from the brain. The exception to this is any solution containing 5% dextrose. These solutions have an effective osmolality 259 mOsm less than the measured osmolality because glucose (osmolality 259 mOsm per kg) is rapidly transported intracellularly into neurons and glia and subsequently metabolized. Five percent dextrose in water (D_5W) thus has an effective osmolality of zero and D_5W/0.2 NaCl has an effective osmolality of 62 mOsm per kg as examples. These dextrose-containing solutions would present a very high concentration of free water within the intracranial intravascular space and result in water movement into the brain causing an increase in ICP or brain bulk.

It is now accepted that hyperglycemia before or during an episode of cerebral ischemia worsens outcomes. The mechanisms are not clear. One hypothesis is that during a hyperglycemic episode, increased intraparenchymal glucose leads to lactic acid production during the ischemic period, which is thought to have a negative effect enhancing neuronal death.

This being said, solutions containing dextrose are not routinely used during intracranial surgery.

Mannitol 20% is the most widely used IVF for treatment of elevated ICP. It also acts to decrease CSF production and as a scavenger of oxygen free radicals. Mannitol should be given intravenously over 10 to 15 minutes to prevent a sudden exposure of the cerebral circulation to extreme hyperosmolality (mannitol has an osmolality of 1,280 mOsm per kg), which could lead to a vasodilatory effect with resultant increased CBV, possible brain engorgement, and increased ICP. Increased urine output secondary to osmotic diuresis should be replaced with normal saline. The usual mannitol dose is 0.25 to 1 g per kg. Mannitol use in renal failure is contraindicated because it can exacerbate renal insufficiency and in cases of severe oliguric renal failure accumulate in the intravascular space leading to volume overload and pulmonary edema.

Hypertonic saline comes in a range of concentrations, with 3% being the most commonly used during intracranial surgery. A recent study has shown no difference between equiosmolar mannitol and hypertonic saline infusions for providing brain relaxation.

Normal saline has been the fluid of choice for intracranial procedures and is used to cover fluid requirements and replace blood loss until red blood cells are required. A drawback to its use is that a hyperchloremic, hypokalemic nonanion gap metabolic acidosis can occur when large volumes are given. This can mask other forms of acidosis and cloud the diagnostic picture. Lactated Ringer's solution (osmolality 250 mOsm per kg) would not theoretically, based on the prior discussion, be an ideal replacement for blood loss, insensible loss, or third-space losses. The crystalloid versus colloid debate seems to be never ending and is usually centered on head injury. Colloid, in the form of 5% or 25% albumin is rarely, if ever, needed in an

awake craniotomy.

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2017:152–165.

Fandino W. Understanding the physiological changes induced by mannitol: from the theory to the clinical practice in neuroanesthesia. *J Neuroanesthesiol Crit Care*. 2017;4:138–146.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1868–1910.

Myburgh J, Cooper J, Finfer S, et al. Saline or albumin for fluid resuscitation in patients with traumatic brain injury. *N Engl J Med*. 2007;357:874–884.

Rozet I, Tontisirin N, Muangman S, et al. Effect of equiosmolar solutions of mannitol versus hypertonic saline on intraoperative brain relaxation and electrolyte balance. *Anesthesiology*. 2007;107:697–704.

Suarez JI, Shannon I, Zaidat OO, et al. Effect of human albumin administration on clinical outcome and hospital cost in patients with subarachnoid hemorrhage. *J Neurosurg*. 2004; 100:585–590.

C.6. Would a lumbar drain for cerebrospinal fluid (CSF) removal benefit this patient?

The lesions in the eloquent cortex are usually small, so a lumbar drain is not indicated. Historically, neurosurgeons have placed a lumbar drain before the start of the surgery to allow CSF to be drained slowly, usually 10 mL per hour, to decrease brain bulk. This might have been placed in an "open" position when the time came to open the dura, allowing for maximal brain relaxation and visualization in addition to preventing any intracranial contents from herniating through the craniotomy site.

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2017:189–208.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1868–1910.

C.7. Venous air embolism (VAE): Is it a concern in this case?

VAE is the entrainment of air into open, noncollapsible vascular structures located above the level of the heart. Therefore, the short answer is yes, because the level of the surgical site meets this definition. VAE is usually associated with posterior fossa craniotomies and cervical spine surgery in the sitting position. Fatal VAE has been described with as little as 3 to 5 cm of surgical site elevation above the heart during lumbar spinal surgery using a four-poster support device in the prone position.

In this case, tumors are usually small and within the cortex, and the patient is either supine or in a nearly horizontal lateral decubitus position. Parasagittal and falcine meningiomas encroaching on the posterior portion of the sagittal sinus are the most common situations for VAE. Fortunately, the eloquent cortical areas are not in this location. Nonetheless, VAE has been reported after pin head holder placement and after craniotomy but before dural opening. This implies that free air can be entrained through the diploic space of the skull unless adequately sealed during the cranial opening. This is usually done with wax. Therefore, as stated earlier, VAE is a possibility during awake craniotomy.

Although transesophageal echocardiography is the most sensitive means of detecting VAE, it is impractical in the setting of awake craniotomy. The precordial Doppler device is the monitor of choice for this particular scenario if the head will be elevated above the level of the heart. When placed in the right or left parasternal region between the third and fourth ribs, Doppler has a high detection rate for VAE. Often, the awake patient may experience an episode of paroxysmal coughing with entrainment of air. The best chance of aspirating a VAE is through a properly placed, multiorificed central line that is positioned 2 cm below the superior vena caval–atrial junction by using intravascular ECG. Lead II is observed while the electrode of the CVL is attached to the leg lead. An equibiphasic P wave indicates that

the tip of the catheter is in the midatrial position.

Treatment for VAE is supportive. If VAE is suspected, the surgeon must be immediately informed and the surgical field flooded with saline to help prevent further air entrainment. Jugular compression and lowering the head are also maneuvers to help stop air entrainment. If it is present, an attempt should be made to aspirate air through the CVL simultaneously with the surgeon addressing the surgical field. Vasopressors or inotropes as needed are given to support hemodynamics and cardiopulmonary resuscitation initiated for cardiac arrest.

Albin MS, Ritter RR, Pruett CE, et al. Venous air embolism during lumbar laminectomy in the prone position: report of three cases. *Anesth Analg*. 1991;73:346–349.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1868–1910.

Jellish WS, Murdoch J, Leonetti JP. Perioperative management of complex skull base surgery: the anesthesiologist's point of view. *Neurosurg Focus*. 2002;12:e5.

C.8. How is the eloquent cortex mapped?

Before the start of the case, the neurologist and or a speech pathologist, will go over the intraoperative testing procedure with the patient. This usually consists of various confrontational type testing in which the patient may be asked to simply count. At other times, the patient may be asked to name items on a card preceded with the phrase "that is a . . . ." Patients are sometimes asked to do simple math problems. It is important to realize that a patient who speaks multiple languages may need to have each of those languages tested separately. Not all learned languages are "laid down" in the same cortical area. This requires extensive preoperative planning to have the needed interpreters available to help with this testing.

Once the craniotomy is completed, the dura opened, and the patient awakened, testing can begin. The tumor surface is often

visible and helps guide the surgeon as to where to start the mapping. A handheld wand with two probes, separated by 5 mm, is gently placed on the brain surface about 2 cm from the tumor edge. This is connected to a constant-current, biphasic stimulator. Neurologists or speech pathologists usually stimulate for 2 to 5 seconds with a frequency of 50 Hz and a pulse width of 200 milliseconds. Responses are usually noted with a constant current range of 4 to 6 mA. After each test, the surgeon moves the wand freely to other areas of the cortex, repeating this procedure until satisfied that functional areas of the cortex have been localized and marked and that an area of negative mapping has been identified through which the tumor or epileptic foci can be resected.

In the case of seizure focus resection, there are no visible signs to follow. Often, the areas of eloquent cortex in danger will have been mapped out by magnetoencephalography (MEG). This is a noninvasive technique for mapping brain activity by recording the magnetic fields produced by the electrical currents of the brain. These studies can then be "laid over" an MRI study and appear as colored squares representing areas of the eloquent cortex tested and can be used for tumor or epilepsy surgery to help identify the functional areas. Mapping can then start outside of these designated areas looking, again, for a quiet area.

Moore TA II, Markert JM, Knowlton RC. Dexmedetomidine as a rescue drug during awake craniotomy for cortical mapping and tumor resection. *Anesth Analg*. 2006;102:1556–1558.

C.9. How are intraoperative seizures treated?

Intraoperative seizures can be either the baseline type, for which the patient presented, or they can be caused by the cortical surface stimulation used to map the cortex. The surgeon usually will not stimulate the same area more than two consecutive times to avoid this complication. If a seizure should occur, it

usually will take the form of the patient no longer answering questions, but maintaining their airway, and at times maybe a slow moaning sound will be made. This usually responds rapidly to application of cold irrigation solution, usually lactated Ringer's solution, to the cortex by the surgeon. If this fails, small doses of propofol, 10 to 20 mg, will usually suffice to stop the seizure. An uncontrolled seizure that is not terminated with these measures can progress into a surgical emergency. The spreading electrical activity will dramatically increase the CBF and blood volume in the cortex exposed beneath the cranial defect. Here, the rapid increase in blood volume pushes the exposed cortex up through the craniotomy defect, a process which can tear delicate cortical veins and result in a cortical venous infarction.

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2017:296–316.

C.10. How will you conduct this anesthetic?

The conduct of this type of anesthetic actually begins long before the patient enters the operating room. The patient must be very motivated for this experience to be successful. The patient must realize fully that this is a lengthy procedure, and 4 to 8 hours is not unusual for being in the operating room. The patient's family must also be involved and have the same understanding. Most important is a motivated and experienced neurosurgeon, neurologist or speech pathologist, and neuroanesthesiologist. Each must realize that time is of the essence and the procedures must be completed as quickly as is safely possible.

The neurosurgeon will be the first person to suggest or inform the patient that this form of surgery is necessary to preserve the language or motor-sensory function. Ideally, the neurosurgeon and the neuroanesthesiologist have a successful history of

performing this procedure. They have developed a technique that has allowed them to have an awake, cooperative patient when the time comes for cortical or subcortical mapping and resection.

In the operating room, before patient arrival, several steps are taken to make the patient as comfortable as possible during this long and demanding procedure. A full-length gel pad is placed on the operating room table under the sheets, an underbody warmer is placed and in some cases the room temperature is set at 70°F or higher. Additional gel pads and foam sheets are available as needed as well as warm blankets.

Following the preoperative visit and IV line placement, the patient is brought to the operating room. Premedications that interfere with ability to cooperate and follow instructions are contraindicated. Standard intraoperative monitors are placed, and a CO_2 monitoring nasal oxygen cannula is placed.

The literature is replete with reports of various anesthetic techniques for awake craniotomy. The common theme is a triphasic “asleep-awake-asleep” technique utilizing a combination of moderate reversible sedation and regional scalp blocks. Some of these techniques use intubation of the trachea and potent inhalational agents until approximately 20 to 30 minutes before cortex mapping when the anesthetic is discontinued and the patient extubated. Others, use a supraglottic airway in the same fashion. Use of propofol, fentanyl, remifentanil, dexmedetomidine, and combinations of these drugs is added to these approaches as a means of transitioning the patient from a general anesthetic to the awake state for mapping and surgery within the eloquent cortex. The use of total IV anesthesia using the same drugs has also been described with the airway controlled by a supraglottic airway with controlled or spontaneous breathing or an unprotected airway (sometimes supported with a nasal trumpet) with

spontaneous respirations.

The literature describes cases in which similar, but not identical, approaches for mapping or other tasking has been successful for one group and not for another. This can lead to frustration in trying to decide how to administer this anesthetic. Many times, the technique is institutionally defined and has worked well for many years. One of the most important things is to fully understand the pharmacology of the anesthetic regimen chosen.

Our institution uses a triphasic total IV anesthesia technique with spontaneous breathing without LMA or tracheal intubation. After standard monitors are placed, two separate infusions are started. Dexmedetomidine is started at 1.0 μg/kg/hr and continued for 10 minutes and reduced to 0.5 to 0.75 μg/kg/hr. Propofol is started at 50 to 100 μg/kg/min. These drugs are titrated as needed to achieve a sedated yet spontaneously breathing patient; corresponding to an Observer's Assessment of Alertness/Sedation scale (OAA/S) of 3 to 4 or a Richmond Agitation-Sedation Scale (RASS) of −2 to −3. Patients on multiple AEDs often require higher doses of sedatives to achieve an adequately sedated patient for this procedure. When the patient no longer responds to name call, a urethral catheter, additional IV lines, and an arterial line, as deemed necessary, are placed. Small bolus doses of propofol 10 to 20 mg are given depending on patient response to these procedures. A loading dose of dexmedetomidine can be given at the discretion of the attending neuroanesthesiologist. The recommended dose is 1 μg per kg over 10 minutes, followed by a maintenance infusion. Reports of persistent bradycardia and hypotension have been reported with this approach versus starting the infusion without a loading dose. Bradycardia is treated with small doses (0.2 to 0.4 mg) of glycopyrrolate, and hypotension is easily treated with a low-dose (0.1 to 0.3 μg/kg/min) phenylephrine infusion. The

dexmedetomidine and propofol combination provides good sedation, anxiolysis, and some amnesia without causing significant respiratory depression.

The success of this procedure lies almost entirely with the precision and adequacy of the scalp blocks performed by the anesthesiologist or neurosurgeon. No amount of sedation will compensate for poorly performed blocks. The scalp block addresses the supratrochlear, supraorbital, zygomaticotemporal, auriculotemporal, greater auricular, and the lesser and greater occipital nerves. A combination of equal volumes of 2% lidocaine with epinephrine 1:100,000 and 0.5% bupivacaine with epinephrine 1:200,000 provides a rapid onset and longer duration than either component separately, although no convincing data support this practice. Use of ropivacaine alone for the same purpose is also described. Following the individual nerve blocks, an intradermal ring of the local anesthetic solution is placed around the operative side of the scalp. Each pin site for the pin head holder device is injected. The surgical incision site is also infiltrated by the surgeon after the patient is prepped and draped.

The dexmedetomidine and propofol infusions are continued as cranial opening proceeds. When the surgeon has made the final burr hole, propofol infusion is terminated and dexmedetomidine dose is reduced to 0.2 μg/kg/hr. The cranial opening continues, and approximately 15 to 20 minutes later, the patient is awake and conversant. The neurosurgeon and neurologist or speech pathologist begin the mapping process, which can take several hours, but usually about 1 hour. Dexmedetomidine is continued at 0.2 μg/kg/hr throughput the mapping process. When satisfied that areas of the eloquent cortex adjacent to the tumor have been localized and an area of negative mapping have been demonstrated, the surgeon proceeds with tumor resection. If the patient is resting comfortably, no

changes in the anesthetic are necessary. For deeper sedation, dexmedetomidine is increased to 0.35 μg/kg/hr; this usually keeps the patient comfortable for the remainder of the procedure. From time to time, the surgeon may ask to remap certain areas, and the dexmedetomidine is again lowered to 0.2 μg/kg/hr. The dexmedetomidine is stopped with skin stapling. The pin head holder is removed, dressings are placed, and preparations are made for leaving the operating room and transferring to the neurosurgery intensive care unit.

A transport monitor capable of providing pulse oximetry, blood pressure measurements, and ECG tracing is attached, and nasal cannula oxygen is continued during the transport.

Bustillo MA, Lazar RM, Finck AD, et al. Dexmedetomidine may impair cognitive testing during endovascular embolization of cerebral arteriovenous malformations: a retrospective case report series. *J Neurosurg Anesthesiol*. 2002;14:209–212.

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D. Postoperative Management

D.1. What are the major concerns following craniotomy?

Several problems can occur in the immediate postoperative period following craniotomy. In general, the patient is transported to the neurosurgical intensive care unit and monitored as described. The head of the bed is usually elevated 20 to 30 degrees to maximize cerebral venous drainage with care of the patient transferred to the neurointensivist and the neurosurgical service.

The key feature of a good neuroanesthetic is the ability to quickly awaken the patient following the procedure so that a neurologic exam can be performed. Typically, with the current regimen the patient will awaken within 5 minutes after the end of the procedure. However, awakening in patients who have required larger doses of medication to achieve an adequate level of sedation (OAA/S 3 to 4) may take 10 to 20 minutes until a suitable neurologic exam can be obtained. Not infrequently, the patient may have a subtle diminution of the neurologic exam compared to the end of the tumor resection. These small differences are likely due to residual anesthetics and progressive edema around the resection site. The former will usually improve over the next 1 to 2 hours and the latter can take several days to resolve completely.

Emergence hypertension is not uncommon in the perioperative period. The incidence of postcraniotomy hypertension has been reported to be 57%. In this series of 11,214 craniotomies, perioperative systemic hypertension was associated with postoperative intracranial hematoma, with resultant increased mortality and increased length of hospital stay. Other possible causes are pain, hypercapnia, and shivering. Eighty-five percent of postoperative intracranial hematomas become evident within 6 hours of surgery and usually present as

a progressive decrease in level of consciousness. Up to 17% of these hematomas present at sites remote to the surgical site. Aggressive efforts at controlling this hypertension are required to prevent possible devastating complications such as bleeding into the tumor bed, requiring a second surgical procedure to evacuate that clot.

Systolic blood pressure goals in a normotensive patient are typically 120 to 140 mmHg and for a chronically poorly controlled hypertensive patient 140 to 160 mmHg. In both cases, aggressive measures to maintain blood pressures at the lower end of the range are warranted if the resection site was large and/or hemostasis was difficult. Often, if not contraindicated, bolus doses of labetalol 5 to 10 mg IV (to a total of 60 mg) is effective. Persistent hypertension, without signs of intracranial hypertension, may require additional treatment. Given the strict blood pressure parameters, failing suitable control with labetalol or hydralazine 5 to 10 mg IV, patients are usually transferred to the intensive care unit on an infusion of nicardipine 5 to 15 mg per hour or clevidipine 1 to 2 mg per hour rapidly titrated up to 16 mg per hour. Alternatively, depending on the patient's comorbid conditions, infusions of sodium nitroprusside or nitroglycerin are possible. A combination of enalapril and labetalol versus nicardipine alone has been reported, with little difference in the ability to control emergence hypertension.

Acute pain control is essential in the postoperative period. Not only are patients more comfortable with adequate pain relief but this also helps control postoperative hypertension and decreases the possibility of intracranial hematomas. Pain following craniotomy has probably been vastly understated secondary to concern about respiratory depression and sedation as well as the traditional thought that craniotomies are less painful than other operations. The incidence of postcraniotomy pain may be as high as 70%. However, our experience is that

pain following an awake procedure is much less common as the duration of the scalp blocks can extend well into the postoperative period. Another helpful adjunct is IV acetaminophen either given during the operative course or at the end of the procedure.

In the immediate postoperative period, almost all pain control medications are given intravenously. Morphine sulfate patient-controlled analgesia has been reported with good results and without respiratory depression or need for reintubation. One regimen consists of morphine 1.5 mg with a lockout period of 8 minutes and a total dose not to exceed 40 mg in 4 hours.

Nonsteroidal anti-inflammatory drugs have been associated with postoperative intracranial hematoma. Administration of antiplatelet agents (aspirin and nonsteroidal anti-inflammatory drugs) was the most common risk factor. Therefore, this class of analgesics should be avoided in the immediate postoperative period.

Postoperative nausea and vomiting is common following craniotomy and can cause hypertension and an increase in ICP. Infratentorial surgery, female sex, and a young age are associated risk factors. Ondansetron 4 to 8 mg IV can provide effective treatment.

Seizures can occur following intracranial tumor resections and can cause serious complications such as secondary intracranial bleeding, hypoxemia, and possibly aspiration. An intracranial mass, such as a hematoma (**Fig. 19.6**), should be suspected if the patient does not regain consciousness within a short period after the seizure has ceased. Small doses of midazolam, 1 to 2 mg, or other benzodiazepines can treat seizures effectively without compromising the airway.

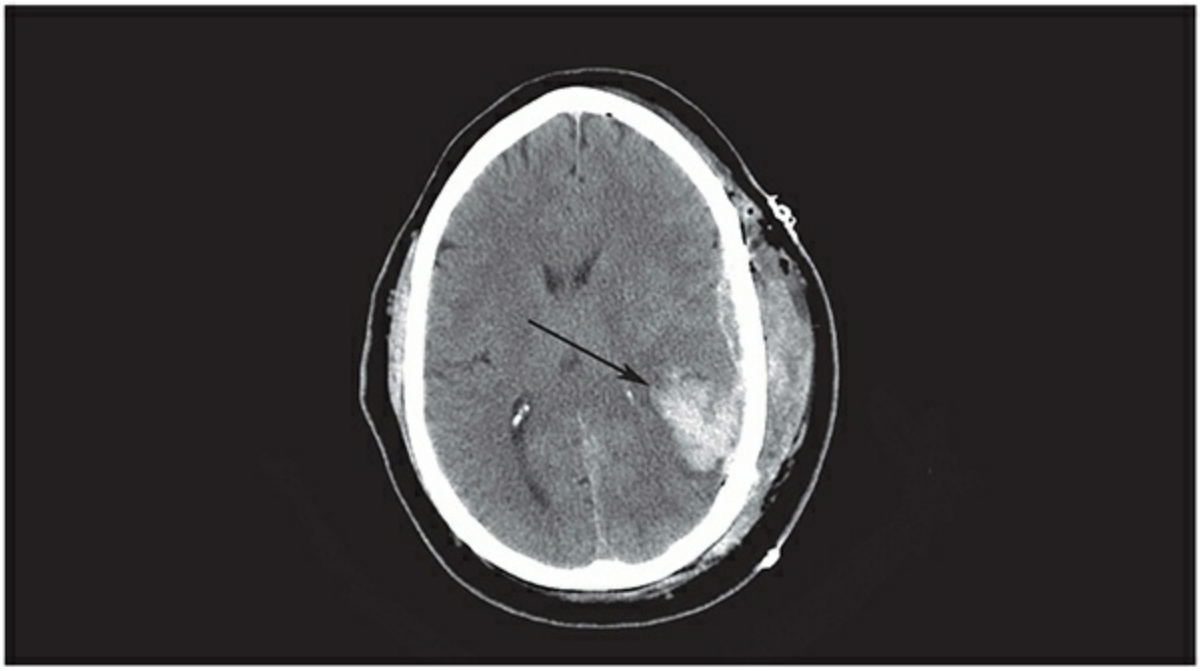

FIGURE 19.6. CT scan of a 73-year-old man who underwent an uneventful left awake craniotomy with motor and language area mapping. On postoperative day 2, he suffered a generalized tonic–clonic seizure and was extremely slow to awaken. CT scan revealed the presence of a large intracranial hematoma (*arrow*) in the operative site requiring return to the operating room for evacuation. Also note the small epidural and subgaleal hematomas. Coagulation studies were normal. The patient was placed on AEDs and did well on follow-up visits without further seizure activity. AEDs were successfully weaned over several weeks. Final pathology revealed glioblastoma multiforme.

Increased ICP commonly occurs after intracranial surgery, with the most common finding on CT scan being brain edema. Maximum pressures are usually recorded within 16 hours of surgery. Associated risk factors are glioblastoma resection and surgery lasting more than 6 hours. Continuing corticosteroids, such as dexamethasone 4 to 10 mg every 6 hours, usually controls this problem.

Peripheral nerve injuries are uncommon after awake craniotomy because patient comfort or discomfort can easily be assessed, and minor movements made if needed. Blister formation along the down side of morbidly obese patients' upper leg can occur after about 5 hours in the lateral decubitus position despite gel pads beneath the thigh.

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20 Head Injury

Chris C. Lee , Susan A. Ironstone, and M. Angele Theard

A 52-year-old woman with an unknown past medical history, who was involved in a high-speed motorcycle collision, was airlifted to a trauma center. On the scene, she was combative, unresponsive, and intubated. She was found to have a left small pneumothorax, rib fractures, and an open tibial/fibular fracture that was reduced and fixed with return of pulses after an initial pulseless left leg. She had a skull fracture extending to the left parietal bone, occipital bone, clivus sphenoid sinus fracture, and temporal bone that was diagnosed at an outside hospital.

On admission, the patient had a Glasgow Coma Scale (GCS) of 7T, and her vital signs were a blood pressure (BP) of 69/40 mmHg, heart rate 150 beats per minute, respiratory rate 20 breaths per minute, and oxygen saturation 100% on 60% fraction of inspired oxygen (F_{IO_2}). The patient was aggressively resuscitated with packed red blood cell transfusions, 0.9% normal saline (NS), and placed on a norepinephrine infusion.

Head computed tomography (CT) scans showed bilateral traumatic subarachnoid hemorrhage (tSAH) and subdural hematomas (**Figs. 20.1** and **20.2**). Her laboratory values were as follows: hemoglobin, 9.8 g per dL/hematocrit, 29.5%; platelets, 137,000 per μL; lactate, 6.5

mmol per L; international normalized ratio (INR), 1.73; troponin-I, 1.27 ng per mL; glucose, 418 mg per dL; sodium (Na), 141 mEq per L; potassium (K), 3.6 mEq per L; and creatinine, 1.36 mg per dL. Fresh frozen plasma (FFP) and prothrombin complex concentrate (PCC) were given immediately to correct the coagulopathy.

The patient was GCS 7T; therefore, a right frontal external ventriculostomy drain (EVD) was emergently placed for intracranial pressure (ICP) monitoring and cerebrospinal fluid (CSF) drainage because her CT scan showed tSAH and early sings of cerebral swelling. The patient was managed conservatively for her ICP but required increasing medical treatment, including maximal hyperosmolar therapy, adequate pain control, sedation, and paralysis. Her ICP readings remained in the 30 mmHg range after initially low ICP readings. The patient was taken to the operating room for a bifrontal craniectomy for emergency decompression secondary to severe bifrontal contusions with malignant cerebral edema (**Figs. 20.3** and **20.4**).

FIGURE 20.1. Initial head CT scan (basal): bilateral tSAH.

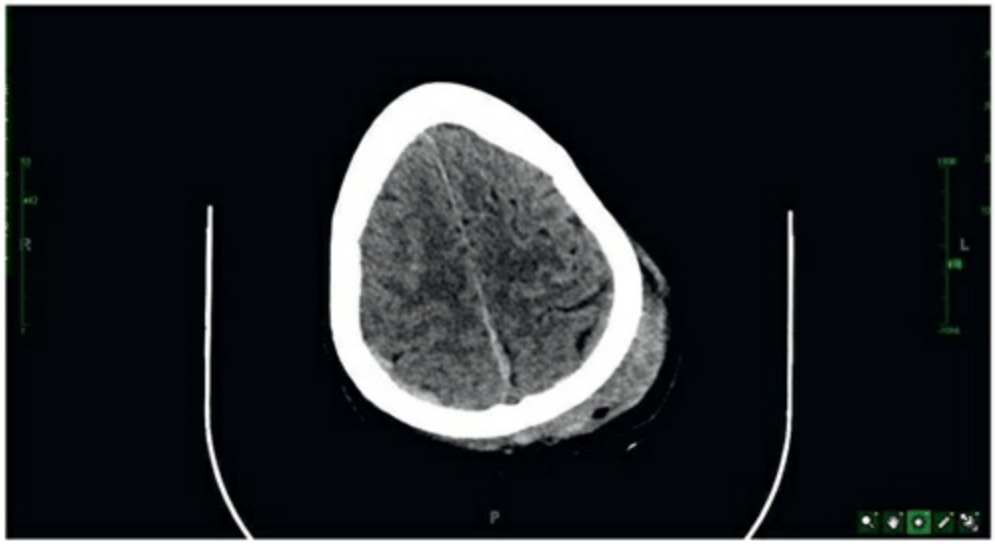

FIGURE 20.2. **Initial head CT scan (vertex): bilateral tSAH.**

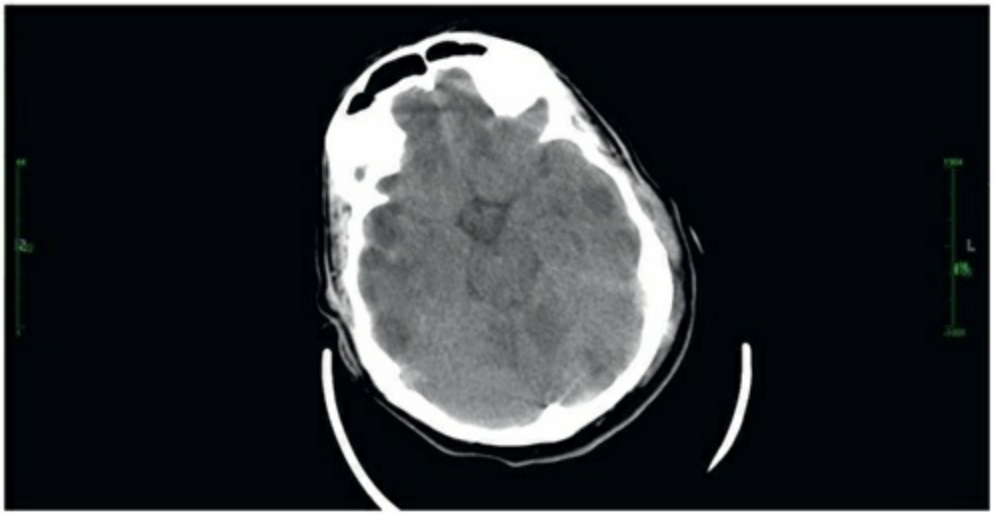

FIGURE 20.3. **Follow-up head CT scan: contusions with malignant cerebral edema.**

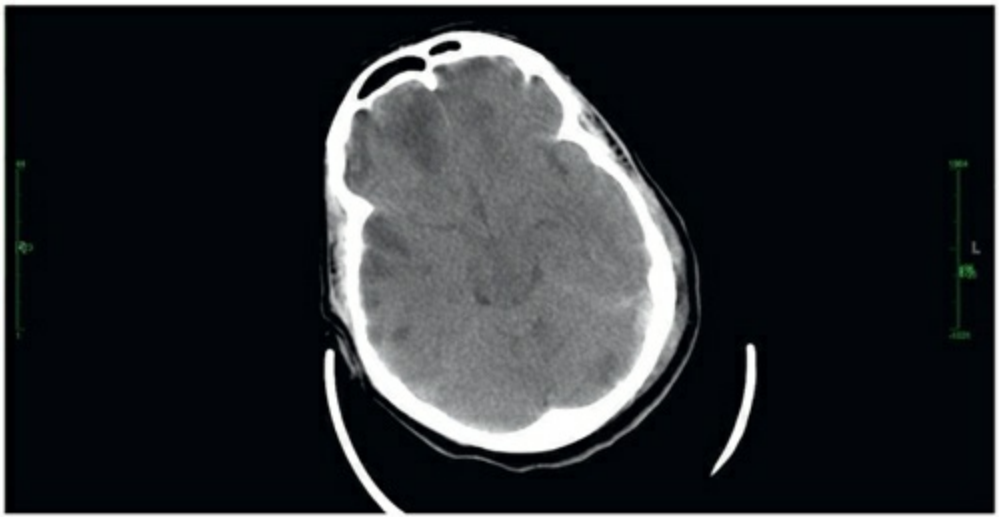

FIGURE 20.4. Follow-up head CT scan: contusions with brain swelling and effacement of sulci and basal cisterns.

A. Pathophysiology and Differential Diagnosis

1. What types of intracranial injuries are most likely to have occurred in this patient?
2. What is the difference between primary and secondary injury? What factors contribute to secondary injury?
3. What are the benefits and risks of administering mannitol?
4. What is the effect of hyperglycemia on neurologic outcome following head trauma?
5. What alterations in sodium and potassium balance can occur in patients with head injury?
6. In addition to sodium and potassium, what other electrolyte abnormalities can be present after head trauma?
7. What are the neuroprotective effects of administering magnesium (Mg)?
8. What role do gender and female sex hormones have in the pathophysiology of traumatic brain injury (TBI)?
9. What is the role of decompressive craniectomy (DC) as a treatment option for ICP control after head injury?
10. Do genetic factors play a role in the outcome after head injury?

B. Preoperative Evaluation and Preparation

1. What is the GCS? What is the significance of a GCS of 7T in this patient?
2. In addition to the GCS, what other assessments can be done to evaluate neurologic function?
3. What is the role of CT scanning in the initial evaluation of the patient with head injury? What are the management options in patients whose neurologic condition is deteriorating before obtaining a CT scan?
4. What is the role of ICP monitoring in the management of head injury?
5. How can you clear this patient's cervical spine?
6. What are the advantages of early endotracheal intubation in this patient?
7. What is your plan for airway management in this patient? How would it change if the patient were combative? How would it change if the patient had facial fractures with significant swelling of the head and neck?
8. What are the effects of succinylcholine on ICP? What is the significance of the effect, if any?
9. What coagulation abnormalities are present after TBI? What modalities can be used to provide hemostasis and reduce intracranial hematoma expansion?

C. Intraoperative Management

1. What is appropriate hemodynamic monitoring during CT scanning and during craniotomy for evacuation of a subdural hematoma?
2. Should hyperventilation be used in this patient?
3. What are the implications of arterial hypertension in patients with head injury? How should BP be managed?
4. What should be done about intravenous (IV) fluid replacement? Should corticosteroids be given empirically?
5. Should hypertonic saline (HTS) be administered to this

patient? How is HTS administered?

6. The patient underwent a craniectomy for evacuation of a frontal intracerebral hematoma. Should some anesthetic agents be avoided in this situation? Which ones? What agents might be preferred in this situation?
7. Should hypothermia be employed in this patient?

D. Postoperative Neurointensive Care Management

1. What are the postoperative ventilation concerns in this patient?
2. What specific measure should be used to control the patient's ICP? What type of monitoring devices can be used to measure ICP?
3. What is neurogenic pulmonary edema? Would you avoid positive end-expiratory pressure (PEEP) in a patient with increased ICP?
4. What is the role of antiseizure prophylaxis in the perioperative management of head trauma?
5. How can cerebral oxygenation monitoring be used in the clinical management of TBI?
6. What methods can be used in the neurointensive care unit to prevent hyperthermia?

A. Pathophysiology and Differential Diagnosis

A.1. What types of intracranial injuries are most likely to have occurred in this patient?

The common causes of TBI include falls, motor vehicle accidents (MVA), assaults, and gunshots. TBI is a leading cause of death and disability after injury in the United States. The following types of intracranial injuries are most likely to have occurred in this patient:

- **Concussion** is both the most common type of TBI and the least apparent on imaging. It is often completely invisible to

any type of imaging and must be assessed and diagnosed clinically. It is also the most common type of TBI to result in ongoing morbidity, causing decreased job and school performance from lasting cognitive symptoms. This is a very complex type of injury and is a big focus of professional sports team injury experts. There is currently a social movement occurring now to raise awareness of these injuries, particularly in young athletes.

- **Diffuse axonal injury (DAI)** is difficult to see on CT of the brain, although small punctate hemorrhages in white matter tracts can be seen. Magnetic resonance imaging (MRI), particularly susceptible weighted imaging, is a more sensitive way to detect it. DAI can produce severe neurologic impairment with a poor prognosis.
- **tSAH** is the most common type of posttraumatic intracranial hemorrhage and the least severe indicator of injury. Although this finding often signals the presence of significant concussion injury, it does not require surgical intervention. tSAH resolves within days and carries a far lower risk of the secondary consequences than those associated with spontaneous aneurysmal subarachnoid hemorrhage (e.g., hydrocephalus and stroke from intracerebral vasospasm). Follow-up CT scans are usually not necessary due to this low risk of secondary neurologic injury.
- **Epidural hematoma** (located between the skull and dura mater) is classically associated with displaced temporal bone skull fractures causing a laceration of the middle meningeal artery. This arterial pressure hemorrhage results in a rapidly expanding hematoma lateral to the temporal lobe, which can lead to death from herniation if it is not emergently surgically evacuated. Injury to large venous structures including dural sinuses or venous bleeding from fractured bone can lead to a so-called venous epidural hematoma. Due to the fact that

these hemorrhages occur at venous pressure, they are thought to be less likely to expand to dangerous volume, but sometimes surgical treatment is required. Patients with acute epidural hematoma often exhibit a lucid interval after the initial impact before deteriorating. The signs of this deterioration can include depressed mental status, an ipsilateral fixed and dilated pupil, contralateral hemiplegia, and imaging demonstrating uncal herniation due to the rapidly expanding hematoma. Arterial epidural hematomas are almost always a true neurosurgical emergency; rapid intervention makes the difference between a good prognosis and death.

- **Subdural hematomas** (located between the brain and dura) arise from a tear in the dural sinuses or bridging veins and may accumulate more insidiously than an epidural hematoma. They are classified as acute (up to 48 hours), subacute (48 hours to 12 days), and chronic (more than 12 days) according to the interval of time between the TBI and the onset of symptoms. Subdural hematomas greater than 1 cm in thickness or causing more than 1 cm of midline shift are generally associated with significant lateralizing neurologic symptoms and often constitute a surgical emergency. Small subdural hematomas can expand in volume as they grow more chronic and can produce delays in onset of significant neurologic signs and symptoms.
- **Intracerebral hematomas and hemorrhages** arise from the tearing of small vessels in the white matter and are due to penetrating head injury or caused by acceleration-deceleration injuries that involve laceration of cortical arteries. These hemorrhages and hematomas can often be managed medically with serial follow-up head CT scans. Surgical evacuation of intracerebral hematomas is rarely indicated due to the deep location of many of these

hemorrhages. Although they can be associated with trauma, hypertension, amyloid angiopathy, and/or profound coagulopathy are more common causes.

- **Cerebral contusions** are superficial hemorrhages that occur mainly when the anterior temporal and frontal lobes strike the rough edges of the tentorium (contrecoup contusion). In a patient without focal neurologic deficits, the most probable intracranial injury is a cerebral contusion after ruling out other focal brain injuries. This type of injury is often associated with cerebral edema and can require aggressive management with hyperosmolar therapies or surgical craniectomy for decompression.

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Ghajar J. Traumatic brain injury. *Lancet*. 2000;356:923–929.

Jaffe RA, Schmiesing CA, Golianu B, eds. *Anesthesiologist's Manual of Surgical Procedures*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2014:37–44.

A.2. What is the difference between primary and secondary injury? What factors contribute to secondary injury?

Primary injury refers to the direct injury of tissue at the moment of head trauma.

Secondary injury occurs minutes, hours, and even days after the initial head trauma and is the consequence of ischemic insults to the brain. The factors contributing to secondary injury include systemic causes (i.e., hypoxia, hypotension, hypo- or hypercarbia, fever, and hypo- or hyperglycemia) and intracranial

causes (i.e., intracranial hypertension, elevated ICP, and herniation). Systemic hypotension and intracranial hypertension are factors related to increased morbidity and mortality in patients with severe TBI. Mental status changes suggest inadequate cerebral perfusion, either from decreased systemic BP or elevated ICP. Cerebral perfusion pressure equals mean arterial pressure minus either ICP or central venous pressure, whichever is greater (CPP = MAP − ICP or CVP). Achieving a CPP between 60 and 70 mmHg requires maintaining an adequate BP, oxygenation, and a normal $PaCO_2$ in order to decrease the chance of mortality, morbidity, or any deleterious sequelae caused by secondary injury.

Algattas H, Huang JH. Traumatic brain injury pathophysiology and treatments: early, intermediate, and late phases post-injury. *Int J Mol Sci*. 2013;15:309–341.

Carney N, Totten AM, O'Reilly C, et al. Guidelines for the management of severe traumatic brain injury, fourth edition. *Neurosurgery*. 2017;80(1):6–15.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2680–2681.

A.3. What are the benefits and risks of administering mannitol?

Benefits

Mannitol (20%) 0.25 to 1.0 g per kg body weight is effective in acutely reducing cerebral edema, brain volume, and ICP by increasing serum osmolality to 305 to 320 mOsm per L to improve CPP, which also facilitates surgical exposure and reduces tissue trauma from surgical retraction. The use of hyperosmolar agents is theoretically limited by an upper acceptable osmolality limit of about 320 mOsm per L. Its osmotic diuresis takes effect in 5 to 15 minutes, achieves a peak effect in 30 minutes, and lasts for 2 to 3 hours. For decades, mannitol has been commonly accepted as an acute treatment for

cerebral edema.

Risks

- After TBI, the possibility of loss of the blood–brain barrier (BBB) integrity leading to leak of mannitol into cerebral interstitial tissue may actually worsen cerebral edema.
- Osmotic diuresis can cause hypovolemia and the consequent hypotension can aggravate cerebral ischemia.
- It can transiently cause hypervolemia and may worsen or result in congestive heart failure in those patients who have borderline cardiopulmonary function.
- Electrolyte abnormalities (e.g., hypernatremia) due to diuresis can occur.
- A serum osmolality above 320 mOsm per L can cause renal failure.
- It could cause intracranial rebleeding in patients with expanding hematoma by removing a tamponading effect on the hematoma if mannitol is administered before the dura is opened.

Colton K, Yang S, Hu PF, et al. Responsiveness to therapy for increased intracranial pressure in traumatic brain injury is associated with neurological outcome. *Injury*. 2014;45(12):2084–2088.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1874–1875.

A.4. What is the effect of hyperglycemia on neurologic outcome following head trauma?

Hyperglycemia resulting from the nervous system response to injury following moderate to severe head trauma has been associated with an increased odds ratio for an unfavorable neurologic outcome and an increased risk of mortality. Additionally, persistent hyperglycemia has been found to be an independent predictor of an unfavorable outcome in patients with severe TBI. The degree of stress-induced hyperglycemia

(SIH) has been found to correspond to the severity of TBI.

Although there is a possibility that intensive glucose control with blood glucose targets of <126 mg per dL may be associated with improved neurologic outcome, it has not been shown to reduce mortality and does appear to increase the risk of severe hypoglycemia. In critically ill patients, hypoglycemia is strongly correlated with increased morbidity and mortality. Therefore, moderate glucose control targets with a range of 144 to 180 mg per dL are still currently recommended so that hyperglycemia and hypoglycemia can be avoided.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1884.

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Muehlschlegel S, Carandang R, Ouillette C, et al. Frequency and impact of intensive care unit complications on moderate-severe traumatic brain injury: early results of the Outcome Prognostication in Traumatic Brain Injury (OPTIMISM) Study. *Neurocrit Care*. 2013;18:318–331.

A.5. What alterations in sodium and potassium balance can occur in patients with head injury?

Electrolyte abnormalities such as hyponatremia and hypokalemia are commonly seen following head trauma. Hyponatremia may result via several mechanisms, including hypothalamus–pituitary dysfunction, cerebral salt-wasting syndrome, and syndrome of inappropriate antidiuretic hormone (SIADH). Additionally, sodium loss may be exacerbated by medications used to treat cerebral edema. Hyponatremia has been strongly correlated with poor outcomes. Severe hypokalemia has been found to be an independent mortality risk factor in patients with TBI and is likely related to trauma and stress-related catecholamine surge. Hypernatremia, resulting from mannitol use, HTS, or diabetes insipidus, is also frequently

seen in association with severe TBI. Hypernatremia may itself be an independent risk factor for postoperative death in patients with severe TBI.

Hoffman H, Jalal MS, Chin LS. Effect of hypernatremia on outcomes after severe traumatic brain injury: a nationwide inpatient sample analysis. *World Neurosurg*. 2018;118:e880–e886.

Pin-On P, Saringkarinkul A, Punjasawadwong Y, et al. Serum electrolyte imbalance and prognostic factors of postoperative death in adult traumatic brain injury patients: a prospective cohort study. *Medicine (Baltimore)*. 2018;97(45):e13081.

Wu X, Lu X, Lu X, et al. Prevalence of severe hypokalaemia in patients with traumatic brain injury. *Injury*. 2015;46(1):35–41.

Zhang W, Li S, Visocchi M, et al. Clinical analysis of hyponatremia in acute craniocerebral injury. *J Emerg Med*. 2010;39(2):151–157.

A.6. In addition to sodium and potassium, what other electrolyte abnormalities can be present after head trauma?

Multiple electrolyte abnormalities, including hypomagnesemia and hypophosphatemia, are often associated with TBI and can be challenging to treat.

Symptoms of hypomagnesemia include ventricular arrhythmias, widened QRS, prolonged PR interval, weakness, and seizures. Symptomatic hypomagnesemia, or magnesium (Mg) level of less than 0.8 mEq per L, should be treated with IV Mg, although oral Mg should be used for asymptomatic patients. Mg repletion may also be required for successful correction of hypokalemia or hypocalcemia.

Patients with hypophosphatemia can present with hypotension, seizures, as well as cardiac or respiratory failure. Treatment of hypophosphatemia can result in severe hypocalcemia and so should only be considered in moderate to severe hypophosphatemia or symptomatic patients.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed.

Philadelphia, PA: Elsevier; 2020:2672.

Wu X, Lu X, Lu X, et al. Prevalence of severe hypokalaemia in patients with traumatic brain injury. *Injury*. 2015;46(1):35–41.

A.7. What are the neuroprotective effects of administering magnesium (Mg)?

N-methyl-D-aspartate (NMDA) receptors are stimulated by excitatory amino acids, like glutamate, in the central nervous system. Once stimulated, the NMDA receptor ion channels will facilitate calcium entry into the cell. In the face of ischemia (TBI), Mg levels in the brain are reduced, and this has been associated with excess glutamate causing excitotoxicity and consequent increased intracellular calcium and cell death. Mg, a noncompetitive inhibitor of the NMDA receptor ion channel, will limit the influx of calcium, thereby decreasing cell death. Other effects of Mg include down regulation of the membrane protein, aquaporin 4, which is known to increase cerebral edema and decrease upregulation of the tumor suppressor gene *TP53*, which causes apoptosis. The benefits of Mg have been translated into decreased cortical damage noted in the rat brain after brain injury.

Despite encouraging preclinical data of the benefits of Mg as well as established safety studies, human outcome studies on the impact of Mg after TBI are varied. Mg administered 12 hours after TBI led to a significant decrease in mortality at 3 months: 13% mortality for patients treated with Mg versus 47% in the placebo group. Of those who survived, good recovery (Glasgow outcome score) was observed in 54% of the patients treated with Mg and 38% of patients treated with placebo. In another study, however, Mg administered to patients within 8 hours of brain injury had no beneficial effect based on mortality, seizures, functional status, or neuropsychological testing at 6 months postinjury. Study design problems, such as missing baseline vital signs, glucose values, concurrent injuries, and neurologic

scores at discharge, contributed to the mixed results. Another challenge in translating the benefit of Mg seen in preclinical studies to human research is the notably small, possibly inadequate, increase in ionized Mg in CSF affected by increasing serum Mg levels. This finding may relate to the integrity of the BBB. Finally, the multifactorial etiology of TBI may necessitate research examining combination therapy (e.g., combinations of hypothermia and/or hyperoxia that restore mitochondrial function with Mg administration) in order to achieve more consistent and favorable outcomes.

Dhandapani SS, Gupta A, Vivekanandhan S, et al, Randomized controlled trial of magnesium sulphate in severe closed traumatic brain injury. *Indian J Neurotrauma*. 2008;5(1):27–33.

Li W, Bai Y, Li Y, et al. Magnesium sulfate for acute traumatic brain injury. *J Craniofac Surg*. 2015;26:393–398.

Sen AP, Gulati A. Use of magnesium in traumatic brain injury. *Neurotherapeutics*. 2010;7(1):91–99.

Temkin NR, Anderson GD, Winn HR, et al. Magnesium sulfate for neuroprotection after traumatic brain injury: a randomised controlled trial. *Lancet Neurol*. 2007;6:29–38.

A.8. What role do gender and female sex hormones have in the pathophysiology of traumatic brain injury (TBI)?

The estimated cost of care for the 3.5 million TBI victims in the United States annually is between $60 and $221 billion dollars. Unwavering efforts to improve TBI outcomes have compelled consideration of evidence, which suggests that women less than 50 years old suffering TBI have a decreased mortality risk compared to men. Additionally, preclinical data suggesting less severe sequelae and reduced mortality from TBI in pubescent compared to prepubescent females has served as the impetus for exploring the influence of sex hormones on outcomes after TBI.

Atella et al. demonstrated improved functional outcome in

pseudopregnant rats (higher progesterone levels) after TBI compared to normal cycling female rats with similar injuries. Other mechanisms by which progesterone may improve outcome after TBI include an anti-inflammatory action by reducing microglia activation and proinflammatory cytokines and stimulation of postinjury remyelination and repair. Estrogen may also be beneficial in cerebral ischemia by stabilizing the BBB and increasing blood flow during and after ischemia as well as improving regeneration and plasticity of new neurons.

Small clinical studies, which demonstrated a more favorable outcome with administration of progesterone 8 hours after injury while encouraging, did not translate into positive findings in two published major progesterone trials. In these two separate randomized controlled trials (RCTs) (SYNAPSE and PRoTECT III trial), progesterone administered to TBI patients did not produce a favorable outcome at 6 months as assessed by Extended Glasgow Outcome Scale (includes an assessment of ability to participate in activities of daily living) or other secondary outcomes. Conclusions from a recent meta-analysis of RCT comparing progesterone to placebo for TBI suggest that although exploration of the neuroprotective potential of progesterone should continue, routine administration of progesterone for TBI is not recommended.

Attella MJ, Nattinville A, Stein DG. Hormonal state affects recovery from frontal cortex lesions in adult female rats. *Behav Neural Biol*. 1987;48:352–367.

Herson PS, Koerner IP, Hurn PD. Sex, sex steroids, and brain injury. *Semin Reprod Med*. 2009;27(3):229–239.

Ley EJ, Short SS, Liou DZ, et al. Gender impacts mortality after traumatic brain injury in teenagers. *J Trauma Acute Care Surg*. 2013;75(4):682–686.

Lin C, He H, Li Z, et al. Efficacy of progesterone for moderate to severe traumatic brain injury: a meta-analysis of randomized clinical trials. *Sci Rep*. 2015;5:13442.

Skolnick BE, Maas AI, Narayan RK, et al. A clinical trial of progesterone for

severe traumatic brain injury. *N Engl J Med*. 2014;371(26):2467–2476.

Wright DW, Espinoza TR, Merck LH, et al. Gender differences in neurological emergencies part II: a consensus summary and research agenda on traumatic brain injury. *Acad Emerg Med*. 2014;21(12):1414–1420.

A.9. What is the role of decompressive craniectomy (DC) as a treatment option for ICP control after head injury?

In TBI, DC has historically been reserved for those patients with increasing ICP refractory to medical therapy (e.g., sedation, hyperventilation, osmotic diuretics, HTS, paralysis, and/or ventriculostomy). A skull flap is removed to make room for the expanding traumatized brain thereby effecting a decrease in ICP and improved cerebral blood flow (CBF). However, this procedure is associated with a 26% mortality rate and is not without risk; contusion expansion, contralateral subdural hematoma or epidural hematoma, CSF leakage, herniation, and infection can occur. Consequently, translating the benefits of DC (i.e., decreased ICP and increase CBF) into a better neurologic outcome in this patient population has been challenging. TBI patients who underwent bifrontal craniectomy as an *early intervention* for increased ICP after failed medical therapy in the DECRA trial had poorer outcomes (worse scores on the Extended Glasgow Coma Scale) compared to patients who received standard care. Rates of death at 6 months were similar between the DC group and the standard care managed group. More recently, the RESCUEicp researchers investigated DC as a *last-tier* treatment for refractory increased ICP in TBI patients. At 6 months, DC for refractory increased ICP conferred an increased survival in TBI patients over patients managed medically; however, more patients in the DC group were in a vegetative state compared to medically managed patients. More investigation is needed to better identify which patients might benefit from DC, with consideration given to patient's quality of

life.

Algattas H, Huang JH. Traumatic brain injury pathophysiology and treatments: early, intermediate, and late phases post-injury. *Int J Mol Sci*. 2014;15(1):309–341.

Cooper DJ, Rosenfeld JV, Murray L, et al. Decompressive craniectomy in diffuse traumatic brain injury. *N Engl J Med*. 2011;364(16):1493–1502.

Hutchinson PJ, Kolias AG, Timofeev IS, et al. Trial of decompressive craniectomy for traumatic intracranial hypertension. *N Engl J Med*. 2016;375:1119–1130.

Shutter LA, Timmons SD. Intracranial pressure rescued by decompressive surgery after traumatic brain injury. *N Engl J Med* 2016;375(12):1183–1184.

Soustiel JF, Sviri GE, Mahamid E, et al. Cerebral blood flow and metabolism following decompressive craniectomy for control of increased intracranial pressure. *Neurosurgery*. 2010;67(1):65–72.

A.10. Do genetic factors play a role in the outcome after head injury?

Genetic factors as modulators of neurologic outcome while far from conclusive are worthwhile considering in order to elucidate varied TBI outcomes and to facilitate more effective treatment strategies. Evidence to date has suggested a role for genetic polymorphism (alterations in the DNA sequence within a given gene) as a contributor to the interindividual variability in outcomes after TBI. Polymorphisms along the coding region of tumor necrosis factor (TNF)-α at position -308 *A* allele (allele 2) may play a role in this proinflammatory cytokine's influence on TBI. In one study, individuals identified with -308 A-allele were more likely to have less favorable outcomes after TBI than noncarriers.

A change from proline to arginine due to a coding polymorphism in the p53 protein (involved in cell death) encoded by total protein 53 on chromosome 17 may help to explain poor outcomes in some TBI patients. Poor neurologic outcome has been associated with a greater rate of individuals homozygous for the arginine allele.

Another genetic polymorphism that may play a role in damage from TBI as well as recovery afterward is the angiotensin-converting enzyme (ACE) gene on chromosome 17. The ACE D (deletion) polymorphism in TBI patients appears to confer worse cognitive performance when compared to patients with the I (insertion) allele. Altered CBF due to increasing levels of ACE in the ACE D/D genotype may be responsible for cerebral ischemia affecting poor outcome.

Polymorphism in the proinflammatory cytokine interleukin (IL)-1 has been associated with more hemorrhagic events after TBI.

Genetic variation in the neurotrophin, brain-derived neurotrophic factor (BDNF), critical to memory and learning may affect processing speed suggesting an influence of the BDNF gene on cognitive performance after TBI.

Apolipoprotein E (APOE), a well-studied gene implicated in neurotrauma outcomes, is synthesized by astrocytes, microglia, and neurons under conditions of stress. This gene plays a role in neuronal repair and growth, maintains synaptodendritic connections, and is a mediator in brain inflammatory responses. Chromosome 19 carries the APOE gene, which has three major alleles. Research has linked the $\varepsilon 4$ allele, arginine/arginine, which differs from the other two major alleles, $\varepsilon 2$ (cysteine/cysteine) and $\varepsilon 3$ (cysteine/arginine), to poor outcomes in patients 6 months after brain injury. Women over 55 years with this polymorphism who suffer TBI have poorer outcomes when compared to men with TBI, and APOE4 has been identified as a risk factor for development of chronic traumatic encephalopathy (CTE).

Laskowitz D, Grant G, eds. *Translational Research in Traumatic Brain Injury*. Boca Raton, FL: CRC Press/Taylor & Francis Group; 2016:179–218.

McAllister TW. Genetic factors modulating outcome after neurotrauma. *PM R*. 2010;2:S241–S252.

B. Preoperative Evaluation and Preparation

B.1. What is the GCS? What is the significance of a GCS of 7T in this patient?

The GCS is an assessment tool in use since 1974 that uses eye opening as well as verbal and motor responses to evaluate neurologic status and severity of TBI (**Table 20.1**). It was initially developed to assess head trauma patients, although its use has expanded to many other patient populations. In this patient, a GCS of 7T signifies that she has a severe TBI and is intubated.

Patients with a GCS score of 13 to 15 are considered to have a mild TBI; moderate TBI is classified by a GCS score of 9 to 12, whereas a GCS score of 8 and below corresponds with severe TBI. Compared to patients with other types of traumatic injury, mortality risk is significantly increased with severe TBI. Even with isolated TBI, these patients are also at high risk of failure of nonneurologic organs. Guidelines published for the management of severe head injury by the American Society of Neurological Surgeons (ASNS) and Brain Trauma Foundation recommend early therapy directed toward avoiding hypotension and hypoxia as well as ICP monitoring in order to guide therapy for maintenance of cerebral perfusion. Adherence to these guidelines has been associated with improved survival following severe head injury.

Bratton SL, Chestnut RM, Ghajar J, et al. Guidelines for the management of severe traumatic brain injury. I. Blood pressure and oxygenation. *J Neurotrauma*. 2007;24(suppl 1):S7–S13.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2680.

Matis G, Birbilis T. The Glasgow Coma Scale—a brief review. Past, present, future. *Acta Neurol Belg*. 2008;108(3):75–89.

Talving P, Karamanos E, Teixeira PG, et al. Intracranial pressure monitoring

in severe head injury: compliance with Brain Trauma Foundation guidelines and effect on outcomes: a prospective study. *J Neurosurg*. 2013;119:1248–1254.

TABLE 20.1 Glasgow Coma Scale

Eye opening:	None	1
	To pain	2
	To verbal command	3
	Spontaneous	4
Best verbal response:	No verbal response	1
	Incomprehensible sounds	2
	Inappropriate words	3
	Disoriented, conversing	4
	Oriented, conversing	5
Best motor response:	No response (flaccid)	1
	Extension (decerebrate)	2
	Abnormal flexion (decorticate)	3
	Flexion/withdrawal	4
	Localizes to pain	5
	Obeys verbal commands	6

B.2. In addition to the GCS, what other assessments can be done to evaluate neurologic function?

Although the GCS is the most commonly used assessment tool, there are other methods available to assess neurologic function. Abnormalities in pupillary size, symmetry, and light reflex may reveal conditions requiring immediate intervention such as uncal or cerebellar herniation. The World Federation of Neurological Surgeons scale is a modified GCS which grades patients according to GCS score and presence or absence of motor deficits. The Hunt and Hess scale is a grading system that predicts mortality in patients with subarachnoid hemorrhage based on clinical presentation and may also be useful for evaluation of TBI patients. The Abbreviated Injury Scale (AIS) is an anatomic scale for assessing the severity of traumatic injuries. It may be useful in conjunction with the GCS in more

accurately evaluating TBI in elderly patients.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2680.

Rau CS, Wu SC, Chen YC, et al. Effect of age on Glasgow Coma Scale in patients with moderate and severe traumatic brain injury: an approach with propensity score-matched population. *Int J Environ Res Public Health*. 2017;14(11):1378.

B.3. What is the role of CT scanning in the initial evaluation of the patient with head injury? What are the management options in patients whose neurologic condition is deteriorating before obtaining a CT scan?

Following head trauma, CT scan can be very useful for revealing acute brain injury. An early CT scan is indicated for a GCS of 9 to 12 (moderate head injury) as well as severe head injury. Any patient with a deteriorating GCS score requires an immediate CT scan.

The Canadian CT Head Rule is a clinical decision-making tool that was developed to guide the use of CT scans in head injury because the vast majority of CT scans performed in the context of head trauma are negative for significant brain injury. The rule is used to assess risk level for neurosurgical intervention and brain injury on CT in patients with minor head injury and GCS of 13 to 15. Patients considered to be at high risk for neurologic intervention have any one of the following findings:

a. GCS score less than 15 at 2 hours beyond the time of injury
b. Any suspected open or depressed skull fracture
c. Signs of basal skull fracture (hemotympanum, Battle sign, raccoon eyes, otorrhea, or rhinorrhea of CSF)
d. Two or more episodes of vomiting
e. 65 years of age or older

Patients with injury resulting from any dangerous mechanism, such as ejection from a motor vehicle, fall from a height of 3 feet or more, or any patient who exhibits amnesia of 30 minutes or more prior to injury are considered to be at medium risk for brain injury findings on CT.

It is important to note that the Canadian CT Head Rule does not apply to trauma patients with GCS <13, obvious open skull fracture, age less than 16 years, or in patients with a bleeding disorder or taking anticoagulant medications.

The airway should be secured with an endotracheal tube as soon as possible in patients with deterioration in neurologic function or in those who are likely to have such changes prior to obtaining a CT scan.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2138.

Stiell IG, Clement CM, Grimshaw JM, et al. A prospective cluster-randomized trial to implement the Canadian CT Head Rule in emergency departments. *CMAJ*. 2010;182(14):1527–1532.

Stiell IG, Wells GA, Vandemheen K, et al. The Canadian CT Head Rule for patients with minor head injury. *Lancet*. 2001;357(9266):1391–1396.

B.4. What is the role of ICP monitoring in the management of head injury?

ASNS/Brain Trauma Foundation (BTF) guidelines recommend early ICP monitoring and concomitant goal-directed therapy for maintenance of cerebral perfusion in patients with severe head injury. Adherence to these guidelines may improve outcome in this patient population, primarily through guiding therapy to minimize secondary insults following the initial injury.

Because of impaired CBF and autoregulation in the injured brain, cerebral perfusion is highly dependent on cranial perfusion pressure for oxygen delivery and the prevention of cerebral ischemia.

Systemic hypotension and intracranial hypertension are

factors related to increased morbidity and mortality in severe TBI. Because CPP values of less than 50 mmHg are correlated with poor outcomes, continuous monitoring of ICP should be used to guide therapy in patients with severe TBI. The target range for CPP is 60 to 70 mmHg according to the most recent ASNS/BTF guidelines.

Currently, recommendations for ICP monitoring include (1) patients with GCS 3 to 8 following resuscitation and abnormal CT scan related to the injury (contusion, swelling, compressed basal cisterns, or hematoma seen on CT) and (2) patients with severe TBI if two or more of the following features are present: age over 40, motor posturing, or systolic BP (SBP) less than 90 mmHg, even if the CT scan is normal. Current recommendations include treating an ICP >22 mmHg, although treatment decisions may also depend on CT findings and clinical presentation.

ICP monitoring can be performed using ventricular catheters or intraparenchymal fiberoptic monitors. Ventricular catheters have the advantage of allowing CSF drainage, although they do carry a higher infection risk. In the setting of a coagulopathy, placing an ICP monitor is contraindicated.

Carney N, Totten AM, O'Reilly C, et al. Guidelines for the management of severe traumatic brain injury, fourth edition. *Neurosurgery*. 2017;80(1):6–15.

Griesdale D, Ortenwall V, Norena M, et al. Adherence to guidelines for management of cerebral perfusion pressure and outcome in patients who have severe traumatic brain injury. *J Crit Care*. 2015;30(1):111–115.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2675–2676.

Talving P, Karamanos E, Teixeira PG, et al. Intracranial pressure monitoring in severe head injury: compliance with Brain Trauma Foundation guidelines and effect on outcomes: a prospective study. *J Neurosurg*. 2013;119:1248–1254.

B.5. How can you clear this patient's cervical spine?

The National Emergency X-Radiography Utilization Study (NEXUS) low-risk criteria are commonly used to determine the need for radiographic imaging in the clinical evaluation of cervical spine injury. A patient is considered to be low risk for cervical spine injury if they meet all of the following criteria:

1. No posterior midline cervical spine tenderness
2. No evidence of intoxication
3. GCS score of 15—normal level of alertness
4. No focal neurologic deficit
5. No painful distracting injuries

However, there is evidence that patients with clinically significant cervical spine injuries, such as ligamentous injury, cervical spine fracture, or dislocation, may be considered low risk according to the NEXUS criteria, particularly elderly patients. This may be a result of variation in determining the extent or presence of distracting injuries.

The Canadian C-spine Rule is another clinical decision-making tool that may be used in evaluating the need for further imaging in cervical spine injury. The criteria take into account the mechanism of injury, midline neck tenderness, and the ability to rotate the neck more than 45 degrees without pain (if it is safe for the patient to do so). A recent comparison of the Canadian C-spine and NEXUS rules indicated that the Canadian C-spine Rule may have greater reliability.

Nevertheless, CT evaluation is still recommended in the case of major trauma because of the possibility of misdiagnosis of a clinically significant cervical spine injury.

Collins NC, McKenzie JV. The NEXUS criteria: do they stand the test of time? *Eur J Emerg Med*. 2013;20:58–60.

Duane TM, Mayglothling J, Wilson SP, et al. National Emergency X-Radiography Utilization Study criteria is inadequate to rule out fracture after significant blunt trauma compared with computed tomography. *J Trauma*. 2011;70:829–831.

Ehrlich F, Wee C, Drongowski R, et al. Canadian C-spine rule and the National Emergency X-Radiography Utilization Low-Risk Criteria for C-spine radiography in young trauma patients. *J Pediatr Surg*. 2009;44:987–991.

Michaleff ZA, Maher CG, Verhagen AP, et al. Accuracy of the Canadian C-spine rule and NEXUS to screen for clinically important cervical spine injury in patients following blunt trauma: a systematic review. *CMAJ*. 2012;184(16):E867–E876.

B.6. What are the advantages of early endotracheal intubation in this patient?

Endotracheal intubation is indicated in this patient with a severe TBI and a strong probability of further neurologic deterioration. Choosing early endotracheal intubation provides the advantage of securing the airway under more controlled and optimized circumstances as well as providing safer conditions for further evaluation and treatments.

Guidelines published by the Eastern Association for the Surgery of Trauma recommend early endotracheal intubation for all patients with a GCS score of 8 or less (level 1 indication). Other level 1 indications include airway obstruction, persistent hypoxemia, hypoventilation, hemorrhagic shock, and cardiac arrest.

Mayglothling J, Duane TM, Gibbs M, et al. Emergency tracheal intubation immediately following traumatic injury: an Eastern Association for the Surgery of Trauma practice management guideline. *J Trauma Acute Care Surg*. 2012;73:S333–S340.

B.7. What is your plan for airway management in this patient? How would it change if the patient were combative? How would it change if the patient had facial fractures with significant swelling of the head and neck?

The practitioner considering airway management in a trauma patient should take into account his or her own skill level and experience with different approaches to intubation. Although

fiberoptic intubation could minimize manipulation of the cervical spine, difficulty is increased substantially under emergent conditions, especially in the presence of bleeding or secretions. Additionally, in a combative, uncooperative patient, attempting an awake or lightly sedated fiberoptic intubation would be inadvisable. Rapid sequence induction (RSI) may provide the best intubating conditions in the trauma patient, who should be considered a full stomach and at high risk for aspiration of gastric contents.

There is some controversy among practitioners regarding the use of both ventilatory breaths and cricoid pressure during RSI of the trauma patient. The risks of oxygen desaturation and hypercarbia for each patient must be taken into consideration when deciding whether ventilation should be used. If ventilatory breaths are necessary, cricoid pressure could limit gastric inflation caused by positive pressure ventilation, although it may also reduce tidal volumes. There is also some evidence that cricoid pressure could degrade laryngoscopic view in up to 30% of patients and should therefore be discontinued if required to improve intubating conditions and expedite securing the airway.

A recent large study conducted in 10 academic centers suggests that the risk of pulmonary aspiration does not increase if cricoid pressure (i.e., Sellick maneuver) is not applied during RSI induction of anesthesia. It is important to note, however, that this trial did not extend to patients outside of the operating room or to pregnant patients.

In-line stabilization (facilitated by removal of the front of the cervical collar if needed) is still recommended in the setting of cervical spine injury. Assistance from one or more individuals will be required in this endeavor, particularly with a combative patient.

Videolaryngoscopy would most likely be highly beneficial under these circumstances (depending on clinician experience)

for facilitation of intubation while reducing stress on the cervical spine. Difficult airway equipment should also be immediately accessible should the need to follow the difficult airway algorithm arise.

If an extremely difficult airway is anticipated, very cautious use or avoidance of neuromuscular blocking drugs (NMBDs) should be exercised, and alternative methods for securing an airway, such as cricothyroidotomy, should be considered.

A primary concern in a patient with facial fractures is the ability to provide adequate ventilation and preoxygenation prior to induction. Additionally, there is also a substantial probability that swelling, blood, and secretions will limit visibility and markedly increase difficulty in securing the airway. Light palpation of the facial bones can help to ascertain the presence of facial fractures.

Oral intubation is highly preferred in trauma situations. Nasal intubation should be avoided in head injury because of the possibility of fractures of the basilar skull and cribriform plate and concerns over entering the cranial vault as well as failed intubation.

Birenbaum A, Hajage D, Roche S, et al. Effect of cricoid pressure compared with a sham procedure in the rapid sequence induction of anesthesia: the IRIS randomized clinical trial. *JAMA Surg*. 2019;154(1):9–17.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2121–2125.

B.8. What are the effects of succinylcholine on ICP? What is the significance of the effect, if any?

The rapid onset and short duration of succinylcholine make it a suitable NMBD for facilitating intubation in trauma patients. Succinylcholine has been shown to transiently increase ICP, but this effect should be weighed against the potential detrimental effects of hypercarbia and hypoxia in patients with severe head

injury and is not a contraindication to its use. The rise in ICP may be attenuated by pretreatment with a small dose of a nondepolarizing NMBD; however, the benefits of this practice have not been proven.

In cases where succinylcholine is not considered to be suitable, high-dose rocuronium (1.2 mg per kg) is an alternative for RSI, particularly when sugammadex is available.

The cyclodextrin sugammadex (Bridion©) is a neuromuscular blockade reversal drug for use with the aminosteroid nondepolarizing agents, rocuronium and vecuronium, that has recently become widely available in the United States. In high doses (16 mg per kg), sugammadex may be considered for emergency reversal of rocuronium. It should be noted, however, that bradycardia and dose-dependent transient elevated activated partial thromboplastin time (aPPT) and prothrombin time/international-normalised-ratio (PT/INR) have been reported with sugammadex.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1872, 2124–2125.

Lee IO, Kim YS, Chang HW, et al. In vitro investigation of the effects of exogenous sugammadex on coagulation in orthopedic surgical patients. *BMC Anesthesiol*. 2018;18(1):56.

Mayglothling J, Duane TM, Gibbs M, et al. Emergency tracheal intubation immediately following traumatic injury: an Eastern Association for the Surgery of Trauma practice management guideline. *J Trauma Acute Care Surg*. 2012;73:S333–S340.

Oliveira C, Marques C, Simões V, et al. Severe bradycardia and asystole associated with sugammadex: case report. *Rev Bras Anestesiol*. 2019;69(2):218–221.

B.9. What coagulation abnormalities are present after TBI? What modalities can be used to provide hemostasis and reduce intracranial hematoma expansion?

Coagulopathy, particularly in the first 24 to 72 hours following severe TBI, is associated with a high risk of mortality and may occur in greater than 60% of these patients. The risk of poor outcome may be increased up to 30 times in TBI patients presenting to the emergency room with abnormal coagulation. Therefore, the initiation of early coagulation monitoring is recommended.

Both hypo- and hypercoagulable states may be present and include disorders of coagulation enzymes, platelet function, thrombocytopenia, and impaired fibrinolysis. Although no specific mechanism has been established, release of tissue factor leading to a consumptive coagulopathy as well as hyperfibrinolysis and abnormal activation of the protein C pathway have been proposed.

Acute coagulopathy following severe head injury is complex and may not be differentiable from coagulopathy associated with other types of trauma. Treatment should address the primary cause with correction of the coagulation abnormality and a focus on controlling bleeding. Although FFP could be useful when there is evidence of a coagulopathy, prophylactic early use in head trauma has not proven to be beneficial and is related to adverse events. Conflicting information exists with respect to platelet administration. Goal-directed platelet use may be effective in reversing platelet dysfunction, particularly in reversal of aspirin therapy, but may not be as effective with other antiplatelet medications. Nevertheless, it is still recommended that an INR above 1.4 and a platelet count at or below 75,000 per μL be corrected.

Recombinant factor VIIa rapidly corrects INR and possibly allows earlier neurosurgical intervention, although a higher incidence of asymptomatic deep vein thrombosis has also been observed. Additionally, administration of recombinant factor VIIa has not been found to improve clinical outcomes and may

be associated with lower GCS at discharge. Four factor prothrombin complex concentrate has been recommended for Vitamin K antagonist reversal, as well as for reversal of Novel Oral Anticoagulants that inhibit Factor Xa, in TBI patients with ICH.

Tranexamic acid has also been investigated and may show some benefit with reduction in intracranial hemorrhage progression particularly in the first 1 to 3 hours following injury. Idarucizumab is a specific antibody now available for the reversal of dabigatran.

de Oliveira Manoel AL, Neto AC, Veigas PV, et al. Traumatic brain injury associated coagulopathy. *Neurocrit Care*. 2015;22(1):34–44.

Furay E, Daley M, Teixeira PG, et al. Goal-directed platelet transfusions correct platelet dysfunction and may improve survival in patients with severe traumatic brain injury. *J Trauma Acute Care Surg*. 2018;85(5):881–887.

Lombardo S, Millar D, Jurkovich GJ, et al. Factor VIIa administration in traumatic brain injury: an AAST-MiTC propensity score analysis. *Trauma Surg Acute Care Open*. 2018;3(1):e000134.

Maegle M. Coagulopathy after traumatic brain injury: incidence, pathogenesis, and treatment options. *Transfusion*. 2013;53(suppl 1):28S–39S.

Medzon R, Bracken M, Rathlev NK, et al. Clinically suspected coagulopathy in blunt head trauma. *J Emerg Med*. 2010;39:399–405.

Qureshi H, Mithaiwala H, Ezell J, et al. Anesthetic management of traumatic brain injury. *Clin Med Rev Case Rep*. 2017;4(3):159.

Wiegele M, Schochi H, Haushofer A, et al. Diagnostic and therapeutic approach in adult patients with traumatic brain injury receiving oral anticoagulation therapy: an Austrian interdisciplinary consensus statement. *Crit Care*. 2019;23:62.

C. Intraoperative Management

C.1. What is appropriate hemodynamic monitoring during CT scanning and during craniotomy for evacuation of a subdural hematoma?

First, the patient should be stabilized prior to CT scanning or

any other diagnostic studies. When a patient, who has sustained a TBI, is uncooperative, combative, or comatose and requires airway control, an emergent endotracheal intubation is necessary to protect airway, facilitate diagnostic procedures, such as head CT scan or MRI, and prevent hypoxia and hypercarbia which are two important secondary insults. Hemodynamic monitoring should include standard American Society of Anesthesiologists (ASA) monitors: noninvasive BP, electrocardiography (ECG), pulse oximetry, capnography (end-tidal carbon dioxide [$EtCO_2$]), and temperature. Patent airway, adequate ventilation, and stable circulation are initial priorities.

If the patient with TBI shows signs of intracranial hypertension (defined as sustained ICP greater than 20 mmHg), such as headache, nausea/vomiting (N/V), papilledema, focal neurologic deficits, altered consciousness, or Cushing triad (reflex arterial hypertension, bradycardia, and bradypnea), hyperosmolar therapy (e.g., mannitol) should be started immediately to lower ICP without direct ICP measurement during CT scanning.

In addition to the aforementioned standard ASA monitors, during the craniotomy for evacuation of a subdural hematoma, which is much more common than epidural hematoma and carries a worse prognosis, an intra-arterial catheter for continuous BP monitoring and urine output monitoring are appropriate in this patient. Central line placement should be considered if the patient has difficult peripheral IV access, the injury is extensive or unknown, or the patient is unstable requiring norepinephrine infusions. ICP monitoring is indicated in this patient because she has severe TBI and abnormal findings on her head CT scans. Important objectives in the management of the patient with TBI are to maintain adequate MAP, keep ICP less than 20 mmHg, prevent or reverse herniation, minimize retractor pressure, and facilitate surgical access. Furthermore,

CPP monitoring and novel techniques, such as jugular venous oxygen saturation ($SjvO_2$) for advanced cerebral monitoring (ACM), may help guide management and improve outcome. Normal $SjvO_2$ threshold is 55% to 75% (see section D.5 for additional information). Medical treatment and surgical intervention decisions are ideally driven by multiple monitoring approaches and ongoing clinical assessment. In addition, monitoring for venous air embolism is reasonable if the patient's head is elevated above the heart.

Carney N, Totten AM, O'Reilly C, et al. Guidelines for the management of severe traumatic brain injury, fourth edition. *Neurosurgery*. 2017;80(1):6–15.

Cooper DJ, Rosenfeld JV, Murray L, et al. Decompressive craniectomy in diffuse traumatic brain injury. *N Engl J Med*. 2011;364(16):1493–1502.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1881–1882.

Jaffe RA, Schmiesing CA, Golianu B, eds. *Anesthesiologist's Manual of Surgical Procedures*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2014:37–44.

Smith M. Physiological brain monitoring. *ASA Refresher Courses in Anesthesiology*. 2014;42(1):119–128.

C.2. Should hyperventilation be used in this patient?

The 2017 BTF guidelines recommend that hyperventilation be avoided during the first 24 hours after TBI when CBF is often critically reduced during the stage of primary brain injury. Hyperventilation with maintenance of $PaCO_2$ 30 to 35 mmHg is an acceptable temporizing measure to reduce elevated ICP unresponsive to sedation, neutrally positioned head elevated to 15 to 30 degrees, osmotic diuretics, and/or CSF drainage but should be as brief as possible. When prolonged hyperventilation is required, monitoring cerebral oxygenation with $SjvO_2$ and CBF with transcranial Doppler should be considered.

$PaCO_2$ is a powerful determinant of CBF. The target $PaCO_2$ is 35 to 45 mmHg. Generally speaking, alterations of $PaCO_2$ within

the range of 20 to 80 mmHg cause changes in CBF accordingly, that is, a decreased $PaCO_2$ or hypocapnia results in decreased CBF and ICP. Moderate hyperventilation ($PaCO_2$ 30 to 33 mmHg), therefore, is often very helpful in reducing CBF and normalizing ICP. A modest decrease in $PaCO_2$ is valuable to counteract the vasodilating effects of volatile anesthetics. However, hypocapnia with resultant vasoconstriction can cause cerebral ischemia, which may worsen cerebral injury in patients with focal ischemia, particularly in a recently injured brain and in a brain beneath a retractor. The most recent BTF guidelines are that hyperventilation should be employed selectively rather than routinely in the management of patients with TBI. Prolonged prophylactic hyperventilation with $PaCO_2$ of ≤25 mmHg is not recommended. Hyperventilation should be reserved for patients in which herniation is imminent.

Brain Trauma Foundation, American Association of Neurological Surgeons, Joint Section on Neurotrauma and Critical Care. Hyperventilation. *J Neurotrauma*. 2000;17(6–7):513–520.

Carney N, Totten AM, O'Reilly C, et al. Guidelines for the management of severe traumatic brain injury, fourth edition. *Neurosurgery*. 2017;80(1):6–15.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1873.

C.3. What are the implications of arterial hypertension in patients with head injury? How should BP be managed?

Hypertension is common in head injury patients who do not have other injuries associated with massive blood loss. There are at least four important implications of arterial hypertension in patients with head injury. (1) Higher SBP may be required to achieve adequate CPP (CPP = MAP − ICP or CVP), particularly in patient with severely elevated ICP. This may be the body's compensatory mechanism. MAP and CPP must be considered in

addition to SBP. Efforts to optimize CPP should first lower ICP. (2) Because autoregulation of CBF is usually impaired in areas of brain injury, arterial hypertension can worsen cerebral edema, leads to secondary hemorrhage, and increases ICP because of the increased cerebral blood volume and hyperemia ("pressure-passive" in TBI patients with impaired cerebral autoregulation). Intra-arterial BP monitoring is necessary. (3) Cushing triad is reflex systemic hypertension, bradycardia, and bradypnea in association with elevated ICP. It is a late and unreliable sign that usually precedes brain herniation. (4) Other etiologies of arterial hypertension might be related to pain or catecholamine surge and can be treated with opioids and deepening anesthesia only after hypoxemia and hypercarbia are ruled out as causes.

It is prudent to maintain SBP ≥100 mmHg for patients 50 to 69 years old or at ≥110 mmHg for patients 15 to 49 or over 70 years old. Recent guidelines recommend keeping CPP between 60 and 70 mmHg to ensure adequate brain perfusion and avoid secondary brain injury in order to improve outcomes. However, patients with TBI associated with multiple trauma injuries are at risk for arterial hypotension (SBP <90 mmHg) related to bleeding, especially when combined with tachycardia. Avoiding hypotension in patients with severe TBI is a primary perioperative goal. Hypotension can cause cerebral ischemia and is related to poor neurologic outcome in TBI patients; treatment includes the judicious use of IV fluids, blood transfusion, and vasopressors. Interventions to stop bleeding and restore intravascular volume should precede surgical management of TBI. Attention to fluid resuscitation is in order because aggressive IV fluids to maintain CPP >70 mmHg may lead to acute respiratory failure.

Brain Trauma Foundation. *Guidelines for the Management of Severe Traumatic Brain Injury*. 4th ed. Palo Alto, CA: Brain Trauma Foundation; 2016:164–172.

Carney N, Totten AM, O'Reilly C, et al. Guidelines for the management of severe traumatic brain injury, fourth edition. *Neurosurgery*. 2017;80(1):6–15.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2139–2140.

C.4. What should be done about intravenous (IV) fluid replacement? Should corticosteroids be given empirically?

Hypotension (SBP <90 mmHg) after head injury is associated with a greater than 70% increased incidence of morbidity and mortality when compared to patients with higher SBPs. Fluid resuscitation should be initiated prior to induction of anesthesia. IV fluids are replaced in trauma patients to restore circulation secondary to blood loss and to maintain MAP and CPP. The important principles are that the chosen fluids should be able to prevent decreases in serum osmolality and colloid oncotic pressure. The choice of the best resuscitation fluids for patients with severe TBI is still controversial. The SAFE-TBI study (2007) indicated that resuscitation with 4% albumin (vs. saline) may be linked with greater mortality in TBI; therefore, 0.9% NS is preferable. Lactated Ringer's solution should be avoided because it was associated with increased mortality compared with NS in patients with TBI.

Corticosteroids should not be given empirically in the operating room because there are no benefits in these patients. In patients with severe TBI, high-dose methylprednisolone was associated with increased mortality and is contraindicated; this is unlike the beneficial role they play in mitigating the swelling and edema that can occur with brain tumors, subdural hematomas, postoperative swelling, and acute spinal cord injury.

Edwards P, Arango M, Balica L, et al. Final results of MRC CRASH, a randomised placebo-controlled trial of intravenous corticosteroid in adults with head injury-outcomes at 6 months. *Lancet*. 2005;365(9475):1957–1959.

Fuller G, Hasler RM, Mealing N, et al. The association between admission

systolic blood pressure and mortality in significant traumatic brain injury: a multi-centre cohort study. *Injury*. 2014;45(3):612–617.

Jungner M, Grände P, Mattiasson G, et al. Effects on brain edema of crystalloid and albumin fluid resuscitation after brain trauma and hemorrhage in the rat. *Anesthesiology*. 2010;112(5):1194–1203.

Myburgh J, Cooper DJ, Finfer S, et al. Saline or albumin for fluid resuscitation in patients with traumatic brain injury. *N Engl J Med*. 2007;357(9):874–884.

Roswell SE, Fair KA, Barbosa RR, et al. The impact of pre-hospital administration of lactated Ringer's solution versus normal saline in patients with traumatic brain injury. *J Neurotrauma*. 2016;33(11):1054–1059.

Semler MW, Self WH, Wanderer JP, et al. Balanced crystalloids versus saline in critically ill adults. *N Engl J Med*. 2018;378(9):829–839.

C.5. Should hypertonic saline (HTS) be administered to this patient? How is HTS administered?

Even though mannitol is used most commonly intraoperatively because of its rapid onset, efficacy in decreasing ICP, and improvement in brain relaxation, HTS has been used as an alternative agent for the effective treatment of elevated ICP. HTS can be administered if this patient is refractory to mannitol or if repeated administration of mannitol results in the adverse effects such as renal injury, hypovolemia, or electrolyte disturbances from profound diuresis.

HTS (3% most commonly used), like mannitol, creates a hyperosmotic state in the intravascular compartment but does not cross the intact BBB. As a result of the osmotic gradient formed across the BBB, water flux from the extravascular to the intravascular compartment occurs. At this time, however, there is insufficient evidence to support the use of one rather than the other to improve outcomes such as mortality or functional recovery. Three percent HTS is typically administered via a central venous catheter as a continuous infusion with careful attention to serum sodium (keep between 145 and 155 mEq per L). Slow administration is helpful in preventing central pontine myelinolysis.

Hyperosmolar agents (mannitol and HTS) are more widely used in neurosurgery to decrease the brain volume of the intra- and extracellular fluid compartments and ICP. However, loop diuretics help promote diuresis.

Carney N, Totten AM, O'Reilly C, et al. Guidelines for the management of severe traumatic brain injury, fourth edition. *Neurosurgery*. 2017;80(1):6–15.

Cooper DJ, Myles PS, McDermott FT, et al. Prehospital hypertonic saline resuscitation of patients with hypotension and severe traumatic brain injury: a randomized controlled trial. *JAMA*. 2004;291(11):1350–1357.

Kamel H, Navi BB, Nakagawa K, et al. Hypertonic saline versus mannitol for the treatment of elevated intracranial pressure: a meta-analysis of randomized clinical trials. *Crit Care Med*. 2011;39(3):554–559.

C.6. The patient underwent a craniectomy for evacuation of a frontal intracerebral hematoma. Should some anesthetic agents be avoided in this situation? Which ones? What agents might be preferred in this situation?

The three important principles in providing anesthesia for craniectomy for evacuation of an intracerebral hematoma in this patient are to maintain adequate MAP, control cerebral edema, and reduce ICP in order to maintain CPP and provide brain relaxation for surgical access. All inhaled anesthetics (all of the volatile anesthetics and nitrous oxide [N_2O]) have some cerebral vasodilatory effect, increase CBF and ICP, and are best avoided. Volatile anesthetics often uncouple CBF and cerebral metabolic rate for oxygen ($CMRO_2$); they produce a dose-dependent increase in CBF but decrease $CMRO_2$. However, all of the IV anesthetic agents, except ketamine, are cerebral vasoconstrictors and cause coupled decrease in CBF and $CMRO_2$ in dose-dependent manner. The IV anesthetic agents such as propofol and narcotics are preferred in this patient. Even though propofol is most commonly used to help reduce ICP, high-dose propofol

is associated with significant hypotension, which can be prevented as long as you support the patient with vasoactive agents. It is critical to keep in mind that hemodynamic stability is essential before and during high-dose propofol. Like N_2O, ketamine increases both CBF and $CMRO_2$ and should also be avoided.

Carney N, Totten AM, O'Reilly C, et al. Guidelines for the management of severe traumatic brain injury, fourth edition. *Neurosurgery*. 2017;80(1):6–15.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1872.

C.7. Should hypothermia be employed in this patient?

Mild hypothermia (32°C to 34°C) may be the most effective method for protecting the brain during focal and global ischemia because it can reduce both basal and electrical metabolic requirements throughout the brain. Induced hypothermia can be employed if this patient is at high risk of intraoperative ischemia and her elevated ICP is refractory to other therapies after discussion with her family or surrogates. However, early (within 2.5 hours), short-term (48 hours postinjury), routine prophylactic hypothermia in neurosurgery is not recommended to improve clinical outcomes in patients with diffuse injuries. An international multicenter trial of mild hypothermia did not show neurologic improvement in patients with TBI. Clinicians should keep in mind that hypothermia may cause cardiac arrhythmias and coagulopathies (platelet dysfunction) and may worsen acidosis, which are deleterious to patients with TBI. Fever worsens clinical outcomes after severe TBI, presumably by aggravating secondary brain injury. Hyperthermia should be treated aggressively and avoided. Intraoperative normothermia is the goal for temperature management. In witnessed cardiac arrest, mild hypothermia has been shown to improve neurologic outcome in these patients.

Butterworth JF, Wasnick JD, Mackey DC, eds. *Morgan & Mikhail's Clinical Anesthesiology*. New York: McGraw-Hill Education; 2018:601–620, 831.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2675.

Madden LK, DeVon HA. A systematic review of the effects of body temperature on outcome after adult traumatic brain injury. *J Neurosci Nurs*. 2015;47(4):190–203.

D. Postoperative Neurointensive Care Management

D.1. What are the postoperative ventilation concerns in this patient?

This patient will undoubtedly remain intubated after DC due to a presenting GCS of 7, acidosis, hyperglycemia, diabetes insipidus, probable lung injury, and pain due to rib fractures. Necessary fluid resuscitation may exacerbate respiratory failure in a patient who is at risk for cardiac dysfunction due to neurogenic pulmonary edema. ICP monitoring is helpful in managing ventilation in the postoperative period because controlling $Paco_2$ and ensuring adequate oxygenation are critical to limiting secondary brain injury. Additionally, CPP (maintained between 60 and 70 mmHg) and MAP should also be monitored to avoid secondary brain injury. To maintain a favorable balance between decreasing ICP and minimizing the decrease in CBF, hyperventilation to no lower than a $Paco_2$ 35 to 40 mmHg is the goal. A low $Paco_2$ will result in low CBF and consequent cerebral ischemia, whereas high $Paco_2$ levels can result in cerebral hyperemia and high ICP. Prolonged prophylactic hyperventilation with $Paco_2 \leq 25$ mmHg is not recommended (level IIB evidence). A muscle relaxant will be helpful in controlling ventilation and preventing unacceptable spontaneous increases in ICP (e.g., during suctioning). Attention

to avoiding high tidal volumes (<6 mL per kg if possible) in order to avoid barotrauma and positive end expiratory pressure (PEEP ≤15 cm H_2O) as needed to maintain adequate oxygenation (PaO_2 >60 mmHg) is important for limiting additional pulmonary damage. Close hemodynamic and ICP monitoring are essential to avoid increases in ICP and/or decreased venous return with institution of PEEP. Other ventilatory strategies including high-frequency percussive ventilation (HFPV) and extracorporeal membrane oxygenation (ECMO) should also be considered if oxygenation continues to be a problem.

Carney N, Totten AM, O'Reilly C, et al. Guidelines for the management of severe traumatic brain injury, fourth edition. *Neurosurgery*. 2017;80(1):6–15.

Ghajar J. Traumatic brain injury. *Lancet*. 2000;356:923–929.

Maas AIR, Stocchetti N, Bullock R. Moderate and severe traumatic brain injury in adults. *Lancet Neurol*. 2008;7:728–741.

Mascia L. Acute lung injury in patients with severe brain injury: a double hit model. *Neurocrit Care*. 2009;11:417–426.

Stocchetti N, Maas A. Traumatic intracranial hypertension. *N Engl J Med*. 2014;370:2121–2130.

D.2. What specific measure should be used to control the patient's ICP? What type of monitoring devices can be used to measure ICP?

Controlling ICP (normal range: 0 to 10 mmHg) is essential to maintaining cerebral perfusion and improving outcome after TBI. ICP should be monitored in patients with severe TBI (GCS 3 to 8) and a CT scan showing hematomas, contusions, swelling, herniation, or compressed basal cisterns. In the case of a normal CT scan, if that patient has two or more of the following features, then ICP monitoring is indicated: >40 years of age, unilateral or bilateral motor posturing, and/or an SBP <90 mmHg. Surgery is often required initially in order to evacuate a

subdural or epidural hematoma causing ICP. The neurosurgical service will often place a ventricular drain in the patient to drain CSF. The head of the bed is typically elevated 15 degrees to promote venous drainage. Keeping the patient sedated, controlling the pain, and avoiding hyperthermia also help to ensure decreased brain cerebral metabolic requirements for oxygen. Selective hyperventilation, as mentioned earlier, may be necessary to control ICP; however, this maneuver will also decrease CBF. Hyperventilation to a $Paco_2$ of <35 mmHg as a temporizing measure is avoided unless transtentorial herniation is suspected. Assuming that the BBB is intact, hyperosmolar therapy with mannitol or HTS will help increase serum osmolarity so that fluid is mobilized from the brain; the serum osmolarity should be no higher than 320 mOsm per L. Electrolyte abnormalities and changes in fluid status require regular blood sampling, close attention to fluid balance, hemodynamic monitoring, and the availability of vasoactive agents. Induction of a barbiturate coma to decrease cerebral metabolism in a patient whose ICP is refractory to treatment will require continued ventilator support, cardiovascular monitors, hemodynamic support, and electroencephalogram (EEG) monitoring. The decrease in ICP caused by mild hypothermia has not translated into improved outcome in TBI patients.

The intraventricular catheter or ventriculostomy connected to a transducer is the most accurate, reliable, and low-cost method for monitoring ICP and guiding therapy. It can be recalibrated in situ. Intraparenchymal ICP monitors using microstrain pressure transducers have negligible drift but cannot be recalibrated in situ. Furthermore, unlike ventricular catheters these catheters cannot be used for draining CSF to decrease ICP. Subdural, subarachnoid, and epidural monitors are less accurate than the aforementioned devices.

Carney N, Totten AM, O'Reilly C, et al. Guidelines for the management of severe traumatic brain injury, fourth edition. *Neurosurgery*. 2017;80(1):6–15.

Cooper DJ, Nichol AD, Bailey M, et al. Effect of early sustained prophylactic hypothermia on neurologic outcomes among patients with severe traumatic brain injury: the POLAR randomized clinical trial. *JAMA*. 2018;320(21):2211–2220.

Hawthorne C, Piper I. Monitoring of intracranial pressure in patients with traumatic brain injury. *Front Neurol*. 2014;5:121.

Maas AIR, Stocchetti N, Bullock R. Moderate and severe traumatic brain injury in adults. *Lancet Neurol*. 2008;7:728–741.

Stocchetti N, Maas A. Traumatic intracranial hypertension. *N Engl J Med*. 2014;370:2121–2130.

D.3. What is neurogenic pulmonary edema? Would you avoid positive end-expiratory pressure (PEEP) in a patient with increased ICP?

Neurogenic pulmonary edema occurs suddenly as a consequence of sympathetic nervous system stimulation from the hypothalamus and medulla after severe neurologic injury. Patients are dyspneic and tachypneic with pink, frothy sputum. They are often hypoxic, tachycardic, and hypertensive. Crackles and rales can be heard on lung auscultation. The chest x-ray is often significant for bilateral infiltrates and the Pa_{O_2}/F_{IO_2} ratio <200.

Theories explaining the pathophysiology of this consequence of TBI are varied. One theory is that myocardial injury from a surge in catecholamines causes pulmonary edema due to cardiac dysfunction, similar to that seen in reversible Takotsubo cardiomyopathy. Neurohemodynamic neurogenic pulmonary edema occurs secondary to an acute rise in systemic and pulmonary pressures leading to left ventricular failure; fluid then shifts to the low-resistance pulmonary circulation causing pulmonary edema. Damage to the alveolar-capillary membrane from the rise in capillary pressure with a consequent transudative pulmonary edema describes the "blast theory."

Finally, trauma to the pulmonary capillary bed secondary to sympathetic discharge may occur without any systemic changes according to the "pulmonary venule adrenergic hypersensitivity theory." After ruling out other causes of respiratory distress (i.e., congestive heart failure, aspiration, acute respiratory distress syndrome, sepsis, and/or transfusion overload), treatment is supportive while addressing the underlying neurologic cause.

Adequate oxygenation of the patient is essential to ensuring cerebral perfusion. If ventilator support with an increased F_{IO_2} is not effective in maintaining a Pa_{O_2} >60 mmHg, then PEEP may help to improve oxygenation. The unwanted consequences of PEEP may be successfully addressed by regular blood sampling and appropriate monitoring. Avoiding hypercarbia from overdistention of alveoli and increased dead space is essential to managing this patient. Elevation of the head of the bed helps to combat the transient increase in right atrial pressure from PEEP-induced impairment of cerebral venous drainage. Monitoring the central circulation to keep the patient euvolemic and close attention to cardiac function will help avoid decreases in venous return from high PEEP and maintain CPP.

Acosta P, Santisbon E, Varon J. The use of positive end-expiratory pressure in mechanical ventilation. *Crit Care Clin*. 2007;23(2):251–261.

Davison DL, Terek M, Chawla LS. Neurogenic pulmonary edema. *Crit Care*. 2012;16(2):212.

D.4. What is the role of antiseizure prophylaxis in the perioperative management of head trauma?

Approximately 30% of patients with severe TBI are at risk for posttraumatic seizures (PTS) in the first 7 days after their trauma (early seizures). These patients may also be at risk for late seizures (after the seventh day after TBI). Penetrating trauma carries with it the greatest risk of PTS; however, patients presenting with a GCS <8, subdural or intracerebral hematoma,

posttraumatic amnesia, immediate seizures, depressed skull fractures, age <65 years, or chronic alcoholism are also at risk for PTS.

The risk of chronic epilepsy, increased cerebral metabolism, and increased ICP makes seizure prophylaxis a serious consideration. Antiepileptic drugs (AEDs) help prevent seizures in patients with early PTS but have little effect on late PTS. Consequently, prophylactic AED is recommended for the first week after head trauma or surgery. Levetiracetam is beneficial and commonly used for early PTS. This drug does not require serum concentration monitoring as with phenytoin and has favorable pharmacokinetic properties.

Carney N, Totten AM, O'Reilly C, et al. Guidelines for the management of severe traumatic brain injury, fourth edition. *Neurosurgery*. 2017;80(1):6–15.

Ghajar J. Traumatic brain injury. *Lancet*. 2000;356:923–929.

Rowe AS, Goodwin H, Brophy GM, et al. Seizure prophylaxis in neurocritical care: a review of evidence-based support. *Pharmacotherapy*. 2014;34(4):396–409.

D.5. How can cerebral oxygenation monitoring be used in the clinical management of TBI?

Brain hypoxia from ischemia due to BBB disruption and cerebral edema, anemia, hypoxemia, and hyperventilation will worsen secondary brain injury. Monitoring of partial pressure of oxygen in brain tissue ($PbrO_2$) is appealing as a guide for managing TBI patients by helping determine the optimal cerebral perfusion pressure (CPP) for adequate brain tissue oxygen. The parenchymal brain oxygen ($PbrO_2$) monitor is inserted into the brain parenchyma typically at the time of ICP monitor placement and measures tissue oxygen in the immediate area. According to the BTF, evidence of a benefit in using this monitoring device to manage TBI patients is inconclusive. In a retrospective study, 123 TBI patients who had ICP and $PbrO_2$

monitoring had a similar mortality rate to the other 506 patients whose treatment was guided by ICP monitoring only. Although hypoxia detected by brain tissue oxygen monitoring was associated with worse outcomes in this study, these researchers were unable to link treatment in response to $PbrO_2$ monitoring to outcome. Several class 3 studies (low-quality RCTs and noncomparative designs) examining $PbrO_2$ monitoring for TBI patients revealed conflicting results regarding mortality and outcome, which has effectively removed the level III recommendation for this advanced monitor for the management of TBI.

Jugular bulb catheters for $SjvO_2$ monitoring provide information regarding global cerebral oxygenation because arteriovenous difference of oxygen content ($AVDO_2$) is an indicator of cerebral oxygen extraction. A cervical spine x-ray is helpful in confirming placement into the dilated portion of the jugular vein just below the base of the skull. Like $PbrO_2$, there is insufficient evidence to support a level I or II recommendation for the use of $AVDO_2$ in managing TBI patients (level II evidence demonstrated no improvement in outcome for monitored patients). Nonrandomized, nonblinded observational studies suggest that jugular bulb monitoring in TBI patients may effect reduced mortality and improved outcomes at 3 and 6 months postinjury (level III evidence).

Regarding threshold values to target or avoid specific to these advanced cerebral monitors, the BTF reports that there is insufficient evidence to inform level I or II recommendations. However, there is level III evidence to support a jugular venous saturation of <50% as a threshold to avoid in the management of TBI.

Carney N, Totten AM, O'Reilly C, et al. Guidelines for the management of severe traumatic brain injury, fourth edition. *Neurosurgery*. 2017;80(1):6–15.

Oddo M, Bösel J. Monitoring of brain and systemic oxygenation in neurocritical care patients. *Neurocrit Care*. 2014;21(suppl 2):S103–S120.

Schell RM, Cole DJ. Cerebral monitoring: jugular venous oximetry. *Anesth Anal*. 2000;90(3):559–566.

D.6. What methods can be used in the neurointensive care unit to prevent hyperthermia?

Fever (>38.3°C) occurs in approximately 70% of patients with brain injury and may last weeks after injury. After ruling out infections, approximately one-third of patients will require treatment for a central fever due to their injured brain. Damage to or irritation of the hypothalamus, the center for thermoregulation, and increased sympathetic tone are responsible for this elevation in temperature. The elevated temperature exacerbates secondary brain injury by increasing neurotransmitter release, oxygen free radicals, high glutamate concentrations, ischemic damage in the penumbra, and BBB breakdown. Fever after TBI is associated with poor long-term outcome.

Antipyretic agents (e.g., acetaminophen, aspirin, and nonsteroidal anti-inflammatory drugs) inhibit cyclooxygenase-mediated prostaglandin synthesis in the brain and lower the hypothalamic set point. The limited benefit of this mode of treatment relates to damage of the thermoregulatory center in head trauma patients.

Nonpharmacologic interventions include external and intravascular cooling. External cooling includes four modes of promoting heat loss: evaporation via sponge baths, conductive heat loss with water-circulating cooling blankets, convective heat loss using fans and air-circulating cooling blankets, and radiation or exposure of the patient's skin. Combining these modalities appears to be more effective than any single method for decreasing temperature in patients without brain injury. A new system of surface cooling includes tightly wrapped pads

that circulate cold water to promote conductive heat loss. This mode of conductive heat loss reduces fever better and faster than the conventional water-circulating cooling blanket.

Intravascular cooling works by infusing cooled saline intravascularly. This method is more effective at cooling than other nonpharmacologic methods. The solution extracts heat from the blood thereby lowering body temperature. Infusion of NS at 4°C will decrease core temperature by 2.5°C within an hour after the infusion is started with no untoward effects on the patient.

The hyperthermic patient must be continuously monitored for any signs of infection and hypothermia. At temperatures less than 35°C, the risk for dysrhythmias, coagulopathy, electrolyte abnormalities, and hypovolemia will increase. Shivering and vasoconstriction (<36°C) may complicate the cooling process with a significant increase in metabolic demand and unwanted tachycardia and hypertension. Attention when caring for these patients is in order because the injured hypothalamus may reset so that these effects may manifest at normothermia.

Badjatia N. Hyperthermia and fever control in brain injury. *Crit Care Med*. 2009;37(7 suppl):S250–S257.

Badjatia N, Bodock M, Guanci M, et al. Rapid infusion of cold saline (4 degrees C) as adjunctive treatment of fever in patients with brain injury. *Neurology*. 2006;66:1739–1741.

Greer DM, Funk SE, Reaven NL, et al. Impact of fever on outcome in patients with stroke and neurologic injury: a comprehensive meta-analysis. *Stroke*. 2008;39:3029–3035.

Mayer SA, Kowalski RG, Presciutti M, et al. Clinical trial of a novel surface cooling system for fever control in neurocritical care patients. *Crit Care Med*. 2004;32:2508–2515.

Cerebral Aneurysm

Patricia Fogarty Mack

21

A 43-year-old woman presented to the emergency room 2 days ago, complaining of severe headache, nausea, and vomiting, followed by a witnessed 3-minute loss of consciousness. On regaining consciousness, she was noted by her family to be confused. A computed tomography (CT) scan showed subarachnoid bleeding. You are called to the angiography suite because four-vessel angiography has revealed an 18-mm basilar tip aneurysm and a 10-mm right middle cerebral artery aneurysm. The interventional neuroradiologist wishes to coil the basilar tip aneurysm but believes the middle cerebral artery aneurysm will require a craniotomy and clipping. At present, she was oriented only to person. She had no previous medical history; however, she has smoked one pack of cigarettes per day for the last 20 years. Her blood pressure was 130/80 mmHg, pulse 90 beats per minute, and respiration 18 breaths per minute. She had no focal neurologic deficits. Laboratory examination revealed normal electrolytes and complete blood count but elevated creatine phosphokinase myocardial-bound (CPK-MB) and troponin. Electrocardiogram demonstrated normal sinus rhythm with flipped T waves throughout the precordium.

A. Medical Disease and Differential Diagnosis

1. What are the incidence, prevalence, and causes of

subarachnoid hemorrhage (SAH), and what are the risk factors associated with rupture of intracranial aneurysms?
2. What are common sizes and locations of intracranial aneurysms?
3. What is the pathophysiology of aneurysmal rupture and SAH?
4. What are symptoms and signs of SAH?
5. How does one assess the severity of SAH?
6. What are the cardiovascular effects of SAH?
7. How is the diagnosis of SAH made?
8. What is the risk for rebleeding for a patient with SAH?

B. Preoperative Evaluation and Preparation

1. What are some concerns in going to the interventional neuroradiology suite in the midst of an angiogram to be followed immediately with coiling of an aneurysm?
2. What type of anesthesia is required for coiling of an aneurysm?
3. Should one proceed with induction of general anesthesia under these circumstances?
4. What types of emergencies can occur during coiling of an aneurysm, and how should they be managed?
5. What other modalities of endovascular therapy are available?
6. A craniotomy is planned for the following day to clip the middle cerebral artery aneurysm. Should surgery be postponed because of the patient's elevated troponin and CPK-MB fractions?
7. Would you premedicate this patient before craniotomy?

C. Intraoperative Management

1. What are the goals of the induction and maintenance of anesthesia for this patient?
2. Is placement of an arterial catheter necessary for induction of anesthesia in this patient in the interventional neuroradiology suite?

3. How would you assess fluid status in this patient?
4. Would monitoring central venous pressure (CVP) be useful for craniotomy and aneurysm clipping in this patient?
5. What other forms of monitoring would you consider?
6. What are your specific concerns during induction of anesthesia in this patient?
7. How would you accomplish a smooth and safe induction and intubation in this patient?
8. Would you perform a rapid sequence induction and tracheal intubation for this patient?
9. What are the effects of hypoxemia and hypercapnia, such as would be seen with loss of the airway on induction, on cerebral blood flow (CBF)?
10. What is optimal fluid management for aneurysm clipping? Would you use a dextrose-containing solution?
11. After the bone plate was removed and as the dura was being opened, the surgeon complained that the brain was "tight." What could you do to achieve better brain relaxation and facilitate surgical exposure?
12. How might transmural pressure be decreased to allow for aneurysm clip placement?
13. What is the purpose of controlled hypotension, and how is it achieved?
14. What are some of the drawbacks of controlled hypotension?
15. What methods of cerebral protection might you use during this operation?
16. Would you induce mild hypothermia as a means of cerebral protection?
17. What are the indications for deep hypothermic circulatory arrest?
18. What steps should be taken in the case of intraoperative rupture of an intracranial aneurysm?
19. How would you plan the emergence from an anesthetic for

aneurysm clipping?

D. Postoperative Management

1. Would you extubate the patient postoperatively?
2. What would be the differential diagnosis if the patient did not return to her preoperative neurologic condition?
3. On postoperative day 2, the patient became disoriented and developed hemiplegia. A CT scan was obtained, which shows no new intracranial bleeding. What other diagnostic studies should be performed?
4. What is cerebral vasospasm, and what causes it?
5. What are pathophysiologic changes seen in cerebral vasospasm?
6. How is the diagnosis of cerebral vasospasm made?
7. What steps can be taken to prevent cerebral vasospasm?
8. What treatments can be undertaken once a diagnosis of cerebral vasospasm is made?
9. What are other neurologic complications following SAH and aneurysm clipping?
10. What other organ systems may manifest problems postoperatively in aneurysm clipping patients?

A. Medical Disease and Differential Diagnosis

A.1. What are the incidence, prevalence, and causes of subarachnoid hemorrhage (SAH), and what are the risk factors associated with rupture of intracranial aneurysms?

The prevalence of SAH is 2% to 5% with an incidence of 10 to 15 per 100,000 people. Each year, 25,000 cases of SAH occur in the United States, comprising 5% to 10% of all cases of stroke. In China and South America, the incidence is only 2 to 4 cases per 100,000 people, whereas higher rates of 19 to 23 per

100,000 are reported in Finland and Japan. Sixty percent of the cases occur in young individuals between the ages of 40 and 60 years. Therefore, a poor neurologic outcome is a devastating condition to be endured over a potentially long period.

Approximately one-third of patients die as a result of the acute bleed. Of the two-thirds who survive the acute bleed, one-half (one-third of total) later die or are severely disabled and half (one-third of total) have an acceptable outcome.

Cerebral aneurysms account for 75% to 80% of SAH; arteriovenous malformations are the cause in 4% to 5%, whereas no specific cause can be found in 15% to 20% of SAH. Other causes of SAH include trauma, mycotic aneurysm, sickle cell disease, cocaine use, and coagulation disorders.

According to a Danish study of 250 patients with SAH compared to 250 control patients, the four strongest independent predictors of aneurysmal SAH are current smoking (odd ratio [OR] 5.9; 95% confidence interval [CI] 4.1 to 8.6), family history of aneurysmal SAH (OR, 4.3; 95% CI 2.4 to 7.5), hypertension (OR, 2.3; 95% CI 1.5 to 3.7), and excessive alcohol use (>/=18 units per week) (OR, 1.2; 95% CI 1.0 to 2.8). Other risk factors include pregnancy and vascular abnormalities (e.g., type III collagen deficiency and elastase abnormalities). One-third of patients with polycystic kidney disease have been found to have intracranial aneurysms at autopsy. Genetic predisposition plays a role: Seven percent of berry aneurysms are familial, and 5% to 10% of patients with a ruptured aneurysm have a first-order relative with a ruptured aneurysm. The rupture rate for aneurysm has been estimated at 0.14% per year for a 5-mm lesion to 1.1% per year for a 10-mm lesion.

Smoking and alcohol abuse also appear to predispose to aneurysm formation and rupture. Smoking at any time and female sex are related to the presence of multiple intracranial aneurysms as well as accelerated aneurysm growth. Cocaine

abuse and resultant episodic hypertension may predispose to aneurysmal rupture at an early age.

Death and disability are primarily due to the initial bleed, vasospasm, and rebleeding. Other causes include surgical complications, parenchymal hemorrhage, hydrocephalus, and complications of medical therapy.

Chang HS. Simulation of the natural history of cerebral aneurysms based on data from the International Study of Unruptured Intracranial Aneurysms. *J Neurosurg*. 2006;104:188–194.

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2017:222–247.

de Rooij NK, Linn FH, van der Plas JA, et al. Incidence of subarachnoid haemorrhage: a systematic review with emphasis on region, age, gender and time trends. *J Neurol Neurosurg Psychiatry*. 2007;78(12):1365–1372.

Vlak MH, Rinkel GJ, Greebe P, et al. Lifetime risks for aneurysmal subarachnoid haemorrhage: multivariable risk stratification. *J Neurol Neurosurg Psychiatry*. 2013;84(6):619–623.

Yoshimoto Y. A mathematical model of the natural history of intracranial aneurysm: quantification of the benefit of prophylactic treatment. *J Neurosurg*. 2006;104:195–200.

A.2. What are common sizes and locations of intracranial aneurysms?

Small (less than 12 mm) aneurysms make up 78% of the total, whereas large (12 to 24 mm) are 20%, and giant (greater than 24 mm) comprise 2%. Most aneurysms are located in the anterior circulation, with the junction of the anterior communicating and anterior cerebral arteries being the most common (39%). Thirty percent of aneurysms occur in the internal carotid artery, 22% in the middle cerebral artery, and 8% in the posterior circulation (posterior cerebral, basilar, and vertebral arteries).

Kassell NF, Torner JC, Haley EC Jr, et al. The international cooperative study on the timing of aneurysm surgery. Part 1: overall management results. *J Neurosurg*. 1990;73:18–32.

A.3. What is the pathophysiology of aneurysmal rupture and SAH?

On the basis of experimental models, aneurysmal rupture leads to the leakage of arterial blood and a rapid increase in intracranial pressure (ICP), approaching diastolic blood pressure in the proximal intracerebral arteries. This increase in ICP causes a decrease in cerebral perfusion pressure (CPP) and a fall in CBF, leading to a loss of consciousness. The decrease in CBF diminishes bleeding and the SAH. A gradual reduction in ICP and an increase in CBF indicate improved cerebral function and possibly a return to consciousness. A persistent increase in ICP (perhaps resulting from thrombi in the cranial cisterns), however, results in a persistent no-flow pattern with acute vasospasm, cell swelling, and death.

A.4. What are symptoms and signs of SAH?

Headache occurs in 85% to 95% of patients. Often, a brief loss of consciousness occurs, followed by diminished mentation; consciousness may be impaired to any degree or may be unaffected at the time of presentation. Symptoms secondary to subarachnoid blood may be similar to those of infectious meningitis (nausea, vomiting, and photophobia). The patient may also experience motor and sensory deficits, visual field disturbances, and cranial nerve palsies. Finally, blood in the subarachnoid space may cause an elevated temperature.

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2017:222–247.

A.5. How does one assess the severity of SAH?

Two grading scales are commonly used to assess neurologic status following SAH, the Hunt and Hess grade (**Table 21.1**) and the World Federation of Neurologic Surgeons' grade (**Table 21.2**), based on the Glasgow Coma Scale. The scales are useful

in identifying a baseline neurologic status from which any acute changes should be assessed. In addition, the scales may correlate with physiologic status. Patients who are Hunt and Hess grades I and II have near-normal cerebral autoregulation and ICP.

TABLE 21.1 Modified Hunt and Hess Clinical Grades

Grade[a]	Criteria
0	Unruptured aneurysm
I	Asymptomatic or minimal headache and slight nuchal rigidity
II	Moderate to severe headache, nuchal rigidity, but no neurologic deficit other than cranial nerve palsy
III	Drowsiness, confusion, or mild focal deficit
IV	Stupor, mild to severe hemiparesis, possible early decerebrate rigidity, vegetative disturbance
V	Deep coma, decerebrate rigidity, moribund appearance

[a]Serious systemic disease such as hypertension, diabetes, severe arteriosclerosis, chronic pulmonary disease, and severe vasospasm seen on arteriography result in placement of the patient in the next less favorable category.

From Hunt WE, Hess RM. Surgical risk as related to time of intervention in the repair of intracranial aneurysms. *J Neurosurg*. 1968;28:14–20, with permission.

TABLE 21.2 World Federation of Neurological Surgeons (WFNS) Grading Scale

WFNS Grade	Glasgow Coma Scale	Motor Deficit
I	15	Absent
II	14–13	Absent
III	14–13	Present
IV	12–7	Present or absent
V	6–3	Present or absent

From Drake CG. Report of World Federation of Neurological Surgeons committee on a universal subarachnoid hemorrhage grading scale. *J Neurosurg*. 1988;68:985–986, with permission.

Drake CG. Report of World Federation of Neurological Surgeons Committee on a universal subarachnoid hemorrhage grading scale. *J Neurosurg*. 1988;68:985–986.

Hunt WE, Hess RM. Surgical risk as related to time of intervention in the repair of intracranial aneurysms. *J Neurosurg*. 1968;28:14–20.

A.6. What are the cardiovascular effects of SAH?

Injury to the posterior hypothalamus from SAH causes the release of norepinephrine from the adrenal medulla and cardiac sympathetic efferents. Norepinephrine can cause an increase in afterload and direct myocardial toxicity, leading to subendocardial ischemia. Pathologic analysis of the myocardium of patients who have died of acute SAH has revealed microscopic subendocardial hemorrhage and myocytolysis.

Electrocardiographic abnormalities are present in 50% to 80% of patients with SAH. Most commonly, these involve ST-segment changes and T-wave inversions but also include prolonged QT interval, U waves, and P-wave changes. ST-T wave changes are usually scattered and not related to a particular distribution.

Dysrhythmias occur in 80% of patients, usually in the first 48 hours. Premature ventricular contractions are the most common abnormality, but any type of dysrhythmia is possible. They include severely prolonged QT interval, torsades de pointes, and ventricular fibrillation. In one series, 66% of arrhythmias were considered mild, 29% moderate, and 5% severe. In addition to increased catecholamine secretion, hypercortisolism and hypokalemia have been suggested as causes for the dysrhythmias seen with SAH.

Ventricular dysfunction, possibly leading to pulmonary edema, is present in approximately 30% of patients with SAH.

Cardiac troponin I predicts myocardial dysfunction in SAH with a sensitivity of 100% and a specificity of 91%. This compares with a sensitivity and specificity of 60% and 94% for CPK-MB in predicting myocardial dysfunction. In order to plan optional anesthetic management, it is important to determine if any cardiac dysfunction is due to a myocardial infarction or reversible neurogenic left ventricular dysfunction. A retrospective study found that reversible neurogenic cardiac dysfunction was associated with a troponin level of 0.22 to 0.25

ng per mL and an ejection fraction of less than 40% by echocardiography.

Bulsara KR, McGirt MJ, Liao L, et al. Use of the peak troponin value to differentiate myocardial infarction from reversible neurogenic left ventricular dysfunction associated with aneurysmal subarachnoid hemorrhage. *J Neurosurg*. 2003;98:524–528.

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2017:222–247.

A.7. How is the diagnosis of SAH made?

Noncontrast CT scan can determine the magnitude and location of the bleed. It may also be useful in assessing ventricular size and aneurysm location. High-resolution CT (CT angiogram) with contrast can more precisely determine the location of the aneurysm.

Lumbar puncture can be used to diagnose SAH if CT is negative, especially when the patient presents more than 1 week after an initial bleed. Xanthochromia, a yellow discoloration of the cerebrospinal fluid (CSF) after centrifugation, is present from 4 hours to 3 weeks after SAH. A lumbar puncture can cause herniation or rebleeding. Therefore, a CT scan should be performed first if the patient presents within 72 hours of suspected SAH.

Four-vessel angiography (right and left carotid and vertebral arteries) has been considered the gold standard in the diagnosis of a intracranial aneurysm; however, CT angiography has been used with increasing frequency and currently is used to determine whether an aneurysm is amenable to coiling or requires surgical clip placement. The goal is to visualize all of the intracranial vessels, to localize the source of bleeding, and to rule out multiple aneurysms (5% to 33% of patients). Three-dimensional reconstructive angiograms and magnetic resonance angiography also may be used to further delineate the intracranial vasculature.

Guy J, McGrath BJ, Borel CO, et al. Perioperative management of aneurysmal subarachnoid hemorrhage: part 1. Operative management. *Anesth Analg*. 1995;81:1060–1072.

Lin A, Rawal R, Agid R, et al. Cerebrovascular imaging: which test is best? *Neurosurgery*. 2018;83:5–18.

Zhang LJ, Wu SY, Niu JB, et al. Dual-energy CT angiography in the evaluation of intracranial aneurysms: image quality, radiation dose, and comparison with 3D rotational digital subtraction angiography. *AJR Am J Roentgenol*. 2010;194:23–30.

A.8. What is the risk for rebleeding for a patient with SAH?

The risk of rebleeding from a ruptured aneurysm is highest, 4%, in the first 24 hours after the initial bleed and 1.5% per day thereafter. The cumulative risk is 19% in 14 days and 50% at 6 months. After 6 months, the rebleeding risk is 3% per year.

Kassell NF, Torner JC. Aneurysmal rebleeding: a preliminary report from the Cooperative Aneurysm Study. *Neurosurgery*. 1983;13:479–481.

B. Preoperative Evaluation and Preparation

B.1. What are some concerns in going to the interventional neuroradiology suite in the midst of an angiogram to be followed immediately with coiling of an aneurysm?

Whenever an anesthesiologist assumes care of a patient when the patient is already sedated, it may be more difficult to obtain an accurate medical history. In addition, the physical examination will be limited by the patient's position for the diagnostic study. Finally, the patient's capacity to consent may also be impaired by previous sedation.

B.2. What type of anesthesia is required for coiling of an aneurysm?

Although there is a case series of aneurysm coiling under

monitored anesthesia care with dexmedetomidine infusion without loading dose, in most institutions, general anesthesia is required for coiling of an intracranial aneurysm. First, intraoperative neurologic testing is generally not required. Second, immobility is very important not only when the coils or stent are actually deployed but also while the interventionist is navigating the intracranial vessels to reach the aneurysm.

Lee H-H, Jung Y-J, Choi B-Y, et al. Usefulness of dexmedetomidine during intracerebral aneurysm coiling. *J Korean Neurosurg Soc*. 2014;55:185–189.

B.3. Should one proceed with induction of general anesthesia under these circumstances?

Obliteration of the aneurysm with coils has become the standard of care for basilar tip aneurysm, and it would be best for the patient to have this done in the same setting as the angiography, provided there were no contraindications to induction of general anesthesia (e.g., hemodynamic instability).

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2017:222–247.

Lee CZ, Young WL. Anesthetic considerations for interventional neuroradiology. *ASA Refresher Course Anesthesiol*. 2005;33:145–154.

B.4. What types of emergencies can occur during coiling of an aneurysm, and how should they be managed?

Intraoperative emergencies can be divided into two categories—hemorrhage and thrombosis. Appropriate management requires constant communication between the radiologist, surgeon, and anesthesiologist. If an intracranial hemorrhage occurs, the interventionalist may try to "glue" the hole in the aneurysm or embolize the parent vessel. If this is not possible, heparin should be rapidly reversed with protamine, and a ventriculostomy will generally be placed by the surgical team. Management of arterial carbon dioxide partial pressure ($PaCO_2$) can then be guided by

the ICP.

As the technology of endovascular therapy has advanced to include balloon- or stent-assisted coiling, treatment of more complex aneurysms has increased. The rate of intraprocedural rupture (IPR) has increased as well. The rate of IPR may be as high as 7.5% in ruptured aneurysms and 2.5% in unruptured aneurysms. IPR may lead to significant clinical deterioration in previously unruptured aneurysms but does not appear to have a severe an impact in patients undergoing endovascular treatment for SAH.

In the case of catheter-induced thrombosis, induced hypertension is usually desirable while tissue plasminogen activator or antiglycoprotein IIb/IIIa therapy is considered.

If a coil was malpositioned, anticoagulation would be continued while the interventional radiologist attempts to snare the coil. As with thrombosis, it may be desirable to augment the blood pressure.

Kocur D, Przybyłko N, Bażowski P, et al. Rupture during coiling of intracranial aneurysms: predictors and clinical outcome. *Clin Neurol Neurosurg*. 2018;165:81–87.

Park YK, Yi H-J, Choi K-S, et al. Intraprocedural rupture during endovascular treatment of intracranial aneurysm: clinical results and literature review. *World Neurosurg*. 2018;114:e605–e615.

Petr O, Brinjikji W, Cloft H, et al. Current trends and results of endovascular treatment of unruptured intracranial aneurysms at a single institution in the flow-diverter era. *AJNR Am J Neuroradiol*. 2016;37:1106–1113.

B.5. What other modalities of endovascular therapy are available?

Flow diverting devices (stents) have been utilized as an endovascular treatment for wide necked and fusiform aneurysms, which are otherwise not amenable to coiling. When these procedures are planned, the patient is prepared with acetylsalicylic acid (ASA) and clopidogrel to prevent stent

thrombosis. A recent meta-analysis found that the complication rate for flow diverting stents is greater in ruptured versus unruptured aneurysms with an overall complication rate of 17% and mortality of 2.8%.

Several additional devices to stent bifurcations as well as wide necked aneurysms have been developed and approved for use in specific circumstances. Assessments of efficacy and complication rates are ongoing.

Finally, in the case of cavernous carotid or otherwise non-clippable aneurysms without the possibility of tradition coil or stent embolization the internal carotid artery might be occluded itself if sufficient cerebral blood flow can be maintained.

Arthur AS, Molyneux A, Coon AL, et al; for WEB-IT Study Investigators. The safety and effectiveness of the Woven EndoBridge (WEB) system for the treatment of wide-necked bifurcation aneurysms: final 12-month results of the pivotal WEB Intrasaccular Therapy (WEB-IT) Study. *J Neurointerv Surg*. 2019;11:924–930.

Bechan RS, Majoie CB, Sprengers ME, et al. Therapeutic internal carotid artery occlusion for large and giant aneurysms: a single center cohort of 146 patients. *AJNR Am J Neuroradiol*. 2016;37(1):125–129. doi:10.3174/ajnr.A4487.

Srinivasan VM, Srivatsan A, Spiotta AM, et al. Early postmarket results with PulseRider for treatment of wide-necked intracranial aneurysms: a multicenter experience. *J Neurosurg*. 2019;1–10. doi:10.3171/2019.5.JNS19313.

Zhou G, Su M, Yin YL, et al. Complications associated with the use of flow-diverting devices for cerebral aneurysms: a systematic review and meta-analysis. *Neurosurg Focus*. 2017;42:E17.

B.6. A craniotomy is planned for the following day to clip the middle cerebral artery aneurysm. Should surgery be postponed because of the patient's elevated troponin and CPK-MB fractions?

Fifty percent of patients will have an increase in CPK-MB fraction; however, CPK-MB per total CPK fraction is usually not consistent with a transmural myocardial infarction. As

discussed previously, troponin I levels are more sensitive. In addition, although some patients (0.7%) do sustain a myocardial infarction in the setting of SAH, little correlation is found between electrocardiographic abnormalities and ischemia in this population.

An echocardiogram may be useful in determining the severity of reversible neurogenic left ventricular dysfunction. If left ventricular function is found to be depressed, a pulmonary artery catheter, noninvasive cardiac output monitor, or intraoperative transesophageal echocardiography may be helpful for intraoperative management.

The desire to delay surgery because of cardiac abnormalities must be weighed against the risk of rebleeding and vasospasm. In most cases, the risk of recurrent hemorrhage outweighs the risk of perioperative myocardial infarction. Furthermore, even if coronary artery disease is present, these patients are not candidates for angioplasty or myocardial revascularization, which requires heparinization. If pulmonary edema or malignant dysrhythmias are present, it may be prudent to postpone surgery until such problems are controlled medically. However, if these problems are not present, then clipping of the aneurysm may be indicated. In a study by Bulsara et al., 2.9% of patients had severe cardiac dysfunction, and neurogenic left ventricular dysfunction resolved over 4 to 5 days.

Bulsara KR, McGirt MJ, Liao L, et al. Use of the peak troponin value to differentiate myocardial infarction from reversible neurogenic left ventricular dysfunction associated with aneurysmal subarachnoid hemorrhage. *J Neurosurg*. 2003;98:524–528.

B.7. Would you premedicate this patient before craniotomy?

No. When the patient is in a Hunt and Hess grade III to V state, anxiety is unlikely. Furthermore, heavy sedation may decrease

ventilation, raising $PaCO_2$ and increasing CBF and ICP, which, at the very least, may hinder preoperative and postoperative neurologic evaluation. If patients are Hunt and Hess grade I to II and it appears that preoperative anxiety might lead to hemodynamic instability, a small dose of a benzodiazepine may be appropriate.

Medications such as calcium channel blockers (nicardipine), anticonvulsants, and corticosteroids should be continued preoperatively on the day of surgery.

If the patient is at risk for aspiration, medications to decrease gastric acidity and volume are appropriate. Most patients will already be receiving a histamine-2 blocker or proton pump inhibitor if they are receiving a glucocorticoid.

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2017:222–247.

C. Intraoperative Management

C.1. What are the goals of the induction and maintenance of anesthesia for this patient?

The primary goal is to prevent aneurysm rupture, either on induction or intraoperatively, while maintaining adequate CPP. The goal of matching anesthetic depth to surgical stimulation is more important than the specific drugs used. In general, the anesthesiologist should provide for rapid and reversible titration of blood pressure, maintain CPP, and protect against cerebral ischemia. An additional goal is to provide a relaxed brain for ease of surgical exposure with minimal brain retraction. Finally, the anesthetic should be planned to achieve a rapid, smooth emergence, allowing prompt neurologic assessment. This can be accomplished with a combination of balanced anesthesia, muscle relaxation, and sympathetic blockers as well as with total

intravenous anesthesia.

Bendo AA. Intracranial vascular surgery. *Anesthesiol Clin North Am*. 2002;20:377–388.

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2017:222–247.

C.2. Is placement of an arterial catheter necessary for induction of anesthesia in this patient in the interventional neuroradiology suite?

In this case, because a femoral sheath is in place at the time that anesthesia is induced, one may transduce femoral arterial pressure during induction. However, because the patient has two aneurysms and because the sheath will be removed at the end of the procedure, an additional arterial catheter should be placed before the removal of the sheath. When a large coaxial catheter is placed through the femoral sheath, systolic pressure is underestimated, but mean pressure should be accurate. Studies have suggested that the placement of an arterial catheter prior to induction is not essential when an unruptured aneurysm is to be coiled.

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2017:222–247.

Lai YC, Manninen PH. Anesthesia for cerebral aneurysms: a comparison between interventional neuroradiology and surgery. *Can J Anaesth*. 2001;48:391–395.

C.3. How would you assess fluid status in this patient?

Several issues in interventional radiology complicate fluid management. First, contrast material acts as an osmotic diuretic. Often, these patients have had a CT scan with contrast in addition to an angiogram and may become intravascularly depleted. Second, the femoral sheath and other catheters are constantly flushed with a heparinized saline solution. It is not uncommon for a patient to receive 1,000 mL or more of flush

fluid during the case. This must be taken into account when calculating fluid balance.

C.4. Would monitoring central venous pressure (CVP) be useful for craniotomy and aneurysm clipping in this patient?

Many have suggested that CVP monitoring is essential in assessing volume replacement needs because urine output will be affected by osmotic or loop diuretics administered to facilitate surgical exposure. In addition, should vasoactive medication become necessary, it may be most effectively administered through a central venous catheter.

One disadvantage of CVP monitoring in the neurosurgical patient is catheter placement. Some clinicians are concerned that placement of an internal jugular venous CVP will compromise venous outflow of the head, thereby predisposing to bleeding or brain swelling, although this remains controversial. A "long-arm" or peripheral antecubital CVP catheter may be more difficult to insert and have a higher incidence of thrombophlebitis. Multiple studies have shown the complication rate of central catheter placement to be as high as 14%. When including failure to place the catheter, the complication rate rises to 54%. Nevertheless, use of an ultrasound-guided approach to placement of central venous catheters reduces the complication rates to less than 2% to 5% and should be the standard of care whenever possible.

Finally, a poor correlation between CVP and left ventricular end-diastolic pressure has been documented in SAH, so a pulmonary artery catheter may be more useful in assessing volume status as well as providing a monitor of cardiac output in those patients who have had preoperative cardiac problems. Patients who are expected to be candidates for hypertensive hypervolemic hemodilution (HHH) therapy for vasospasm or for

drug-induced coma may also benefit from placement of a pulmonary artery catheter.

Central pressure monitoring is usually instituted after the patient is anesthetized to minimize patient stress. One should be careful to use the minimal degree of head-down tilt necessary to access the central circulation because the Trendelenburg position can increase ICP and thereby decrease CPP.

Based on the risk and benefits of central venous and pulmonary artery access, placement of CVP and pulmonary artery catheters is reserved for patients who have documented cardiac dysfunction, cerebral vasospasm or poor peripheral intravenous access. Volume status may be assessed by noninvasive monitors that calculate stroke volume or by careful assessment of the arterial waveform utilizing calculated pulse pressure variation available on many monitoring systems.

Akmal AH, Hasan M, Mariam A. The incidence of complications of central venous catheters at an intensive care unit. *Ann Thorac Med*. 2007;2:61–63.

Eisen LA, Narasimhan M, Berger JS, et al. Mechanical complications of central venous catheters. *J Intensive Care Med*. 2006;21:40–46.

Marik PE, Cavallazzi R, Vasu T, et al. Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: a systematic review of the literature. *Crit Care Med*. 2009;37: 2642–2647.

C.5. What other forms of monitoring would you consider?

Electroencephalography (EEG) and somatosensory evoked potentials (SSEPs) have been advocated by some, although they are not standard monitoring in most hospitals. Although EEG has been used to monitor cerebral ischemia, scalp electrodes may not reflect activity of brain areas most at risk. Cortical electrodes, such as those used in epilepsy surgery, may avoid the problem of attenuation of the scalp electroencephalographic signal by CSF drainage and air between scalp electrodes and brain surface during surgery. EEG is useful in a titrating intravenous anesthetic infusion if burst suppression is desired

during temporary clipping.

SSEPs may detect reversible ischemia during temporary vessel occlusion, but they may not detect ischemia in subcortical structures and motor cortex. Furthermore, SSEPs have relatively high false-positive (38% to 60%) and false-negative (5% to 34%) rates. Brainstem auditory evoked responses may be useful for monitoring during posterior circulation aneurysm clipping. Motor evoked potentials may be superior in detecting subcortical ischemia. The use of SSEP and motor evoked potential monitoring usually warrants use of total intravenous anesthesia and avoidance of muscle relaxants.

Microvascular Doppler ultrasound evaluation may detect inadvertent vessel occlusion, but it cannot assess the adequacy of collateral perfusion.

Monitoring of ICP is common, with the probability of increased ICP being greatest 24 to 48 hours after SAH. An intraventricular catheter not only allows for ICP monitoring but also allows for CSF drainage to improve operating conditions. If an intraventricular catheter is not present, lumbar spinal drain may be placed. One must be careful not to allow substantial CSF drainage before dural opening because this may decrease ICP leading to an increase in transmural pressure and possible rupture.

Intraoperative angiography is one means to assess complete obliteration of the aneurysm without clip occlusion of the parent artery or perforating branches. Its use has increased with the installation of hybrid operating rooms that are fully equipped with advanced angiography equipment.

Horiuchi K, Suzuki K, Sasaki T, et al. Intraoperative monitoring of blood flow insufficiency during surgery of middle cerebral artery aneurysms. *J Neurosurg*. 2005;103:275–283.

Neuloh G, Schramm J. Monitoring of motor evoked potentials compared with somatosensory evoked potentials and microvascular Doppler ultrasonography

in cerebral aneurysm surgery. *J Neurosurg*. 2004;100;389–399.

Szelényi A, Langer D, Kothbauer K, et al. Monitoring of muscle motor evoked potentials during cerebral aneurysm surgery: intraoperative changes and postoperative outcome. *J Neurosurg*. 2006;105:675–681.

C.6. What are your specific concerns during induction of anesthesia in this patient?

If an aneurysm ruptures during anesthetic induction, mortality is high (approximately 75%). Therefore, precise control of transmural pressure is important in preventing aneurysm rupture.

Transmural pressure = CPP = MAP – ICP or CVP (whichever is greater), where MAP = mean arterial pressure

On the other hand, one does not want CPP to be so low that ischemia develops, especially in areas of vasospasm.

Chowdhury T, Cappellani RB, Sandu N, et al. Perioperative variables contributing to the rupture of intracranial aneurysm: an update. *ScientificWorldJournal*. 2013;2013:396404.

Tsementzis SA, Hitchcock ER. Outcome from "rescue clipping" of ruptured intracranial aneurysms during induction of anesthesia and endotracheal intubation. *J Neurol Neurosurg Psychiatry*. 1985;48:160–163.

C.7. How would you accomplish a smooth and safe induction and intubation in this patient?

Assuming that evaluation of the airway indicated that tracheal intubation is unlikely to be difficult, induction would begin with preoxygenation followed by propofol 1.5 to 2.5 mg per kg, thiopental 3 to 5 mg per kg, or etomidate 0.5 to 1 mg per kg, which have similar effects on CBF and cerebral metabolic rate. Given that this patient had no other medical problems, propofol is a reasonable choice. One may want to avoid ketamine for induction because of its potential to increase in CBF and ICP. Thiopental is not presently available in North America but may be available elsewhere.

After loss of consciousness and apnea, care must be taken to

maintain a normal $Paco_2$. Vigorous hyperventilation will lower $Paco_2$, decreasing CBF. This may lower ICP to such a degree that if MAP is maintained or increased, transmural pressure may be increased, leading to rupture of the aneurysm.

A nondepolarizing muscle relaxant, which has no effect on ICP or CBF, should be given to facilitate tracheal intubation. The neuromuscular junction should be monitored to ensure that paralysis is adequate to avoid coughing with intubation.

Fentanyl 3 to 5 μg per kg, sufentanil 0.5 to 1 μg per kg, or remifentanil 0.25 to 1 μg per kg can be given 3 to 5 minutes before laryngoscopy to blunt the hemodynamic response. Isoflurane, desflurane, or sevoflurane can be used to deepen the anesthetic. Finally, approximately 90 seconds before laryngoscopy, lidocaine 1.5 to 2 mg per kg or esmolol 0.5 mg per kg can be given to blunt the hemodynamic response to intubation.

Lidocaine decreases both CBF and cerebral metabolic rate for oxygen ($CMRO_2$), and at high concentrations can cause seizures. Esmolol and labetalol have no effect on CBF and ICP, even in brain areas where autoregulation may not be intact. Extreme reductions in MAP (greater than 35%) may compromise CPP in patients with increased ICP.

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2017:222–247.

C.8. Would you perform a rapid sequence induction and tracheal intubation for this patient?

No indication is seen for a rapid sequence induction and intubation in this patient. Overall risk of aspiration during general anesthesia has been estimated at 0.05%; however, the risk of aneurysm rupture during induction is 1% to 2%. Therefore, unless a clear indication exists for rapid sequence

induction, it is best avoided.

If a rapid sequence induction is indicated, one may consider using vecuronium 0.15 to 0.20 mg per kg or rocuronium 0.9 to 1.2 mg per kg rather than succinylcholine. Succinylcholine may increase in ICP, although some recent studies have noted no increase in ICP with administration of succinylcholine, but rather with intubation. The increase in ICP can be attenuated or eliminated by deep anesthesia or prior defasciculation. Succinylcholine, more importantly, may lead to hyperkalemia and possibly ventricular fibrillation in those patients presenting with motor deficits following SAH or in those patients who have been bedridden for some time.

In the case of a full stomach or an anticipated difficult airway, an awake fiberoptic intubation, with the use of appropriate sedation and topical application of local anesthesia, may be an appropriate alternative. Under such circumstances, it is useful to have an assistant so that while one person is securing the airway, the other is solely focused on controlling the hemodynamics with titration of appropriate medication. Videolaryngoscopy may reduce the need for awake fiberoptic intubation. In addition, the use of a supraglottic devices to maintain an airway during a difficult intubation may be useful in patients with an unanticipated difficult airway.

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2017:222–247.

Guy J, McGrath BJ, Borel CO, et al. Perioperative management of aneurysmal subarachnoid hemorrhage: part 1. Operative management. *Anesth Analg*. 1995;81:1060–1072.

Zura A. Succinylcholine in the patient with increased intracranial pressure. In: Mashour GA, Farag E, eds. *Case Studies in Neuroanesthesia and Neurocritical Care*. Cambridge, United Kingdom: Cambridge University Press; 2011:309–310.

C.9. What are the effects of hypoxemia and hypercapnia,

such as would be seen with loss of the airway on induction, on cerebral blood flow (CBF)?

Each millimeter of mercury increase in $PaCO_2$ increases CBF 3% to 4%, when $PaCO_2$ is in the range of 20 to 80 mmHg. In addition, hypoxemia will ensue if the airway is not secured in a timely manner and will also cause an increase in CBF once arterial oxygen partial pressure (PaO_2) is less than 60 mmHg (**Fig. 21.1**).

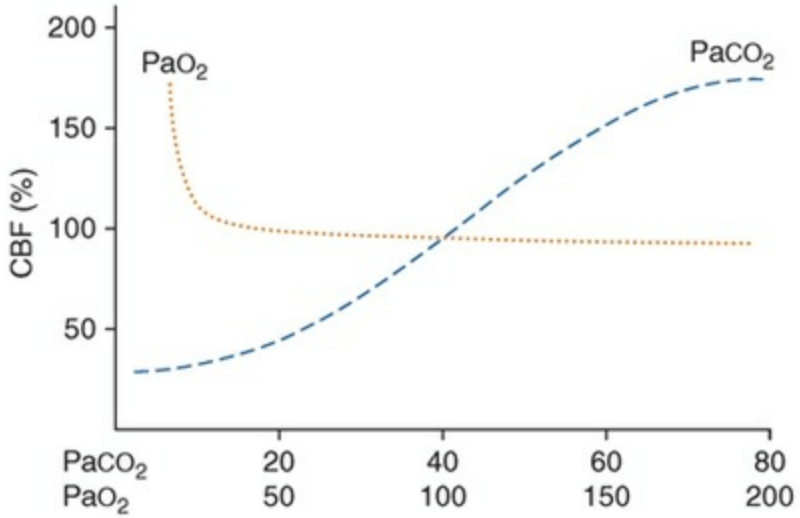

FIGURE 21.1. Change in CBF as a function of $PaCO_2$ and PaO_2 tension. (*From Albin MS, ed.* Textbook of Neuroanesthesia: With Neurosurgical and Neuroscience Perspectives. *1st ed. New York, NY: McGraw-Hill; 1997:30. Copyright © 1997 McGraw-Hill. With permission.*)

C.10. What is optimal fluid management for aneurysm clipping? Would you use a dextrose-containing solution?

Maintenance fluid requirements and blood loss should be replaced. One wants to avoid profound hypovolemia not only for its detrimental cardiovascular effects but also because it is associated with cerebral ischemia and perioperative neurologic deficits resulting from vasospasm. Some authors advocate mild hypervolemia to maximize cerebral CBF and minimize vasospasm; however, one must keep in mind the possibility of

cerebral edema as well as acute congestive heart failure.

In general, dextrose-containing solutions should be avoided because an increased incidence of neurologic deficits associated with glucose administration has been found in experimental models of focal cerebral ischemia. Blood glucose should be maintained less than 180 mg per dL.

Use of crystalloid versus colloid for fluid management and which type of crystalloid solution has long been a matter of controversy. Although some authors advocate colloid solutions to diminish the risk of brain swelling, evidence exists that the solution may predispose to brain edema and contribute to hyponatremia, which may increase the incidence of delayed ischemic neurologic deficits. Hypotonic crystalloid solutions are avoided in the neurosurgical patient; acceptable solutions include normal saline and balanced electrolyte solutions such as Normosol® and Plasma-Lyte®.

A moderate degree of hemodilution to a hematocrit of 30% to 35% usually lowers blood viscosity, thereby increasing CBF. The goal is to increase oxygen delivery by increasing CBF, without allowing the hematocrit to decrease to a degree that reduction in oxygen content negates the increase in CBF. Hematocrit, serum sodium, and serum osmolality measurements may be used to guide fluid therapy. Serum sodium should be maintained within normal limits, both to maintain serum oncotic pressure and to avoid the hyponatremia associated with cerebral salt wasting.

Guy J, McGrath BJ, Borel CO, et al. Perioperative management of aneurysmal subarachnoid hemorrhage: part 1. Operative management. *Anesth Analg*. 1995;81:1060–1072.

Ibrahim GM, Macdonald RL. The effects of fluid balance and colloid administration on outcomes in patients with aneurysmal subarachnoid hemorrhage: a propensity score-matched analysis. *Neurocrit Care*. 2013;19:140–149.

Lanier WL, Stangland KJ, Scheithauer BW, et al. The effects of dextrose infusion and head position on neurologic outcome after complete cerebral ischemia in primates: examination of a model. *Anesthesiology*. 1987;66:39–48.

Perel P, Roberts I, Ker K. Colloids versus crystalloids for fluid resuscitation in critically ill patients. *Cochrane Database Syst Rev*. 2013;(2):CD000567.

C.11. After the bone plate was removed and as the dura was being opened, the surgeon complained that the brain was "tight." What could you do to achieve better brain relaxation and facilitate surgical exposure?

Any method that rapidly decreases ICP before dural opening may suddenly increase transmural pressure and lead to aneurysm rupture. After dural opening, one of the fastest ways to decrease cerebral blood volume and improve exposure is through hyperventilation. Mild hypocarbia ($PaCO_2$ = 30 to 35 mmHg) can usually be established before dural opening, with moderate hypocarbia ($PaCO_2$ = 25 to 30 mmHg) after dural opening. Because of the risk of cerebral ischemia secondary to diminished CBF, normocarbia should be maintained whenever possible in patients with vasospasm.

Mannitol is the most frequently used diuretic to reduce brain swelling. It is given as an infusion to a total dose of 0.7 g per kg (0.25 to 1 g per kg). Its immediate effect is a transient rise in intravascular volume, which may pose problems in patients with impaired ventricular function. In addition, too rapid infusion can lead to decreases in systemic vascular resistance. Its onset of diuretic action is in 10 to 15 minutes, with peak effect occurring at 60 to 90 minutes. If mannitol does not produce the desired brain relaxation and the serum osmolality is greater than 320 mOsm, additional mannitol is unlikely to produce additional effect. In those patients who may not tolerate the initial effects of mannitol, intravenous furosemide 0.1 to 0.3 mg per kg can be

substituted. Both medications can cause derangements in fluid status and serum electrolytes that require close monitoring.

Drainage of CSF from either a lumbar drain or an intraventricular catheter is usually effective in optimizing surgical exposure. One must be careful to avoid significant CSF drainage before dural opening to prevent either brainstem herniation or a sudden decrease in transmural pressure. Similarly, hemodynamic instability can ensue if CSF is drained too rapidly at any point in the operation.

If tight brain remains a problem, one must ascertain that there is no hypoxemia or hypercarbia. In addition, one should consider eliminating nitrous oxide (N_2O) and reducing the amount of volatile anesthetic because all inhalational agents are cerebral vasodilators and may potentially increase ICP. Of course, if inhaled agents are reduced, appropriate intravenous agents should be substituted to ensure adequate anesthesia. Total intravenous anesthesia may be useful in this situation.

One may give a bolus of propofol or thiopental to decrease $CMRO_2$ and CBF; nevertheless, one must maintain MAP to maintain CPP. At the time of patient positioning, one must ensure that no impediment exists to venous outflow of the brain (i.e., extreme flexion or rotation of the head should be avoided and no monitor cables [electrocardiogram] should be draped across the neck). Even 10 degrees of head-up positioning has been found to be effective at reducing ICP.

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2017:222–247.

Sullivan HG, Keenan RL, Isrow L. The critical importance of $PaCO_2$ during intracranial aneurysm surgery. Case report. *J Neurosurg*. 1980;52:426–430.

C.12. How might transmural pressure be decreased to allow for aneurysm clip placement?

The most widely accepted method for producing a slack

aneurysm to allow for clip placement is the use of temporary clip occlusion of one or more parent vessels. For example, to place a permanent clip on an anterior communicating artery aneurysm, a temporary clip can be placed on either the right or left anterior cerebral artery or both. Advantages of temporary clip use include a greater reduction in transmural pressure, a greater ease in clipping, a decreased incidence of intraoperative rupture, and the avoidance of controlled hypotension.

The maximal duration of temporary clip application before a neurologic deficit occurs is unknown, but it is probably related to the location of the aneurysm and distribution of perforating vessels distal to the temporary clip. White matter and major deep nuclei are likely to be more susceptible than gray matter to temporary ischemia. Risk factors for neurologic deficit following temporary clip placement include poor preoperative neurologic condition, age older than 61 years, and distribution of perforating arteries in distal basilar and horizontal segments of middle cerebral artery. Recent studies suggest that there are regional differences in brain oxygenation during temporary clip occlusion, with the middle cerebral artery distribution being more susceptible to ischemia than the anterior cerebral artery distribution. In addition, patients who underwent multiple brief periods of temporary occlusion had less ischemia than those who underwent a single temporary artery occlusion of greater than 10 minutes.

Adenosine-induced temporary flow arrest has also been reported as a mechanism to produce a slack aneurysm to facilitate clipping.

Bendok BR, Gupta DK, Rahme RJ, et al. Adenosine for temporary flow arrest during intracranial aneurysm surgery: a single-center retrospective review. *Neurosurgery*. 2011;69:815–821.

Ha SK, Lim DJ, Seok BG, et al. Risk of stroke with temporary arterial occlusion in patients undergoing craniotomy for cerebral aneurysm. *J Korean*

Neurosurg Soc. 2009;46:31–37.

Silva PA, Cerejo A, Vilarinho A, et al. Regional variations in brain oxygenation during temporary clipping in aneurysm surgery. *Neurol Res*. 2012;34:971–976.

C.13. What is the purpose of controlled hypotension, and how is it achieved?

In the past, controlled hypotension was used to decrease transmural pressure, making the aneurysm neck slack enough to allow placement of a clip without vessel rupture. Various agents were used to achieve controlled hypotension, including volatile agent, nitroprusside, esmolol, labetalol, nitroglycerin, and trimethaphan. Specific agents were selected based on the patient's preexisting medical conditions, especially coronary ischemia or poor ventricular function. In an otherwise healthy patient, sodium nitroprusside infusion may be used for its rapid onset, easy titratability, and quick offset. An esmolol infusion can be added to augment hypotension and counteract the reflex tachycardia; by decreasing the amount of nitroprusside needed to induce hypotension, the likelihood of cyanide toxicity diminishes. Side effects of nitroprusside include cyanide toxicity, rebound hypertension, and intrapulmonary shunting. Direct measurement of CVP is useful when planning to use controlled hypotension in these patients.

During controlled hypotension, MAP is usually maintained at a minimum of 50 mmHg in previously normotensive individuals. Neurologic function monitors (EEG, SSEP, brainstem auditory evoked response, and cerebral oximetry) may be useful in guiding target level of MAP.

Albin MS, ed. *Textbook of Neuroanesthesia: With Neurosurgical and Neuroscience Perspectives*. New York: McGraw-Hill; 1997:877–878.

Ornstein E, Young WL, Ostapkovich N, et al. Deliberate hypotension in patients with intracranial arteriovenous malformations: esmolol compared with isoflurane and sodium nitroprusside. *Anesth Analg*. 1991;72:639–644.

C.14. What are some of the drawbacks of controlled hypotension?

The main drawback of controlled hypotension is that it leads to a global decrease in CPP. CPP is then further diminished in the presence of vasospasm or in areas of brain retraction. In a retrospective study, multiple regression analysis indicated that patients who underwent even limited periods of controlled hypotension had a worse outcome, both in terms of Glasgow Outcome Scale (multiple regression) and higher incidence and severity of vasospasm. Although further studies indicated that this effect was not seen when corrected for age, controlled hypotension usually is avoided in neurosurgery.

Connolly ES, Rabinstein AA, Carhuapoma JR, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2012;43:11–37.

C.15. What methods of cerebral protection might you use during this operation?

Cerebral protection has long been a matter of much investigation and controversy. Barbiturate loading has been shown in animals to be protective against focal ischemia, although no controlled human studies have been performed. Barbiturates decrease cerebral metabolic rate for glucose and oxygen and lower CBF and ICP. The dose is usually titrated to electroencephalographic silence or burst suppression. At doses used to suppress electroencephalographic activity, the patient may experience cardiovascular depression. The dose of barbiturate traditionally used for cerebral protection may also prolong emergence and hinder postoperative neurologic evaluation. Although barbiturates were originally thought to protect against ischemia through metabolic depression, other factors such as redistribution of blood flow to ischemic areas, blockade of

sodium channels and glutamate receptors, attenuation of *N*-methyl D-aspartate (NMDA), and α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) receptor-mediated glutamate toxicity all play a role.

Propofol has also been used as an alternative to thiopental sodium. Cerebral protection from propofol is thought to result from scavenging of free radicals, inhibition of glutamate release, and prevention of lipid peroxidation. In studies involving both volatile anesthetics and propofol, apoptotic cell death was delayed, but not prevented, if the ischemic result is mild. Propofol may be titrated to burst suppression on EEG monitoring.

Etomidate decreases cerebral metabolic rate at electroencephalographic burst suppression and prevents an increase in excitatory neurotransmitters during cerebral ischemia in animal models; nevertheless, it has been associated with a greater volume of injured brain than thiopental and control groups in focal ischemia in hypertensive rats.

Deliberate mild hypothermia (32.5°C to 35.5°C), although promising in animal models, did not demonstrate efficacy with patients with good-grade aneurysm in the Intraoperative Hypothermia for Aneurysm Surgery Trial (IHAST) 2, although there was a suggestion of a trend toward benefit in subgroup analysis.

Although many pharmacologic targets for cerebral protection, including magnesium, lidocaine, and others, have shown promising results in laboratory analysis, none have consistently proven effective in the clinical setting.

Engelhard K, Werner C, Eberspächer E, et al. Influence of propofol on neuronal damage and apoptotic factors after incomplete cerebral ischemia and reperfusion in rats: a long-term observation. *Anesthesiology*. 2004;101:912–917.

Guy J, McGrath BJ, Borel CO, et al. Perioperative management of aneurysmal

subarachnoid hemorrhage: part 1. Operative management. *Anesth Analg*. 1995;81:1060–1072.

Kawaguchi M, Furuya H, Patel PM. Neuroprotective effects of anesthetic agents. *J Anesth*. 2005;19:150–156.

Todd MM, Hindman BJ, Clarke WR, et al. Intraoperative Hypothermia for Aneurysm Surgery Trial (IHAST)Investigators. Mild intraoperative hypothermia during surgery for intracranial aneurysm. *N Engl J Med*. 2005;352: 135–145.

C.16. Would you induce mild hypothermia as a means of cerebral protection?

Hypothermia causes a greater reduction in cerebral metabolic rate for glucose and oxygen than the level attained at electroencephalographic silence because its reduction of metabolism is caused by a reduction in both neuronal electrical activity and enzyme activity related to maintenance of cellular function. Hypothermia also reduces the release of excitatory neurotransmitters. Significant reduction in infarct size after global and focal ischemia has been demonstrated in several animal studies. Unfortunately, these advantages have not been documented in clinical trials. The IHAST study showed no differences in Glasgow Outcome Scale at 3 months in patients who present with good neurologic grade.

Disadvantages of unintentional hypothermia documented in the literature include an increased incidence of myocardial ischemia in peripheral vascular surgery, increased incidence of postoperative wound infection in abdominal surgery, coagulopathy, prolonged drug clearance, and hyperglycemia. In the IHAST study, the hypothermic group had a small increase in infection rate. The effect of hypothermia in poor clinical grade patients is unknown.

Frank SM, Beattie C, Christopherson R, et al. Unintentional hypothermia is associated with postoperative myocardial ischemia. The Perioperative Ischemia Randomized Anesthesia Trial Study Group. *Anesthesiology*. 1993;78:468–476.

Todd MM, Hindman BJ, Clarke WR, et al. Intraoperative Hypothermia for Aneurysm Surgery Trial (IHAST)Investigators. Mild intraoperative hypothermia during surgery for intracranial aneurysm. *N Engl J Med*. 2005;352: 135–145.

C.17. What are the indications for deep hypothermic circulatory arrest?

Hypothermic circulatory arrest at body temperature less than 22°C (71.6°F) is reserved for giant aneurysms, difficult basilar artery aneurysms, and anatomically complex aneurysms that are not clippable without complete cessation of blood flow and are not amenable to the use of temporary clips. Deep hypothermic circulatory arrest requires cooperation between several services, including anesthesiology, neurosurgery, cardiac surgery, and perfusionists. In addition to the concerns mentioned regarding anesthesia for the person with an intracranial aneurysm and the need for prompt awakening for ease of neurologic assessment, deep hypothermic circulatory arrest adds concerns regarding institution of and separation from cardiopulmonary bypass, systemic heparinization and protamine reversal, and, of course, rewarming from profound hypothermia. This is rarely performed now that coil embolization is possible for many of these aneurysms. Giant and complex aneurysms that are not amenable to coiling may be managed with flow diversion endovascular therapy.

Gross BA, Frerichs KU. Stent usage in the treatment of intracranial aneurysms: past, present and future. *J Neurol Neurosurg Psychiatry*. 2013;84:244–253.

Young WL, Lawton MI, Gupta DK, et al. Anesthetic management of deep hypothermic circulatory arrest for cerebral aneurysm clipping. *Anesthesiology*. 2002;96:497–503.

C.18. What steps should be taken in the case of intraoperative rupture of an intracranial aneurysm?

The incidence of intraoperative rupture is 2% to 19%. The stage

of the operation at which rupture occurs affects outcome, with rupture at induction being the worst. After induction, the most common times for rupture are when the dura mater or arachnoid mater are being opened, during intracranial hematoma removal, and, of course, during dissection exposure of the aneurysm. At any point in the operation, a sudden sustained increase in blood pressure with or without bradycardia is suggestive of rupture. If rupture is suspected on induction, one must institute measures to control ICP while maintaining CPP.

If rupture occurs during surgical dissection, mortality is lower. The primary concern is to control bleeding while maintaining systemic perfusion. Bleeding is controlled by placement of temporary clips or by clamping or compression of the ipsilateral carotid artery in the neck if the aneurysm is too proximal. If bleeding is not controlled in a timely manner and a significant amount of blood accumulates in the subarachnoid space, severe brain swelling that is refractory to all treatment may develop.

Houkin K, Kuroda S, Takahashi A, et al. Intra-operative premature rupture of the cerebral aneurysms. Analysis of the causes and management. *Acta Neurochir (Wien)*. 1999;141:1255–1263.

Lin BF, Kuo CY, Wu ZF. Review of aneurysmal subarachnoid hemorrhage—focus on treatment, anesthesia, cerebral vasospasm prophylaxis, and therapy. *Acta Anaesthesiol Taiwan*. 2014;52:77–84.

C.19. How would you plan the emergence from an anesthetic for aneurysm clipping?

The goal is to have a patient comfortable and not coughing or straining or subject to hypercarbia or wide variations in blood pressure.

After discontinuing all anesthetic agents and reversing neuromuscular blockade, the use of a lidocaine 1.5 mg per kg bolus may minimize coughing and reaction to the endotracheal tube. Strict control of blood pressure must be observed

especially in the presence of ischemic heart disease or in patients suspected of having multiple aneurysms. One should keep the blood pressure within 20% of the patient's normal measurement.

D. Postoperative Management

D.1. Would you extubate the patient postoperatively?

Most patients who are in Hunt and Hess grades I and II can be extubated postoperatively with no need for airway support. Patients in grades IV and V usually require mechanical ventilation postoperatively, whereas grade III patients may or may not require intubation and mechanical ventilation. Patients with vertebral or basilar artery aneurysms may require airway protection secondary to cranial nerve damage and loss of protective reflexes.

If this patient is able to follow commands, is clinically recovered from the effects of muscle relaxants, and has established an adequate ventilatory pattern with return of protective airway reflexes, extubation would be appropriate.

Bendo AA. Intracranial vascular surgery. *Anesthesiol Clin North Am*. 2002;20:377–388.

D.2. What would be the differential diagnosis if the patient did not return to her preoperative neurologic condition?

If the patient had a focal neurologic deficit on awakening in the operating room, the cause most likely would be a surgical one, although new-onset vasospasm is also a possibility.

If the patient failed to regain consciousness, the first step would be to ensure that all inhalational and infused anesthetics had been discontinued. Second, one should make sure that neuromuscular blockade was fully reversed. In addition, ensure that the patient is not hypothermic as hypothermia can prolong

the duration of action of intravenous medications. While considering reversal of benzodiazepines and opioids, one should rule out other causes such as hypoxia, hypercarbia, hyponatremia, and hypoglycemia. One should consider the possibility of intraoperative seizure, with delayed emergence resulting from a postictal state. If after reversal of all anesthetic agents, the patient has not awakened, a CT scan should be obtained to rule out subdural hematoma, intracranial hemorrhage, hydrocephalus, and pneumocephalus. An angiogram may also be obtained to rule out vascular occlusion. An electroencephalogram might be appropriate to rule out subconvulsive status epileptics.

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2017:222–247.

D.3. On postoperative day 2, the patient became disoriented and developed hemiplegia. A CT scan was obtained, which shows no new intracranial bleeding. What other diagnostic studies should be performed?

If transcranial Doppler is available, an increased value for cerebral arterial flow velocity would be suggestive for vasospasm, leading to delayed cerebral ischemia/infarction. Tissue oximetry may also be useful as a monitor for vasospasm. Angiography is the gold standard for diagnosis of cerebral vasospasm and should be performed to confirm the diagnosis and characterize the number and location of the vessels involved.

Cerebral vasospasm may be localized to the area of aneurysm rupture or in an area of the brain remote from SAH. The worst prognosis is in those patients in whom vasospasm is diffuse. Of course, as these studies are being done, laboratory values should

be checked to make sure no new or worsening metabolic derangement is contributing to the neurologic deterioration.

D.4. What is cerebral vasospasm, and what causes it?

Vasospasm, which occurs in 35% of patients with SAH, is a segmental or diffuse narrowing of the lumen of one or more intracranial arteries. It is the most common cause of delayed cerebral ischemia/infarction and may be seen angiographically in 60% of patients, even if clinical manifestations are not apparent. The severity of vasospasm may be related to the amount and location of subarachnoid blood. Injection of blood into the subarachnoid space causes vasospasm in experimental animals and antifibrinolytics apparently worsen the spasm. On a molecular level, one theory is that oxyhemoglobin causes the production of superoxide radicals that lead to a decrease in nitric oxide levels in endothelial cells. This decrease in nitric oxide increases protein kinase C and intracellular calcium, resulting in myofilament activation and vasospasm. Other theories involve prostaglandins and lipid peroxidases. There may also be a genetic predisposition to development of vasospasm. Preliminary studies suggest that patients with the polymorphism of haptoglobin ($\alpha_1\alpha_1$) may be protected against vasospasm compared to patients with haptoglobin $\alpha_2\alpha_2$, which is less effective at neutralizing free radical formation by free hemoglobin. It is clear that endothelial dysfunction is present, particularly in the microcirculation. The risk of vasospasm decreases with advancing age, with patients younger than 50 years old at a fivefold greater risk than older patients.

Borsody M, Burke A, Coplin W, et al. Haptoglobin and the development of cerebral artery vasospasm after subarachnoid hemorrhage. *Neurology*. 2006;66:634–640.

Kale SP, Edgell RC, Alshekhlee A, et al. Age-associated vasospasm in aneurysmal subarachnoid hemorrhage. *J Stroke Cerebrovasc Dis*. 2013;22:22–

27.

D.5. What are pathophysiologic changes seen in cerebral vasospasm?

Structurally, leukocytes, red blood cells, and macrophages are seen in arterial walls. Inflammatory mediators, such as eicosanoids, interleukin 1, and immune complexes, are increased. Eventually, the vessel wall thickens, and smooth muscle proliferation and collagen deposition accompany degenerative changes in the tunica intima and media.

Functionally, carbon dioxide reactivity is impaired, and autoregulation is often impaired, perhaps correlating to the degree of delayed cerebral ischemia/infarction. CBF in some areas appears to be pressure dependent, hence the reasoning behind hypertensive therapy.

Weyer GW, Nolan CP, Macdonald RL. Evidence-based cerebral vasospasm management. *Neurosurg Focus*. 2006;21:E8.

D.6. How is the diagnosis of cerebral vasospasm made?

The clinical diagnosis of cerebral vasospasm is made when the patient experiences an altered level of consciousness (drowsiness, disorientation) or a new focal neurologic deficit. These may be accompanied by increasing headache, meningismus, and fever. Vasospasm is rare in the first 3 days following SAH. It reaches peak incidence at 3 to 10 days and usually resolves by 10 to 14 days after SAH. In this patient, the new onset of hemiplegia suggests that the middle cerebral artery is involved. If vessels in the posterior fossa are involved, respiratory and hemodynamic abnormalities may develop.

The differential diagnosis includes rebleeding, hydrocephalus, seizure, hyponatremia, and drug effects. Transcranial Doppler CBF velocity greater than 120 cm per second in association with a new focal neurologic deficit are usually sufficient to make the diagnosis of cerebral vasospasm; however, a change in

transcranial Doppler values over time may be more useful than an absolute value. CBF velocity greater than 200 cm per second is associated with a high risk of cerebral infarct, whereas a velocity less than 100 cm per second indicates that cerebral vasospasm is unlikely. Recent evidence shows that transcranial Doppler had only 63% sensitivity in identifying delayed cerebral ischemia/infarction, with a positive predictive value of only 22% in grade II and III patients. Cerebral perfusion imaging may be necessary in patients of poor grade who are unable to participate in neurologic examination.

Angiographic cerebral vasospasm can be found in 60% of patients following SAH, but only 50% of these patients develop clinical focal neurologic deficits.

Connolly ES, Rabinstein AA, Carhuapoma JR, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2012;43:11–37.

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2017:222–247.

D.7. What steps can be taken to prevent cerebral vasospasm?

Calcium channel blockers are standard prophylactic therapy to prevent vasospasm. The mechanism is unknown, but presumably, calcium channel blockers aid in maintaining cellular integrity by preventing calcium entry into ischemic cells. Nimodipine, taken orally, improves neurologic outcome. Patients given nimodipine have no change in overall incidence of vasospasm, but they have a lower incidence of severe narrowing. In addition, although no improvement is found in mortality, there is improvement in outcome for survivors.

Use of nicardipine, an intravenous agent, showed a lower incidence of vasospasm, but no improvement in outcome versus a placebo group; both groups received HHH therapy. The main

complication of calcium channel blocker therapy is hypotension (0% to 8%), which may make this therapy difficult to achieve.

Intravenous nimodipine is not available in the United States, although patients are given nimodipine orally or via nasogastric tube every 4 hours. The incidence of vasospasm does not differ significantly from open surgical repair to endovascular procedures. In addition, although calcium channel blockers cross the blood–brain barrier, the dose needed to achieve significant levels at the site necessary may be limited by systemic hypotension. Prolonged-release nicardipine implants placed at the time of surgical clipping were shown to reducing the incidence of vasospasm, improving outcome. In order to deliver calcium channel blockade intrathecally, nicardipine nanoparticles administered via external ventricular drains reduced delayed cerebral ischemia and improved clinical outcome. The microparticles appeared safe and there was no significant hypotension. In addition, there was a reduction in delayed cerebral ischemia/infarction and an improvement in clinical outcome.

Other steps to limit cerebral vasospasm include the removal of subarachnoid blood as quickly as possible, instillation of thrombolytic agents (e.g., tissue plasminogen activator), and use of pharmacologic agents to reduce inflammatory response (high-dose glucocorticoids, ibuprofen). In Europe and Japan, protease inhibitors have been used in the treatment of vasospasm.

Barth M, Capelle HH, Weidauer S, et al. Effect of nicardipine prolonged-release implants on cerebral vasospasm and clinical outcome after severe aneurysmal subarachnoid hemorrhage: a prospective, randomized, double-blind phase IIa study. *Stroke*. 2007;38(2):330–336.

Connolly ES, Rabinstein AA, Carhuapoma JR, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2012;43:11–37.

Hänggi D, Etminan N, Aldrich F, et al; for NEWTON Investigators.

Randomized, open-label, phase 1/2 a study to determine the maximum tolerated dose of intraventricular sustained release nimodipine for subarachnoid hemorrhage (NEWTON [nimodipine microparticles to enhance recovery while reducing toxicity after subarachnoid hemorrhage]). *Stroke*. 2017;48(1):145–151.

D.8. What treatments can be undertaken once a diagnosis of cerebral vasospasm is made?

Treatment for cerebral vasospasm is multifactorial and includes continuation of prophylactic measures. In the past, HHH therapy was used to augment CBF past the stenotic areas. It begins with hypervolemic hypertension, with intravascular volume expansion with crystalloid or colloid to increase cardiac output. Some recommended target values are CVP of 10 to 12 mmHg, pulmonary artery occlusion pressure of 15 to 18 mmHg, cardiac index of 3.0 to 3.5 L/min/m^2, and hematocrit of 30% to 35%. Various blood pressure targets have been reported, but a reasonable plan is systolic blood pressure 160 to 200 mmHg if the aneurysm is clipped and 120 to 150 mmHg if unclipped. Vasoactive infusions are added if hypervolemia alone is inadequate. End points of therapy are resolution of neurologic deficits or occurrence of complications of therapy, such as pulmonary edema (26%), myocardial ischemia, and rebleeding or rupture of a secondary aneurysm. A pulmonary artery catheter is often indicated. Fluid used for HHH should be isotonic and have enough sodium to avoid hyponatremia. Vasopressin, fludrocortisone, or hydrocortisone can be administered to counteract excessive sodium and fluid loss. Recent literature has proven the benefit of maintenance of euvolemia with induced hypertension in contrast to strict HHH.

Other treatments for vasospasm, including intra-arterial vasodilators or angioplasty, are utilized if the patient does not demonstrate prompt improvement with hypertensive therapy.

In spite of all attempted therapy, the outcome in patients with

significant vasospasm is often poor. Most medications investigated to ameliorate the devastating consequences of vasospasm have limited efficacy. Nimodipine has been found to have some efficacy in treating vasospasm and improving outcome. A recent target of pharmacologic therapy has been endothelin, a potent long-lasting vasoconstrictor. Clazosentan, an endothelin receptor antagonist, reduced angiographic vasospasm but did not improve clinical outcome in two appropriately powered trials.

Connolly ES, Rabinstein AA, Carhuapoma JR, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2012;43:11–37.

Dorhout Mees SM, Rinkel GJ, Feigin VL, et al. Calcium antagonists for aneurysmal subarachnoid haemorrhage. *Cochrane Database Syst Rev*. 2007; (3):CD000277.

Hoh BL, Ogilvy CS. Endovascular treatment of cerebral vasospasm: transluminal balloon angioplasty, intra-arterial papaverine, and intra-arterial nicardipine. *Neurosurg Clin N Am*. 2005;16:501–516.

Macdonald RL, Higashida RT, Keller E, et al. Randomised trial of clazosentan, an endothelin receptor antagonist, in patients with aneurysmal subarachnoid hemorrhage undergoing surgical clipping (CONSCIOUS-2). *Acta Neurochir Suppl*. 2013;115:27–31.

Macdonald RL, Higashida RT, Keller E, et al. Randomized trial of clazosentan in patients with aneurysmal subarachnoid hemorrhage undergoing endovascular coiling. *Stroke*. 2012;43(6):1463–1469.

Muench E, Horn P, Bauhuf C, et al. Effects of hypervolemia and hypertension on regional cerebral blood flow, intracranial pressure, and brain tissue oxygenation after subarachnoid hemorrhage. *Crit Care Med*. 2007;35: 1844–1852.

Raabe A, Beck J, Keller M, et al. Relative importance of hypertension compared with hypervolemia for increasing cerebral oxygenation in patients with cerebral vasospasm after subarachnoid hemorrhage. *J Neurosurg*. 2005;103:974–981.

D.9. What are other neurologic complications following SAH and aneurysm clipping?

Hydrocephalus, manifesting with a gradual decrease in level of consciousness, occurs in 25% of patients surviving SAH. Diagnosis is confirmed by CT scan. Treatment is by ventricular drainage.

Seizures occur in 13% of patients with SAH and may herald rebleeding or vasospasm. Seizures can increase MAP, CBF, ICP, and lactate production, predisposing to rebleeding in those patients with unclipped aneurysms and cerebral ischemia in those patients with vasospasm. Most patients receive prophylactic anticonvulsants.

Hyponatremia occurs in 10% to 34% of patients with SAH over a time course that parallels that of vasospasm. It may be due to syndrome of inappropriate antidiuretic hormone secretion, "cerebral salt wasting," or prolonged or excessive mannitol use. Cerebral salt wasting syndrome is thought to be mediated by release of atrial natriuretic factor by the hypothalamus secondary to distention of the cerebral ventricles from hydrocephalus. After SAH, patients also have elevated plasma volume. In these patients, fluid restriction is not the treatment of choice because hypovolemia may predispose to vasospasm. Serum brain natriuretic peptide, which causes diuresis and natriuresis, is elevated after SAH, and patients may require treatment with an isotonic or hypertonic salt-containing fluid. In addition, treatment with hydrocortisone may be considered. Finally, patients may experience brain swelling or edema, which is treated with hypertonic saline, mannitol, and/or dexamethasone.

Cottrell JE, Patel P, eds. *Cottrell and Patel's Neuroanesthesia*. 6th ed. Philadelphia, PA: Elsevier; 2017:222–247.

D.10. What other organ systems may manifest problems postoperatively in aneurysm clipping patients?

The lungs can be affected by pneumonia or neurogenic

pulmonary edema, in which disruption of the pulmonary capillary membrane occurs secondary to increased sympathetic nervous system activity. Because of inactivity, patients may be predisposed to developing deep venous thrombosis (DVT) and pulmonary embolism. Patients (approximately 5%) may develop heparin-induced thrombocytopenia, possibly due to heparin exposure during angiography. These patients tend to have increased rates of both vasospasm and DVT. In general, heparin prophylaxis is often avoided in patients after SAH due to concerns for aneurysmal rebleeding, surgical site bleeding or new bleeding around a ventriculostomy catheter. The incidence of venous thromboembolism in neurocritical care patients may be as high as 14%.

There appears to be a relationship between the use of hypertonic saline in the SAH patient and the incidence of acute kidney injury. Patients may have a fever secondary to subarachnoid blood, which may make the workup of postoperative infection more difficult. Finally, as in most patients with head injury, those with SAH may have increased metabolic rate.

Connolly ES, Rabinstein AA, Carhuapoma JR, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2012;43:11–37.

Kshettry VR, Rosenbaum BP, Seicean A, et al. Incidence and risk factors associated with in-hospital venous thromboembolism after aneurysmal subarachnoid hemorrhage. *J Clin Neurosci*. 2014;21:282–286.

Kumar AB, Shi Y, Shotwell MS, et al. Hypernatremia is a significant risk factor for acute kidney injury after subarachnoid hemorrhage: a retrospective analysis. *Neurocrit Care*. 2015;22:184–191.

SECTION 5 The Endocrine System

22 Pheochromocytoma

Anup Pamnani and Vinod Malhotra

A 39-year-old man has a history of recurrent headaches, diaphoresis, and severe hypertension for several weeks. During a physical examination, he was found to have an exceptionally high blood pressure (BP) of 230/150 mmHg with a heart rate of 112 beats per minute. Prior to this, the patient claims to have been in good health. Further studies were obtained to evaluate the etiology of his arterial hypertension and headaches.

A. Medical Disease and Differential Diagnosis

1. What are some common differential diagnoses for arterial hypertension?
2. What is a pheochromocytoma?
3. Describe the anatomy of the adrenal gland.
4. What substances does the adrenal medulla secrete?
5. What are the mechanisms of action of epinephrine and norepinephrine?
6. What is the pathway for synthesis and breakdown of

catecholamines?

7. What does the adrenal cortex secrete?
8. What are the metabolic actions of the glucocorticoids and the mineralocorticoids?
9. What are the clinical features associated with a pheochromocytoma?
10. What is the prevalence of pheochromocytomas and paragangliomas?

B. Preoperative Evaluation and Preparation

1. How can you diagnose and localize the tumor preoperatively?
2. How do you pharmacologically prepare the patient with a pheochromocytoma for surgery?
3. What other aspects of preoperative management are important?

C. Intraoperative Management

1. What drugs should be avoided during the operation?
2. How would you monitor this patient?
3. Describe the anesthetic management of the patient with pheochromocytoma.
4. What drugs are used to control the effects of catecholamine stimulation during surgery?
5. What are some management concerns after the tumor is removed?
6. What are some of the concerns with laparoscopic adrenalectomy?

D. Postoperative Management

1. What is the significance of postoperative hypotension? How is it treated?
2. What other problems can arise in the postoperative period?

A. Medical Disease and Differential Diagnosis

A.1. What are some common differential diagnoses for arterial hypertension?

The following is a partial list of differential diagnosis of hypertension:

- *Essential hypertension* of unknown etiology
- *Primary renal disease*: nephritis, renal artery stenosis, and renal infarction
- *Endocrine*: adrenocortical *hyperfunction*, hyperthyroidism, pheochromocytoma, acromegaly
- *Sympathetic stimulation*: hypoxia, hypercarbia, pain
- *Neurogenic*: seizure activity, elevated intracranial pressure, and denervation of the carotid sinus
- *Miscellaneous*: malignant hyperthermia, neuroleptic malignant syndrome, carcinoid syndrome, and toxemia of pregnancy

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Longo DL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:2962–2968.

A.2. What is a pheochromocytoma?

Pheochromocytomas are catecholamine-secreting tumors of chromaffin tissue. The precise etiology of these tumors is unknown. They are usually located in the adrenal medulla or sympathetic paraganglia but may be found anywhere chromaffin tissue exists. These locations extend from the base of the skull to the anus. Traditionally, it was thought that 90% of pheochromocytomas were found in the adrenal medulla and 10% occurred elsewhere. Prevalence of extra-adrenal tumors is now thought to be as high as 20%. These are commonly called *paragangliomas*.

Pheochromocytomas account for only 0.1% of all cases of arterial hypertension. They are prevalent in 0.005% to 0.01% of the population. When unsuspected or improperly managed during surgery, the hemodynamic effects of the released

catecholamines can be profound.

Chen H, Sippel RS, O'Dorisio MS, et al. The North American Neuroendocrine Tumor Society consensus guideline for the diagnosis and management of neuroendocrine tumors: pheochromocytoma, paraganglioma, and medullary thyroid cancer. *Pancreas*. 2010;39(6):775–783.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:449–476.

Kinney MA, Narr BJ, Warner MA. Perioperative management of pheochromocytoma. *J Cardiothorac Vasc Anesth*. 2002;16(3):359–369.

A.3. Describe the anatomy of the adrenal gland.

The adrenal glands are paired, mustard-colored structures positioned superior and slightly medial to the kidneys in the retroperitoneal space. Each gland is supplied by three arteries: the superior adrenal arteries derived from the inferior phrenic artery, the middle adrenal arteries derived from the aorta, and the inferior adrenal arteries derived from the renal artery. In contrast to the arterial supply, each adrenal gland usually is drained by a single, major adrenal vein. The right adrenal vein is usually short and drains into the inferior vena cava (IVC), whereas the left adrenal vein is longer and empties into the left renal vein. Accessory veins occur in 5% to 10% of patients and are an important consideration during pheochromocytoma resection.

In most respects, the cortex and medulla of the adrenal gland can be considered as two completely distinct organs that happen to colocalize during development. They are of separate embryologic origin; the medullary portion is derived from the chromaffin ectodermal cells of the neural crest and develops in parallel with the sympathetic system during development, and the cortex originates around the fifth week of gestation from mesodermal tissue near the gonads on the adrenogenital ridge.

The chromaffin cells become enclosed within the cortex to form the medulla. The organs of Zuckerkandl are paraganglia

around the aorta at the level of the kidney anterior to the inferior aorta. Accessory areas for the occurrence of pheochromocytoma are in the mediastinum, in the bladder, occasionally in the neck, in the sacrococcygeal region, or in the anal or vaginal areas.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:1343–1407.

Townsend CM, Beauchamp RD, Evers MB, et al, eds. *Sabiston Textbook of Surgery*. 20th ed. Philadelphia, PA: WB Saunders; 2016:963–995.

A.4. What substances does the adrenal medulla secrete?

The adrenal medulla primarily secretes three catecholamines: epinephrine, norepinephrine, and dopamine. These three compounds are found in all the chromaffin cells of the sympathetic nervous system, which includes the adrenal medulla, aberrant tissue along the sympathetic chain, and paraganglia. Both norepinephrine and dopamine are found at the endings of the postganglionic fibers of the sympathetic nervous system and in the central nervous system.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:1343–1407.

Townsend CM, Beauchamp RD, Evers MB, et al, eds. *Sabiston Textbook of Surgery*. 20th ed. Philadelphia, PA: WB Saunders; 2016:963–995.

A.5. What are the mechanisms of action of epinephrine and norepinephrine?

These catecholamines exert their effects by acting on β-adrenergic and α-adrenergic receptors. β-Receptor stimulation results in G protein–mediated activation of adenylate (adenylyl) cyclase, which increases cyclic adenosine monophosphate (cAMP) levels.

Stimulation of the α_1 subtype of the α-receptor results in G protein–mediated hydrolysis of phospholipid membranes, which cause an increase in cytoplasmic Ca^{2+} levels and subsequent

smooth muscle contraction. The stimulation of α_2 receptors, conversely, inhibits the action of adenylate cyclase and decreases cAMP.

The pharmacologic response is dependent on the location of the catecholamine receptors throughout the body. The distribution and density of the receptors will determine the predominant response to each catecholamine.

Brunton LL, Knollmann BC, Dandan R, eds. *Goodman and Gillman's The Pharmacological Basis of Therapeutics*. 13th ed. New York: McGraw-Hill; 2017:191–224.

Hemmings HC Jr, Egan TD, eds. *Pharmacology and Physiology for Anesthesia*. 2nd ed. Philadelphia, PA: Elsevier; 2018:282–299.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:449–476.

A.6. What is the pathway for synthesis and breakdown of catecholamines?

The synthesis of endogenous catecholamines begins with the active transport of the amino acid tyrosine from the circulation into postganglionic sympathetic nerve endings. The hydroxylation of tyrosine is regarded as the rate-limiting step of the pathway (**Fig. 22.1**). The termination of the action of catecholamines occurs primarily through reuptake at nerve terminals. Diffusion and metabolism, by the enzymes catechol-*O*-methyltransferase (COMT) and monoamine oxidase (MAO), also play a role in termination of action.

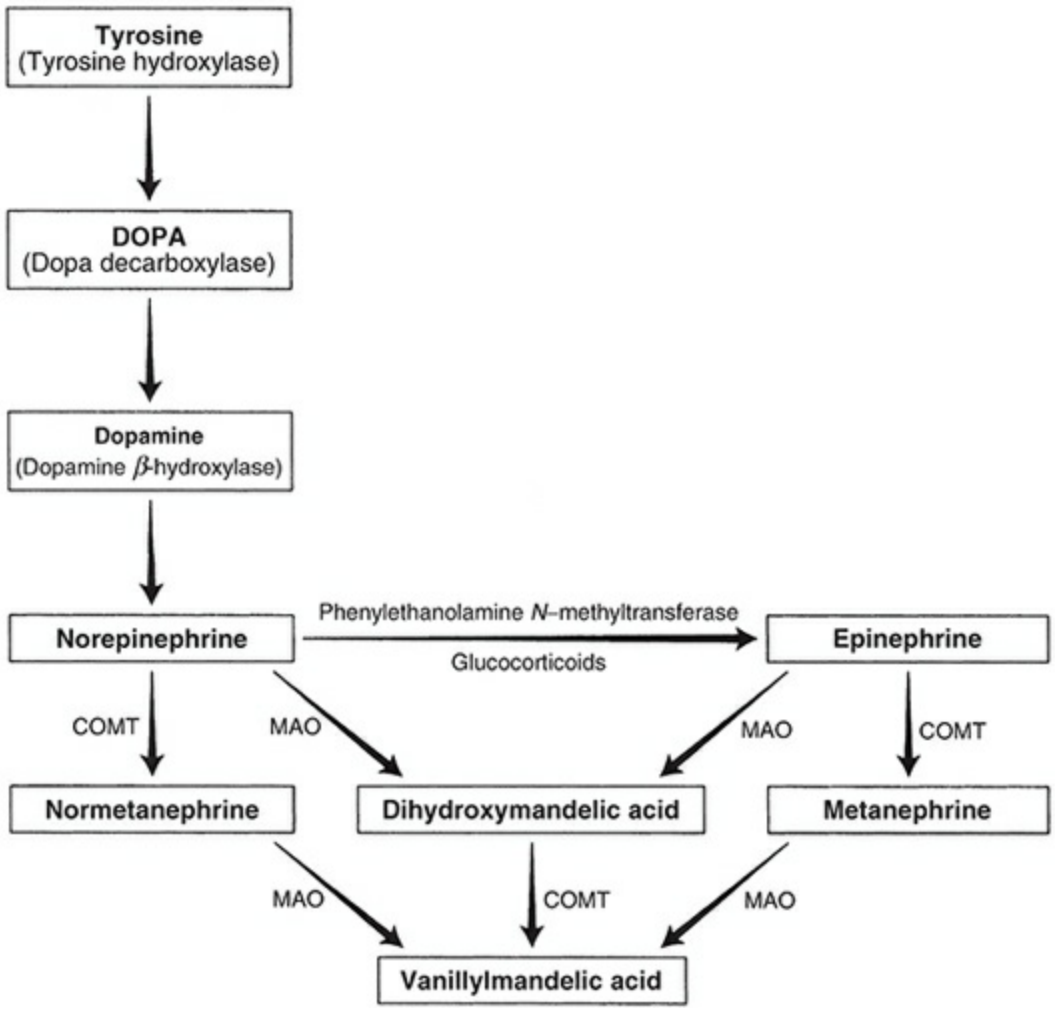

FIGURE 22.1. Synthesis and metabolism of endogenous catecholamine. COMT, catechol-*O*-methyltransferase; MAO, monoamine oxidase. (*Reprinted by permission from Springer: Pullerits J, Ein S, Balfe JW. Anesthesia for phaeochromocytoma.* Can J Anesth. *1988;35[5]:526–534. Copyright © 1988 Canadian Anesthesiologists.*)

Hemmings HC Jr, Egan TD, eds. *Pharmacology and Physiology for Anesthesia*. 2nd ed. Philadelphia, PA: Elsevier; 2018:282–299.

Schulz C, Eisenhofer G, Lehnert H. Principles of catecholamine biosynthesis, metabolism and release. *Front Horm Res*. 2004;31:1–25.

A.7. What does the adrenal cortex secrete?

The adrenal cortex secretes more than 30 different corticosteroids. These can be divided into three major classes: mineralocorticoids, glucocorticoids, and sex steroids (the androgens and estrogen).

The precursor of all corticosteroids is cholesterol.

Aldosterone is the most important mineralocorticoid secreted by the adrenal cortex, whereas cortisol is the most important glucocorticoid secreted. The adrenal cortex is also responsible for secreting sex steroids.

Each of these substances is secreted by different zones. The mineralocorticoids are secreted by the zona glomerulosa, glucocorticoids are secreted by the zona fasciculata, and sex steroids are secreted by the zona reticularis.

Brunton LL, Knollmann BC, Dandan R, eds. *Goodman and Gillman's The Pharmacological Basis of Therapeutics*. 13th ed. New York: McGraw-Hill; 2017:191–224.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:449–476.

A.8. What are the metabolic actions of the glucocorticoids and the mineralocorticoids?

The glucocorticoids have their predominant mechanism of action on intermediary metabolism. These effects include increased gluconeogenesis, fatty acid mobilization, protein catabolism, and anti-inflammatory effects. Cortisol may improve cardiac function by improving responsiveness of β-adrenergic receptors. Approximately 95% of the glucocorticoid activity is from the secretion of cortisol.

The mineralocorticoids predominantly act on the body minerals, such as sodium and potassium. By conserving sodium ions, they sustain extracellular fluid volume. They also help maintain normal potassium plasma concentrations.

Barnes PJ. Molecular mechanisms and cellular effects of glucocorticosteroids. *Immunol Allergy Clin North Am*. 2005;25(3):451–468.

Brunton LL, Knollmann BC, Dandan R, eds. *Goodman and Gillman's The Pharmacological Basis of Therapeutics*. 13th ed. New York: McGraw-Hill; 2017:191–224.

Czock D, Keller F, Rasche FM, et al. Pharmacokinetics and pharmacodynamics of systemically administered glucocorticoids. *Clin*

Pharmacokinet. 2005;44(1):61–98.

A.9. What are the clinical features associated with a pheochromocytoma?

The classic triad is severe headache, diaphoresis, and palpitations. One or more of the following often signal the presence of a pheochromocytoma: sudden severe headaches, perspiration, weight loss, paroxysmal hypertension, pallor, palpitations, diabetes-like syndrome with elevated fasting blood sugar, nausea, vomiting, fever, encephalopathy, anxiety, myocardial infarction, stroke, or acute renal failure. The aforementioned symptoms are usually paroxysmal in nature. These "attacks" may last from a few moments to hours. Although hypertension can be paroxysmal, 65% of adults demonstrate sustained hypertension.

A pressor response to particular drugs suggests the presence of this tumor. These drugs include histamine, glucagon, droperidol, tyramine, metoclopramide, cytotoxic drugs, saralasin, tricyclic antidepressants, and phenothiazines.

Manger WM. An overview of pheochromocytoma: history, current concepts, vagaries, and diagnostic challenges. *Ann N Y Acad Sci*. 2006;1073:1–20.

Townsend CM, Beauchamp RD, Evers MB, et al, eds. *Sabiston Textbook of Surgery*. 20th ed. Philadelphia, PA: WB Saunders; 2016:963–995.

A.10. What is the prevalence of pheochromocytomas and paragangliomas?

Pheochromocytomas occur in both sexes with peak incidence in the third to fifth decades of life. Advances in diagnosis and genetics now challenge the traditional "rule of 10" for pheochromocytomas (10% bilateral, 10% extra-adrenal, 10% familial, 10% malignant). Prevalence of bilateral adrenal tumors is higher than 10% in some familial pheochromocytoma syndromes such as multiple endocrine neoplasia type 2 and von Hippel-Lindau syndrome (see **Table 22.1** for complete list).

Prevalence of extra-adrenal tumors (paragangliomas) is thought to reach as high as 20%. Nearly 25% of these tumors are thought to be hereditary.

TABLE 22.1 Syndromes Associated with Pheochromocytoma

MEN type IIa (Sipple syndrome)	Parathyroid adenoma/hyperplasia
	Medullary carcinoma of thyroid
	Pheochromocytoma
MEN type IIb	Medullary carcinoma of the thyroid
	Mucosal adenomas
	Marfanoid appearance
	Pheochromocytoma
von Hippel-Landau syndrome	Hemangioblastoma of the retina, cerebellum, or other parts of the CNS, pheochromocytoma
Neurofibromatosis	Neurofibromas, café-au-lait spots, axillary or inguinal freckling, optic nerve glioma, pheochromocytoma

CNS, central nervous system; MEN, multiple endocrine neoplasia.

Metastases are low for adrenal pheochromocytomas (up to 5%). The prevalence of malignant disease is about 33% for extra-adrenal pheochromocytomas and even higher in patients with specific mutations such as those causing some forms of familial paragangliomas.

Kinney MA, Narr BJ, Warner MA. Perioperative management of pheochromocytoma. *J Cardiothorac Vasc Anesth*. 2002;16(3):359–369.

Lenders JW, Eisenhofer G, Mannelli M, et al. Phaeochromocytoma. *Lancet*. 2005;366(9486):665–675.

Widimský J Jr. Recent advances in the diagnosis and treatment of pheochromocytoma. *Kidney Blood Press Res*. 2006;29(5):321–326.

B. Preoperative Evaluation and Preparation

B.1. How can you diagnose and localize the tumor preoperatively?

The laboratory tests for pheochromocytoma are shown in **Table**

22.2. Biochemical diagnosis is based on the excess catecholamines and their metabolites released by the tumor.

TABLE 22.2 Biochemical Tests for Diagnosis of Pheochromocytoma

Urine Tests
Norepinephrine
Epinephrine
Dopamine
Total metanephrines
Fractionated metanephrines
Vanillylmandelic acid
Plasma Tests
Norepinephrine
Epinephrine
Dopamine
Plasma-free metanephrines
Clonidine suppression of norepinephrine secretion

In theory, the hydroxy-methoxy-mandelic acid (often misnamed as vanillylmandelic acid [VMA]) level should be the most reliable laboratory test because it is the final common product of both catecholamine metabolic pathways. In practice, however, the intermediate metanephrines have proved to be better discriminators of pheochromocytomas. Hydroxy-methoxy-mandelic acid is often used as an initial "case-finding" test because it has "acceptable" specificity and sensitivity and is relatively inexpensive.

Historically, 24-hour urine tests were generally considered superior to plasma tests in the diagnosis of pheochromocytomas because the tumor secretes catecholamines only intermittently and the catecholamines have a short half-life. These combined factors could result in relatively normal plasma catecholamine levels in the presence of an active tumor.

Measurement of total metanephrines gives the highest true-positive results, approximately 98% to 99%. Compelling

evidence now indicates that initial screening for pheochromocytomas and paragangliomas can include measurements of plasma-free metanephrines or urine-fractionated metanephrines. The plasma test offers advantages over the urine test in that it can additionally help predict size and adrenal versus extra-adrenal locations of tumors as well as presence of metastases and underlying germline mutations of tumor susceptibility genes. However, the plasma test is difficult to implement correctly, rendering the urine test preferable for mainstream use and the plasma test more appropriate for specialized endocrine centers.

Computed tomography (CT) with or without iodine 131 (^{131}I)–labeled metaiodobenzylguanidine (MIBG) is extremely accurate in diagnosing and localizing the tumor. Use of arteriography, once popular, should be performed cautiously because dye can stimulate catecholamine release. CT scanning and magnetic resonance imaging (MRI) scanning are excellent imaging techniques that visualize normal adrenal glands when the diagnosis is equivocal. For extra-adrenal locations and in pregnant patients, MRI scanning may be a more desirable choice.

Brunicardi FC, Andersen DK, Billiar TR, et al, eds. *Schwartz's Principles of Surgery*. 10th ed. New York: McGraw-Hill; 2015:1343–1407.

Chen H, Sippel RS, O'Dorisio MS, et al. The North American Neuroendocrine Tumor Society consensus guideline for the diagnosis and management of neuroendocrine tumors: pheochromocytoma, paraganglioma, and medullary thyroid cancer. *Pancreas*. 2010;39(6):775–783.

Eisenhofer G, Peitzsch M. Laboratory evaluation of pheochromocytoma and paraganglioma. *Clin Chem*. 2014;60(12):1486–1499.

Widimský J Jr. Recent advances in the diagnosis and treatment of pheochromocytoma. *Kidney Blood Press Res*. 2006;29(5):321–326.

B.2. How do you pharmacologically prepare the patient with a pheochromocytoma for surgery?

The major goals of pharmacologic therapy in the preoperative period are to control hypertension and to facilitate intravascular volume expansion.

Administration of α-adrenergic blockers has been the cornerstone of preoperative management. Phenoxybenzamine, prazosin, terazosin, and doxazosin may all be employed to facilitate preoperative α-blockade. Phenoxybenzamine is most commonly used due to its relatively long duration of action and ease of administration. It irreversibly and nonselectively alkylates α-adrenergic receptors, including α_1-receptors on vascular smooth muscle, rendering them nonfunctional. Preoperative medical therapy is started 1 to 3 weeks prior to surgery. Therapy is titrated to resolution of symptoms and decrease of BP to low normal values for age. During this period, the patient is encouraged to liberally imbibe fluids and salt in order to facilitate volume replacement and minimize postural hypotension.

Reflex tachycardia is a frequent side effect of preoperative α-blockade. Tachycardia can be managed by subsequent addition of β-blocker therapy. It is worth noting, however, that β-blockade is best avoided in the initial phases of treatment. In the absence of adequate α-blockade, inhibition of β-receptor–mediated vasodilation can result in unopposed α-receptor–mediated vasoconstriction due to catecholamines secreted by the tumor. This can precipitate a hypertensive crisis, heart failure, and possibly end-organ damage.

α-Methyl-para-tyrosine (α-metyrosine) is also an option for preoperative management of pheochromocytoma. This agent decreases the biosynthesis of catecholamines through competitive inhibition of the enzyme tyrosine hydroxylase. The significant depletion of catecholamine stores reduces hemodynamic fluctuations during tumor manipulation. For maximal effect, α-metyrosine must be administered a minimum

of 2 to 3 days before surgery.

Recently, the calcium channel blocker nicardipine has been used as an alternative to phenoxybenzamine for preoperative management. Preoperative use of phenoxybenzamine can often be limited by its frequent and sometimes severe side effect profile (postural hypotension, reflex tachycardia, nasal stuffiness, syncope, etc.) as well as its uncommon use and high cost. Oral nicardipine therapy appears to be an equivalent alternative to phenoxybenzamine therapy and may be better tolerated, cheaper, and more accessible.

Brunaud L, Boutami M, Nguyen-Thi PL, et al. Both preoperative alpha and calcium channel blockade impact intraoperative hemodynamic stability similarly in the management of pheochromocytoma. *Surgery*. 2014;156(6):1410–1417.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:449–476.

Lenders JW, Duh QY, Eisenhofer G, et al. Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2014;99(6):1915–1942.

Naranjo J, Dodd S, Martin YN. Perioperative management of pheochromocytoma. *J Cardiothorac Vasc Anesth*. 2017;31(4):1427–1439.

Siddiqi HK, Yang HY, Laird AM, et al. Utility of oral nicardipine and magnesium sulfate infusion during preparation and resection of pheochromocytomas. *Surgery*. 2012;152(6):1027–1036.

B.3. What other aspects of preoperative management are important?

The circulating blood volume is frequently decreased in these patients due to vasoconstriction from high levels of circulating catecholamines. Patients are encouraged to consume fluid and salt in order to facilitate volume expansion once α-blocker therapy is initiated. However, volume expansion should be undertaken with caution in those with decreased myocardial function to avoid precipitating congestive heart failure.

Sedation in the immediate preoperative period can be

particularly helpful to attenuate catecholamine release secondary to anxiety. It may also help reduce vasodilator requirement subsequently in the intraoperative phase. Adequate sedation and analgesia should also be provided during invasive procedures such as arterial line access. Preoperative treatment of the airway with nebulized lidocaine can help significantly attenuate the tracheal response to intubation.

Lenders JW, Duh QY, Eisenhofer G, et al. Pheochromocytoma and paraganglioma: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2014;99(6):1915–1942.

Pacak K. Preoperative management of the pheochromocytoma patient. *J Clin Endocrinol Metab*. 2007;92(11):4069–4079.

C. Intraoperative Management

C.1. What drugs should be avoided during the operation?

Some of the commonly administered drugs that should be avoided in patients with pheochromocytoma are listed in **Table 22.3**. Many of these agents release histamine (e.g., morphine, atracurium), which is a potent catalyst of catecholamine release from the tumor. Agents that cause indirect increase of catecholamine levels (e.g., ketamine, ephedrine) should also be avoided. It should be noted, however, that these are not absolute contraindications and many of these agents can be used if clinically necessary, provided they are used judiciously with close monitoring.

TABLE 22.3 Suggested Drugs to Avoid in Patients with Pheochromocytoma

Droperidol
Morphine
Atracurium
Pancuronium
Ketamine

Ephedrine
Halothane
Cocaine
Metoclopramide

Connery LE, Coursin DB. Assessment and therapy of selected endocrine disorders. *Anesthesiol Clin North America*. 2004;22(1):93–123.

Kinney MA, Narr BJ, Warner MA. Perioperative management of pheochromocytoma. *J Cardiothorac Vasc Anesth*. 2002;16(3):359–369.

C.2. How would you monitor this patient?

Monitoring in these patients generally includes an electrocardiogram with a V_5 lead, core temperature, pulse oximetry, intra-arterial BP monitoring, central venous pressure monitoring, and a urinary catheter. For patients with known or suspected myocardial dysfunction, a pulmonary artery catheter or transesophageal echocardiography should be considered. Devices that measure cardiac output and stroke volume variation noninvasively can be particularly helpful in titrating fluid therapy.

Most tumors nowadays are excised using laparoscopic technique with minimal blood loss. With the increasing availability of noninvasive monitors of cardiac function, patients who are adequately optimized in the preoperative period and display minimal hemodynamic perturbation do not require central venous pressure monitoring.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:449–476.

Kinney MA, Narr BJ, Warner MA. Perioperative management of pheochromocytoma. *J Cardiothorac Vasc Anesth*. 2002;16(3):359–369.

C.3. Describe the anesthetic management of the patient with pheochromocytoma.

General anesthesia is frequently employed for tumor resection because most resections are performed by laparoscopic

technique. Neuromuscular relaxation and controlled ventilation allow for adequate gas exchange during CO_2 insufflation for pneumoperitoneum.

The anesthetic induction technique should minimize hemodynamic changes and allow for adequate depth of anesthesia during tracheal intubation. Lidocaine 4% solution administered prior to intubation, via mucosal atomizer device, or 1.5 mg per kg intravenously 2 minutes before laryngoscopy can significantly attenuate the response to tracheal intubation. Other measures to attenuate hemodynamic responses to intubation are described in Chapter 11, sections C.5 and C.6. Most of the inhaled agents can be employed during the maintenance phase. However, caution should be used when desflurane is utilized because it may provoke sympathetic stimulation and subsequent catecholamine release. Halothane, now infrequently used in most clinical settings, should be avoided because it has the potential to incite arrhythmias in the presence of high levels of circulating catecholamines.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:449–476.

C.4. What drugs are used to control the effects of catecholamine stimulation during surgery?

Drugs used to control intraoperative hypertension are listed in **Table 22.4**.

TABLE 22.4 Intravenous Drugs to Control Intraoperative Hypertension

Drug	Dose
Nicardipine	Infusion of 5–15 mg/hr. Increase by 2.5 mg/hr every 15 min to effect.
Phentolamine	1-mg IV boluses every 5–10 min. Start infusion 0.1–2 mg/min and titrate to effect.
Nitroglycerin	20–40 μg boluses every 5–10 min to effect. Infusion 5–20 μg/min initial (maximum dose 400 μg/min)

Nitroprusside	Infuse initially with 0.5–1.5 μg/kg/min to maximum of 8 μg/kg/min over 1–3 hr.
Propranolol	1-mg boluses to total 10 mg
Esmolol	Load with 5–10-mg boluses and infuse at 0.25–0.5 μg/kg/min.
Labetalol	5–10-mg boluses every 20–30 min to maximum dose 150 mg

IV, intravenous.

Nicardipine infusion can be easily titrated and is particularly effective at achieving systemic vasodilation. It is a good choice in patients that have already been started on oral nicardipine in the preoperative period. Sodium nitroprusside was used extensively previously. Concerns over toxic metabolites and handling precautions to prevent its degradation by light have largely resulted in nicardipine replacing it as a first-line agent. Phentolamine, a short-acting α-blocking agent, can also be given as a bolus medication or a continuous infusion to control BP.

Magnesium sulfate ($MgSO_4$) has been occasionally used in selected cases as an adjunct vasodilator. Data is still being gathered on its efficacy. Administration of $MgSO_4$ should be accompanied by close monitoring of plasma magnesium levels and other clinical signs of hypermagnesemia.

β-Blockers can be a useful adjunct to control BP in the intraoperative phase, particularly if tachycardia accompanies use of systemic vasodilators. They should, however, not be used as the first-line agent for treatment of intraoperative hypertension due to the concern about unopposed α-agonism.

Hodin R, Lubitz C, Phitayakorn R, et al. Diagnosis and management of pheochromocytoma. *Curr Probl Surg*. 2014;51(4):151–187.

James MF, Cronjé L. Pheochromocytoma crisis: the use of magnesium sulfate. *Anesth Analg*. 2004;99(3):680–686.

Kinney MA, Narr BJ, Warner MA. Perioperative management of pheochromocytoma. *J Cardiothorac Vasc Anesth*. 2002;16(3):359–369.

C.5. What are some management concerns after the tumor is removed?

It is important to be aware of the fact that BP may decrease very quickly after venous drainage of the tumor is interrupted. Any vasodilators being administered should be discontinued. BP support may be maintained by administering vasopressors, such as norepinephrine and vasopressin, and administering fluids. Norepinephrine requirements can be substantial in the post–tumor resection period due to receptor insensitivity from chronic catecholamine exposure. Additional vasopressors, such as vasopressin, may also need to be initiated.

Close communication between the anesthesia and surgical teams is essential during this period. Continued vasodilator support may indicate inadequate resection or previously undiagnosed extra-adrenal tumor.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:449–476.

Hodin R, Lubitz C, Phitayakorn R, et al. Diagnosis and management of pheochromocytoma. *Curr Probl Surg*. 2014;51(4):151–187.

C.6. What are some of the concerns with laparoscopic adrenalectomy?

Insufflation of CO_2, to facilitate pneumoperitoneum, is typically associated with an elevation in catecholamine levels in patients undergoing laparoscopic adrenalectomy, resulting in an associated increase in cardiac output and BP. Close monitoring of vital signs is essential once pneumoperitoneum is initiated. Use of lower intra-abdominal pressures during laparoscopy has been associated with decreased release of catecholamines and less hemodynamic fluctuation. If hemodynamic instability is sustained or refractory, insufflation should be terminated.

Lombardi CP, Raffaelli M, De Crea C, et al. Role of laparoscopy in the management of adrenal malignancies. *J Surg Oncol*. 2006;94(2):128–131.

Sood J, Jayaraman L, Kumra VP, et al. Laparoscopic approach to pheochromocytoma: is a lower intraabdominal pressure helpful? *Anesth*

Analg. 2006;102(2):637–641.

Sprung J, O'Hara JF Jr, Gill IS, et al. Anesthetic aspects of laparoscopic and open adrenalectomy for pheochromocytoma. *Urology*. 2000;55(3):339–343.

D. Postoperative Management

D.1. What is the significance of postoperative hypotension? How is it treated?

Postoperative hypotension can be due to reduced circulating catecholamine levels post–tumor resection, hypovolemia, or residual effects of phenoxybenzamine (which has a long half-life). In addition, downregulation of catecholamine receptors, due to chronically elevated levels of catecholamines, renders administered catecholamines less effective. Post–adrenalectomy hypotension should be treated with volume administration and, if needed, norepinephrine. Vasopressin can be used to treat catecholamine-resistant hypotension. It is important that the clinician rule out other etiologies of hypotension, such as postoperative bleeding as well.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:449–476.

D.2. What other problems can arise in the postoperative period?

Occasionally, patients may be somnolent in the postoperative period. This is possibly due to the sudden removal of activating catecholamines. Narcotic requirement may also be decreased.

Hypoglycemia is another significant concern. Severe hypoglycemia may cause loss of consciousness and respiratory arrest. Hypoglycemia is the result of decreased catecholamine levels (particularly when the tumor is epinephrine-secreting). Neoglycogenesis and glycogenolysis, the result of chronic β-agonism, are no longer present, and chronically elevated insulin

plasma level may decrease more gradually. Close monitoring of plasma glucose levels is essential in the first 24-hours post–tumor resection.

Persistent hypertension after removal of a pheochromocytoma occasionally signifies that a residual pheochromocytoma tumor is present. Be aware that plasma catecholamine levels (norepinephrine) may not decrease to normal levels for many days after removal of the tumor.

Davies MJ, McGlade DP, Banting SW. A comparison of open and laparoscopic approaches to adrenalectomy in patients with phaeochromocytoma. *Anaesth Intensive Care*. 2004;32(2):224–229.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:449–476.

Wilhelm SM, Prinz RA, Barbu AM, et al. Analysis of large versus small pheochromocytomas: operative approaches and patient outcomes. *Surgery*. 2006;140(4):553–559; discussion 559–560.

23 Diabetes Mellitus

Mark E. Nunnally and Vinod Malhotra

A 59-year-old woman presents for vaginal hysterectomy for cervical cancer. She is obese (body mass index 32 kg per m^2) and has had diabetes mellitus (DM) type 2, hypertension, and dyslipidemia for 20 years. She takes enalapril; metoprolol; atorvastatin; metformin; sitagliptin; and recently, insulin glargine, 20 units subcutaneous, daily for refractory hyperglycemia. She measures her serum glucose intermittently at home. Values are generally 150 to 220 mg per dL. She experiences an early and a prolonged sense of fullness after meals and an unpleasant sour taste at night two or three times per week. Laboratory values are notable for a serum creatinine of 2.2 mg per dL and a serum glucose of 206 mg per dL. She has not taken any medications today and has had nothing to eat since midnight.

A. Medical Disease and Differential Diagnosis

1. What is the epidemiology of DM in the general population?
2. What are the factors in the etiology of the disease?
3. How is DM classified?
4. What are the complications of DM?
5. How are the different forms of this illness treated?
6. How is control of the disease adequately monitored?
7. What are some of the factors that alter insulin requirements?

8. What are the principles of management of diabetic ketoacidosis (DKA)?
9. What is a hyperglycemic hyperosmolar state?

B. Preoperative Evaluation and Preparation

1. How should this patient be evaluated?
2. How would the stiff joint syndrome affect her airway management?
3. What are the signs and implications of autonomic neuropathy in the diabetic patient?
4. How should this patient be prepared for anesthesia and surgery?
5. For elective surgery, how are insulin and glucose requirements managed on the day of surgery?
6. How should this patient be premedicated?

C. Intraoperative Management

1. What are the effects of anesthesia and surgery on insulin and glucose metabolism?
2. What anesthetic techniques should be considered?
3. How should this patient be monitored?
4. How is hyperglycemia treated intraoperatively?
5. How is hypoglycemic shock recognized and treated intraoperatively?

D. Postoperative Management

1. How is diabetes controlled in this patient postoperatively?
2. Does diabetes increase perioperative risk?
3. What are the common postoperative complications to be expected in a diabetic patient?
4. Is it necessary to achieve tight perioperative control of glucose?

A. Medical Disease and Differential Diagnosis

A.1. What is the epidemiology of DM in the general population?

DM, literally "sweet urine," is a group of metabolic disorders defined by elevated serum glucose. Data from the National Health and Nutrition Examination Survey from 2010 to 2014 suggest a prevalence of DM in the adult population of 11.9%, with about a quarter of those undiagnosed. For patients 65 years or older, the prevalence is 26.3%. National Health Interview Survey (NHIS) data suggest a doubling of prevalence between 1990 and 2008, but no significant change between 2008 and 2012.

A majority of patients with diabetes (approximately 90%) have type 2 diabetes (DM2); a minority (approximately 10%) have type 1 diabetes (DM1). Finally, 1% to 14% of pregnant women develop gestational diabetes. DM1 and DM2 are very different diseases. In DM1, exogenous insulin is essential for cellular metabolism. Untreated, DM1 is a wasting disease associated with ketoacidosis and severe cumulative organ failure. DM2 is a metabolic disorder associated with resistance to insulin effects. Because of the presence of circulating insulin, ketoacidosis is rare in DM2. However, a hyperglycemic hyperosmolar state is a risk in the inadequately treated patient.

Centers for Disease Control and Prevention. Diabetes prevalence and glycemic control among adults aged 20 and over, by sex, age, and race and Hispanic origin: United States, selected years 1988–1994 through 2011–2014. http://www.cdc.gov/nchs/data/hus/2016/040.pdf. Accessed October 29, 2018.

Geiss LS, Wang J, Cheng YJ, et al. Prevalence and incidence trends for diagnosed diabetes among adults aged 20 to 79 years, United States, 1980-2012. *JAMA*. 2014;312(12):1218–1226.

Hillier TA, Vesco KK, Pedula KL, et al. Screening for gestational diabetes mellitus: a systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2008;148:766–775.

A.2. What are the factors in the etiology of the disease?

Because hyperglycemia defines DM, it is too easy to focus on elevations in serum glucose, ignoring other effects. Lipid and protein metabolism are deranged in both varieties of DM. Tissue growth, signaling, and function are likewise impaired. Simple control of blood sugar may not adequately treat the complex hormonal and metabolic derangements of DM. Inflammation and immune dysfunction are also components of the disease.

In DM1, the immune system destroys insulin-secreting pancreatic β cells. The diagnosis of DM1 is frequently made in childhood. DM2 manifests in a variety of conditions that decrease the hypoglycemic effects of insulin. Among these are obesity and endocrine and inflammatory conditions. In both cases, genetic association is incomplete and there is association with other diseases, including autoimmune disorders, hypertension, and dyslipidemias. Gestational diabetes reflects insulin resistance exacerbated by the effects of pregnancy. It likely signals patients who are at risk of developing DM2.

Cowie CC, Rust KF, Byrd-Holt DD, et al. Prevalence of diabetes and impaired fasting glucose in adults in the U.S. population: National Health and Nutrition Examination Survey 1999-2002. *Diabetes Care*. 2006;29(6):1263–1268.

McDonald M, Hertz RP, Unger AN, et al. Prevalence, awareness, and management of hypertension, dyslipidemia, and diabetes among United States adults aged 65 and older. *J Gerontol Biol Sci Med Sci*. 2009;64(2):256–263.

A.3. How is DM classified?

Table 23.1 lists the criteria for the diagnosis of DM1, DM2, and gestational diabetes. Elevated (≥6.5%) hemoglobin A_1C (Hgb A_1C) or fasting hyperglycemia (≥126 mg per dL) are useful means to confirm metabolic derangement, but random hyperglycemia accompanied by classic symptoms (such as polyuria and polydipsia), or the inability to manage a glucose load, are sufficient to make the diagnosis. Ketoacidosis and the need for insulin reflect DM1, whereas obesity, gradual symptom

onset (usually at an older age), and hyperosmolality without ketosis suggest DM2. Gestational diabetes resembles DM2 only in the setting of pregnancy.

TABLE 23.1 American Diabetes Association Diagnostic Criteria for Diabetes Mellitus

1.	Symptoms of diabetes plus random plasma glucose level >200 mg/dL (11.1 mmol/L)
2.	Hemoglobin A_1C ≥6.5%
3.	Fasting plasma glucose level ≥126 mg/dL (7.0 mmol/L)
4.	Two-hour plasma glucose level ≥200 mg/dL (11.1 mmol/L) during oral glucose tolerance test

From American Diabetes Association. Classification and diagnosis of diabetes: standards of medical care in diabetes—2018. *Diabetes Care*. 2018;41(suppl 1):S13–S27. Copyright © 2017 by the American Diabetes Association. Used with permission of American Diabetes Association.

Therapy for DM varies by type. Insulin is essential in DM1. In DM2 and gestational diabetes, diet, exercise, and drugs that modify insulin secretion or sensitivity can help correct hyperglycemia, although exogenous insulin may be necessary.

American Diabetes Association. Classification and diagnosis of diabetes: standards of medical care in diabetes—2018. *Diabetes Care*. 2018;41(suppl 1):S13–S27.

A.4. What are the complications of DM?

Acute complications of DM include DKA and a hyperglycemic hyperosmolar state. Both are associated with severe systemic illness and a high mortality and will be discussed separately. Hypoglycemia is a serious risk of several diabetes therapies.

Chronically, DM impacts virtually every organ system. Of most concern to the anesthetist are macrovascular disease, including accelerated atherosclerosis, and microvascular nephropathy, neuropathy, and cardiomyopathy. Tissues fail from a combination of advanced glycation end products, inflammation, connective tissue proliferation, and impaired perfusion. Renal failure; neuropathy; and accelerated coronary, cerebral, and peripheral vascular disease are common.

Autonomic neuropathy and the stiff joint syndrome are both factors for preoperative evaluation (see later discussion). Hypertension frequently accompanies DM, exacerbating organ failure. Impaired immune function predisposes to infection. Hypercoagulability exacerbates macrovascular disease. Dyslipidemias accelerate atherosclerotic lesions and may directly contribute to metabolic toxicities.

Cumulatively, the systemic lesions caused or exacerbated by DM reduce life expectancy. When diagnosed before the age of 35 years, DM causes an estimated mean of 25.9 years of lost life. Because complications worsen with time, this effect decreases. About 50% of mortality in diabetic patients comes from cardiovascular disease.

Although it would be helpful to stratify diabetic patients according to their risk of complications, the complexity of the disease and its management makes risk stratification difficult. The safest assumption is that a diabetic is at high risk for coronary and other macrovascular disease, congestive heart failure, and renal insufficiency.

Ford ES, Zhao G, Li C. Pre-diabetes and the risk for cardiovascular disease: a systematic review of evidence. *J Am Coll Cardiol*. 2010;55:1310–1317.

Stolar M. Glycemic control and complications in type 2 diabetes mellitus. *Am J Med*. 2010;123:S3–S11.

A.5. How are the different forms of this illness treated?

Diabetes care is different in chronic and acute settings. It is essential to differentiate between the agents used chronically and those used during acute perioperative stress.

Care of DM1 requires exogenous insulin. **Figure 23.1** illustrates the pharmacodynamics of several insulin preparations. A combination of a short- and a long-acting insulin preparation can help achieve the goals of resting and postprandial glycemic control. In contrast, DM2 responds to insulin, oral insulin

secretagogues, insulin sensitizers, glucose uptake inhibitors, gastrointestinal hormones, weight loss, dietary management, and exercise. **Table 23.2** lists the major classes of drugs for the treatment of DM2, their mechanisms of action, pharmacokinetics, and particular concerns for the anesthetist.

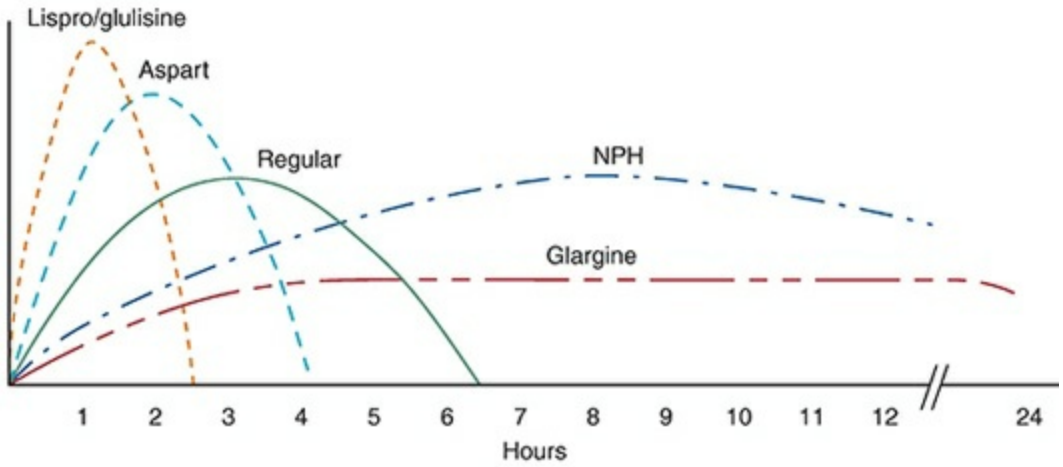

FIGURE 23.1. Onset and duration of action graphic for common subcutaneous insulin preparations. Regular insulin given intravenously fits the best profile for a titratable drug in the operating room, as onset peak and offset all occur within an hour. NPH, neutral protein hagedorn.

TABLE 23.2 Common Therapies for Type 2 Diabetes[a]

Drug Name/Class	Mechanism	Route	Onset	Duration	Important Considerations
First-generation sulfonylureas	↑ β cell insulin secretion	PO			Hypoglycemia
Acetohexamide			3 hr	24 hr	
Chlorpropamide			2 hr	24 hr	
Tolazamide			4 hr	16 hr	
Tolbutamide			1 hr	12 hr	
Second-generation sulfonylureas	↑ β cell insulin secretion	PO			Hypoglycemia
Glimepiride (Amaryl)			2–3 hr	24 hr	
Glipizide ER (Glucotrol XL)			2–4 hr	24 hr	
Glipizide IR (Glucotrol)			30 min	24 hr	
Glyburide			30 min	24 hr	

(Micronase)					
Biguanides	↑ Peripheral glucose uptake in response to insulin	PO			Lactic acidosis risk may extend up to 72 hr after administration.
Metformin (Glucophage)			1–3 hr	17 hr	
α-Glucosidase inhibitors	↓ Digestive carbohydrate breakdown	PO			No known adverse effects
Acarbose (Precose)			2 hr	NA	
Miglitol (Glyset)			2–3 hr	NA	
Thiazolidinediones (PPAR-γ mediators)	↑ Peripheral glucose uptake	PO			Risk for hepatic injury, fluid retention; congestive heart failure; ongoing concerns about myocardial ischemia
Pioglitazone (Actos)			Hours	$T_{1/2}$ 3–7 hr	
Rosiglitazone (Avandia)			Hours	$T_{1/2}$ 3–4 hr	
Meglitinides (glinides)	↑ β cell insulin secretion	PO			Hypoglycemia
Mitiglinide (Glufast)			Minutes	Hours	
Nateglinide (Starlix)			20 min	$T_{1/2}$ 1.5 hr	
Repaglinide (Prandin)			15–60 min	4–6 hr	
Incretin-mimetics (glucagon-like peptide-1 agonists)	↑ Insulin, ↓ glucagon, hepatic glucose production, gastric emptying, and appetite	SC			Observational data associated with renal failure, delayed gastric emptying, hypoglycemia, pancreatitis
Albiglutide (Tanzeum)			Days	$T_{1/2}$ 5 days	
Dulaglutide (Trulicity)			Hours (48 hr median)	$T_{1/2}$ 5 days	
Exenatide (Byetta, Bydureon)			10 min	6–8 hr	
Liraglutide (Saxenda, Victoza)			Minutes	$T_{1/2}$ 13 hr	
Lixisenatide (Adlyxin)			Hours	$T_{1/2}$ 3 hr	

Semaglutide (Ozempic)			Days	$T_{1/2}$ 1 week	
Dipeptidyl peptidase-4 (DPP-IV) inhibitors	Inhibits incretin breakdown	PO			May have effects on immune function and heart failure
Alogliptin (Nesina)			1–2 hr	$T_{1/2}$ 21 hr	
Linagliptin (Tradjenta)			1.5 hr	$T_{1/2}$ 12 hr	
Saxagliptin (Onglyza)			Hours	24 hr	
Sitagliptin (Januvia)			Hours	Days	
Amylin analogues	↑ Satiety, ↓ glucagon, and appetite, indication for DM1	SC			Hypoglycemia
Pramlintide (Symlin)			Minutes	Hours	
Sodium glucose cotransporter-2 (SGLT-2) inhibitors	Inhibit renal reabsorption of glucose	PO			Hypoglycemia, urinary tract infections. Bladder cancer. Antihyperglycemic effects may mask diabetic ketoacidosis.
Canagliflozin (Invokana)			Hours	$T_{1/2}$ 13 hr	
Dapagliflozin (Farxiga)			Hours	$T_{1/2}$ 13 hr	
Empagliflozin (Jardiance)			Hours	$T_{1/2}$ 12 hr	
Ertugliflozin (Steglatro)			1 hr	$T_{1/2}$ 17 hr	
Dopamine agonist	↓ Sympathetic tone, ↓ hepatic glucose production, ↓ postmeal free fatty acid levels	PO			Hypotension
Bromocriptine (Cycloset)			Minutes	$T_{1/2}$ 6 hr	
Bile acid sequestrant	Binds bile acids in GI tract, preventing reabsorption.	PO			May increase serum triglycerides, transaminases. GI discomfort

	Mechanism for controlling blood sugar unknown		
Colesevelam (Welchol)		Minutes	Works concurrently with meals

[a]Onset and duration data are approximate only and subject to variability.
DM1, type 1 diabetes; ER, extended release; GI, gastrointestinal; IR, immediate release; NA, not applicable; PO, per os (by mouth); PPAR-γ, peroxisome proliferator-activated receptor gamma; SC, subcutaneous; $T_{½}$, half-life.

Certain medications have adverse effects that deserve consideration. Biguanides, such as metformin, increase peripheral glucose uptake but also predispose patients to greater production of lactic acid and acidosis. The significance of this finding is not clear, but many recommend discontinuing these drugs perioperatively because they might increase the risk of lactic acidosis with hypoperfusion during surgery. Because of its long half-life, metformin may take up to 72 hours to clear from the bloodstream, so discontinuation on the day of surgery does not minimize the risk of acidosis. Thiazolidinediones have been associated with hepatic injury and congestive heart failure. Exenatide is associated with reports of kidney dysfunction. Sulfonylureas, pramlintide, and sitagliptin may be associated with hypoglycemia. Glucose transporter type 2 inhibitors, such as dapagliflozin, may be associated with urogenital infections. Long-term risks remain poorly characterized for this and other new agents, such as glucagon-like peptide agonists and inhaled insulin preparations.

For these reasons, as well as unreliable pharmacokinetics, the best option for acute treatment of all types of diabetic hyperglycemia is insulin. Although subcutaneous dosing is often used in the hospital setting, intravenous insulin best meets the profile of an ideal titratable agent. It has a short time to onset (10 to 15 minutes), peak effect (less than 30 minutes), and duration

of action (45 minutes). Frequent glucose monitoring is essential to titrate the therapy.

Although serum glucose or other markers of chronic hyperglycemia, such as Hgb A_1C, are currently standard end points for chronic therapy, other factors such as serum lipid and blood pressure management may be just as important. Anesthesiologists should inquire about agents treating these conditions during preoperative evaluation.

Bagry HS, Raghavendran S, Carli F. Metabolic syndrome and insulin resistance: perioperative considerations. *Anesthesiology*. 2008;108:506–523.

Chen D, Lee SL, Peterfreund RA. New therapeutic agents for diabetes mellitus: implications for anesthetic management. *Anesth Analg*. 2009;108:1803–1810.

Gourgari E, Wilhelm EE, Hassanzadeh H, et al. A comprehensive review of the FDA-approved labels of diabetes drugs: indications, safety, and emerging cardiovascular safety data. *J Diabetes Complications*. 2017;31:1719–1727.

Jung CH, Chung EJ, Park JY. A novel therapeutic agent for type 2 diabetes mellitus: SGLT2 inhibitor. *Diabetes Metab J*. 2014;38:261–273.

A.6. How is control of the disease adequately monitored?

Self-monitoring of blood glucose is possible in all forms of diabetes, usually by using finger-stick blood samples and portable monitors. This method is the established standard of care in DM1 for carefully titrated control to prevent hypoglycemia and ketoacidosis. Many advocate self-monitoring for patients with DM2, especially if they take insulin, but compliance varies, and self-monitoring may not be beneficial in all patients. Hgb A_1C, the product of Hgb exposure to hyperglycemic conditions, is a marker of long-term glycemic control. It may help identify subgroups of patients for whom the risk for complications is higher and can be a marker of disease control. The relationship between levels of glycemic control and Hgb A_1C is not linear, so a single laboratory value does not completely reveal the glycemic profile over time. Patients with

DM have blood pressure and serum lipid profiles monitored as part of their long-term care because these factors increase the risk of lifetime complications.

In the operating room, serum glucose can be measured by pinprick or vascular blood sample. Samples from a venous or arterial line offer greater reliability during low perfusion. If insulin is being used, monitoring is recommended every hour.

Kolb H, Kempf K, Martin S, et al. On what evidence-base do we recommend self-monitoring of blood glucose? *Diabetes Res Clin Pract*. 2010;87:150–156.

Moitra V, Sladen RN. Monitoring endocrine function. *Anesthesiol Clin*. 2009;27:355–364.

A.7. What are some of the factors that alter insulin requirements?

Insulin responsiveness is dynamic during stress or illness. Tissue injury from surgery, trauma, or inflammatory states, such as infection, decreases glycemic responsiveness to insulin as part of the stress response. Under ideal circumstances, these effects are maximal 2 to 3 days after injury and resolve over the course of a week, but there is substantial variability. Besides stress, any other condition that increases counter-regulatory hormones such as glucagon, cortisol, and catecholamines decreases insulin sensitivity and increases insulin requirements. Cushing disease and pheochromocytoma are examples of conditions that cause insulin resistance. Several medications, including corticosteroids, thyroid replacement preparations, oral contraceptives, and thiazide diuretics, also increase insulin resistance. In solid organ transplant recipients, steroids and the calcineurin inhibitors tacrolimus and cyclosporine have been associated with insulin resistance or onset of diabetes. Exercise and ethanol can decrease insulin requirements.

Shah T, Kasravi A, Huang E, et al. Risk factors for development of new-onset diabetes mellitus after kidney transplantation. *Transplantation*. 2006;82:1673–

1676.

Tanaka T, Nabatame H, Tanifuji Y. Insulin secretion and glucose utilization are impaired under general anesthesia with sevoflurane as well as isoflurane in a concentration-independent manner. *J Anesth*. 2005;19:277–281.

Thorell A, Nygren J, Ljungqvist O. Insulin resistance: a marker of surgical stress. *Curr Opin Clin Nutr Metab Care*. 1999;2(1):69–78.

A.8. What are the principles of management of diabetic ketoacidosis (DKA)?

A hyperglycemic patient should be assessed for DKA before surgery. Because DKA is associated with higher perioperative mortality, patients should be monitored for intravascular volume and electrolyte abnormalities.

Withholding insulin contributes to DKA. Infection or tissue injury exacerbates diabetes and sets off a chain of events that can result in DKA. Because of increased risk to the patient, DKA is corrected before surgery. When it is triggered by a surgical condition, time to correct it may be limited by the urgency of the surgery.

Patients with DKA have an anion gap metabolic acidosis in addition to hyperglycemia. Elevated serum ketone levels can help confirm the diagnosis, but urine ketones are frequently easier to assay. Commonly, a patient will be hypovolemic from polyuria and incomplete hydration, and resuscitation with isotonic fluids is appropriate. Lactate and acetate are converted to glucose by the liver, and this fact should be considered in selecting solutions for the initial resuscitation and weighed against the risks of hyperchloremic acidosis. Ketosis is corrected with insulin, which is best as an intravenous infusion. Because glucose levels frequently normalize before ketosis clears, insulin therapy is continued even after hyperglycemia corrects. Dextrose is administered simultaneously to avoid hypoglycemia. During acidemia, hyperkalemia is common, resulting from shifts in body stores. However, a patient will frequently have a net

potassium deficit. Hypokalemia during correction, which can reflect a deficit of up to 10 mEq potassium per kg body mass, should be treated aggressively. Likewise, hypocalcemia and hypomagnesemia should be anticipated and treated.

Kitabchi AE, Murphy MB, Spencer J, et al. Is a priming dose of insulin necessary in a low-dose insulin protocol for the treatment of diabetic ketoacidosis? *Diabetes Care*. 2008;31:2081–2085.

Kitabchi AE, Nyenwe EA. Hyperglycemic crises in diabetes mellitus: diabetic ketoacidosis and hyperglycemic hyperosmolar state. *Endocrinol Metab Clin North Am*. 2006;35:725–751.

A.9. What is a hyperglycemic hyperosmolar state?

Any hyperglycemic patient should be evaluated for a hyperglycemic hyperosmolar state, another potentially fatal condition. The syndrome is more frequent in DM2. It includes hyperglycemia, hyperosmolarity, volume depletion, and changes in mental status. Adverse effects result from hyperosmolarity and hypovolemic shock. Glucose levels exceeding 1,000 mg per dL have been described. Mortality can be high. Glycosuria and inadequate fluid intake contribute to the condition. Treatment consists of fluid resuscitation and intravenous insulin to correct the hyperglycemia. Sodium, potassium, calcium, and magnesium levels should be evaluated and normalized.

Kitabchi AE, Nyenwe EA. Hyperglycemic crises in diabetes mellitus: diabetic ketoacidosis and hyperglycemic hyperosmolar state. *Endocrinol Metab Clin North Am*. 2006;35:725–751.

B. Preoperative Evaluation and Preparation

B.1. How should this patient be evaluated?

The goals of preoperative evaluation are to stratify perioperative risk, ensure optimal management of concurrent illness, and screen for specific anesthetic-related problems. A diabetic patient is evaluated for cardiovascular disease, renal function,

stiff joint syndrome, autonomic neuropathy, aspiration risk, and acute diabetic emergencies.

Both DM1 and DM2 increase the risk of coronary artery disease. The 2014 American College of Cardiology (ACC)/American Heart Association (AHA) Guideline on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery recommends the use of the Revised Cardiac Risk Index (RCRI). This index uses a history of diabetes, ischemic heart disease, heart failure, cerebrovascular disease, and renal insufficiency to predict perioperative cardiovascular risk. According to the 2014 guidelines, patients are triaged based on risk for major adverse cardiac events (MACE). The RCRI, the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) Surgical Risk Calculator, and the Myocardial Infarction and Cardiac Arrest (MICA) calculators are three tools to measure this risk. In the case of the RCRI, diabetes requiring insulin is one of six criteria used in the score. In the Surgical Risk Calculator, risk is calculated from a larger group of factors, including surgery type and a diagnosis of diabetes. The MICA calculator risk is calculated based on surgery type, American Society of Anesthesiologists patient classification, serum creatinine, and patient age. If MACE risk from these indices is greater than or equal to 1%, poor or unknown exercise tolerance and whether the results will change perioperative care determine the need for stress testing. A diagnosis of diabetes is thus a major factor for deciding whether to supplement a patient assessment preoperatively because of cardiovascular risk. Preoperative β-blocker therapy is recommended (level of evidence: B) in diabetic patients with three or more RCRI risk factors, although starting these agents on the day of surgery in patients who have never had the therapy is discouraged.

Optimizing the patient's medical status is a consideration for

all patients but particularly for diabetics who have many comorbidities. Optimal management of coexisting hypertension and congestive heart failure can minimize perioperative risk. The decision to proceed or delay a procedure for medical management depends on the urgency of the surgery and the potential for improving the patient's medical condition.

Diabetes is a leading cause of renal insufficiency and failure. Because this patient already has an increased serum creatinine, she should be screened for renal insufficiency and any fluid and metabolic derangements should be corrected. A metabolic panel, including serum creatinine, blood urea nitrogen, potassium, sodium, chloride, bicarbonate, and base deficit can be useful, especially because angiotensin mediators, β-blockers, and insulin itself can affect serum potassium levels. Joint stiffness is assessed with a comprehensive airway examination and the "prayer sign," in which a patient's hands are placed against each other at the palmar surface to see whether the fingers touch. Other considerations in the diabetic include the risks of aspiration and autonomic instability. Although Hgb A_1C levels correlate with perioperative risk, the test does not add any information to the decision paradigm.

In addition to its chronic consequences, diabetes may produce a hyperglycemic hyperosmolar state and DKA. Both syndromes reflect severe metabolic abnormalities, most commonly resulting from infection. Because these syndromes may manifest as a result of a surgical emergency, patients with these conditions will present for perioperative management. Ideally, metabolic derangements should be corrected before anesthetic induction, but sometimes, patients must go to surgery urgently or emergently. Anesthesia providers should be prepared for hemodynamic instability, rapid fluid infusion, electrolyte repletion, and frequent monitoring of serum glucose and electrolytes. In both conditions, intravenous insulin infusion is

indicated, titrated to normoglycemia in the hyperglycemic hyperosmolar state and the clearance of ketones in DKA. Supplemental dextrose is usually necessary to maintain insulin infusion in DKA.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management for patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;64:e77–e137.

Lee TH, Marcantonio ER, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation*. 1999;100(10):1043–1049.

B.2. How would the stiff joint syndrome affect her airway management?

The stiff joint syndrome is thought to result from glycation of connective tissue with chronic exposure to hyperglycemia. This collagen glycation starts in the fourth and fifth interphalangeal joints resulting in the patient not able to completely appose the palms and fingers of the hands—the "prayer sign." The degree of interphalangeal involvement can also be assessed by scoring the ink impression made by the palm of the dominant hand "palm print (PP) sign." These are good screening tests for joint stiffness and indicate a reduced range of motion in the cervical spine, temporomandibular, arytenoid joints, and glottic structures making endotracheal intubation difficult. The PP test and the prayer sign are sensitive and specific predictors of difficult airway that may likely require a smaller endotracheal tube and difficult airway adjuncts.

Hashim KV, Thomas M. Sensitivity of palm print sign in prediction of difficult laryngoscopy in diabetes: a comparison with other airway indices. *Indian J Anaesth*. 2014;58(3):298–302.

Hogan K, Rusy D, Springman SR. Difficult laryngoscopy and diabetes mellitus. *Anesth Analg*. 1988;67:1162–1165.

Nadal JL, Fernandez BG, Escobar IC, et al. The palm print as a sensitive predictor of difficult laryngoscopy in diabetics. *Acta Anaesthesiol Scand*. 1998;42:199–203.

Salzarulo HH, Taylor LA. Diabetic "stiff joint syndrome" as a cause of difficult endotracheal intubation. *Anesthesiology*. 1986;64:366–368.

B.3. What are the signs and implications of autonomic neuropathy in the diabetic patient?

Diabetic neuropathy involves both the peripheral and autonomic nervous system. In the autonomic system, gastric motility, heart rate, and vasomotor tone may be impaired. Cardiac ischemia can be asymptomatic. This patient is at risk for pulmonary aspiration of gastric contents and hemodynamic instability. A history will elicit early satiety, prolonged postprandial fullness, and significant reflux symptoms. Potential difficulties with mask ventilation and intubation are assessed. Heart rate variability, best seen on an electrocardiogram (ECG) tracing in response to deep breathing, Valsalva maneuver, or position changes, identifies patients at risk for hemodynamic instability. Preparation is made to control hemodynamic instability, especially because this patient is taking an angiotensin-converting enzyme inhibitor. Angiotensin-receptor blocking agents also increase the risk of postinduction hypotension. Because of a high likelihood of hemodynamic instability, the anesthesiologist should prepare to use slow titration of anesthetic agents, frequent blood pressure monitoring, and vasoactive agents, if necessary.

Huang CJ, Kuok CH, Kuo TB, et al. Pre-operative measurement of heart rate variability predicts hypotension during general anesthesia. *Acta Anaesthesiol Scand*. 2006;50:542–548.

B.4. How should this patient be prepared for anesthesia and surgery?

This patient's cardiovascular risk is elevated. Her RCRI puts her

risk for MACE between 6% and 11%, but the NSQIP Surgical Risk Calculator puts it at 0.2%. If her exercise tolerance is below 4 metabolic equivalents (METs), about the equivalent of climbing a flight of stairs with a bag of groceries or performing heavy work around the house, noninvasive stress testing may be considered. Insulin therapy is given for hyperglycemia. Because of her elevated serum glucose, she is asked about polyuria, a sign that she might be dehydrated from hyperglycemic diuresis. DKA is unlikely because she has DM2, but a metabolic panel is indicated to rule out electrolyte abnormalities. The presence of an elevated anion gap should provoke further investigation for the possibility of ketoacidosis. An ECG may be indicated based on her risk factors for cardiovascular disease.

Her symptoms, consistent with gastroparesis and gastroesophageal reflux, will influence premedication and airway management. Results from a comprehensive airway examination, including assessment of neck and jaw mobility and a check for the prayer sign, affect anesthetic management decisions. A rapid sequence intubation could minimize aspiration risk but only if intubation is easy. If a difficult airway is suspected, awake intubation techniques should be considered.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management for patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;64:e77–e137.

B.5. For elective surgery, how are insulin and glucose requirements managed on the day of surgery?

The risk of hypoglycemia is balanced against the benefit of glycemic control. Anesthetized patients can have occult hypoglycemia, so serum glucose is checked frequently. Intravenous insulin is titrated for glycemic control. When administered intravenously, either as an infusion or as

intermittent boluses, insulin has a fast onset and a short duration of action. Subcutaneous insulin, with longer lasting effects, is less predictable, especially during the hemodynamic changes of anesthesia and surgery. Subcutaneous insulin pumps should be turned down or off for all but the most minor procedures. Similarly, oral agents should be withheld on the day of surgery, except for minor procedures. Ideally, metformin should be withheld for 72 hours to minimize the risk of lactic acidosis.

Initial enthusiasm for tight glycemic control in critically ill patients has given way to a much more cautious approach. Perioperatively, hyperglycemia is associated with worsened neurologic and cardiac ischemia and poor wound healing. Even though tight control of serum glucose has been associated with better outcomes in some settings, there is risk associated with insulin therapy. Hypoglycemia is a serious risk, and insulin has multiple other effects that remain poorly described.

Evidence is limited to support glycemic control to a "normal" range of 80 to 110 mg per dL in the operating room. Higher targets minimize hypoglycemia. Levels higher than 180 mg per dL may cause protein glycation and osmotic diuresis. Targets within the range of 100 to 180 mg per dL are considered satisfactory.

Preoperative infusion of dextrose minimizes peripheral insulin resistance and reduces the risks of hypoglycemia. When dextrose causes hyperglycemia, the amount of insulin needed is increased. Given that insulin resistance and hyperglycemia are parts of the stress response to surgery, hyperglycemia may be a sign that exogenous carbohydrate infusion is not necessary.

Coursin DB, Connery LE, Ketzler JT. Perioperative diabetic and hyperglycemic management issues. *Crit Care Med*. 2004;32(4 suppl):S116–S125.

Lipshutz AK, Gropper MA. Perioperative glycemic control: an evidence-based review. *Anesthesiology.* 2009;110:408–421.

B.6. How should this patient be premedicated?

Concerns with premedication include sensitivity to sedatives and aspiration risk. Preexisting cardiovascular, cerebrovascular, and renal disease temper the aggressiveness of administration of benzodiazepines and opioids. Because of the symptoms of gastroesophageal reflux and gastroparesis, histamine blockers, liquid antacids, or metoclopramide may be given. Metoclopramide, famotidine, and a liquid antacid like sodium citrate may minimize aspiration risk in this patient.

C. Intraoperative Management

C.1. What are the effects of anesthesia and surgery on insulin and glucose metabolism?

As part of the stress response to surgery, metabolism increases and resistance develops to the hypoglycemic effects of insulin. The response includes the mobilization of protein stores (mostly muscle), more hepatic gluconeogenesis, and greater breakdown and synthesis of triglycerides. Hormones, including catecholamines, cortisol, glucagon, and even insulin, contribute to the metabolic changes. Although glucose metabolism increases, so too does glucose production, adding to the risk of hyperglycemia. Administration of exogenous dextrose can exacerbate hyperglycemia in diabetic patients.

Anesthetic techniques influence metabolism but generally to a lesser extent than the stress from surgical injury. Techniques that mitigate stress hormones, such as neuraxial anesthesia, also may mitigate hyperglycemia. Some drugs affect regulatory hormones directly. Etomidate blocks cortisol synthesis. Benzodiazepines can decrease cortisol secretion. Halogenated agents have in vitro effects on insulin secretion. However, none of these effects impact postoperative glycemic control as much as will the

surgery itself.

McAnulty GR, Robertshaw HJ, Hall GM. Anaesthetic management of patients with diabetes mellitus. *Br J Anaesth*. 2000;85(1):80–90.

C.2. What anesthetic techniques should be considered?

Factors other than glycemic control may influence the choice of anesthetic technique in the patient with diabetes. Regional techniques are chosen based on provider skill, patient preferences, and postoperative pain control. Techniques that speed the time to oral intake by reducing nausea or minimizing ileus make glycemic management easier postoperatively. For this reason, antiemetics and the spare use of opioids might be beneficial. Although not a contraindication to nerve blockade, peripheral neuropathy should be documented in a preoperative neurologic examination. Nerve injury from local anesthetics or abnormalities on neurologic examination may complicate postoperative management. Infection risk from regional techniques may be increased in patients with diabetes.

Sedated or anesthetized patients cannot complain of hypoglycemic symptoms the same way unsedated patients can. Serum glucose is monitored regularly in all but the shortest cases.

In this patient, general endotracheal anesthesia with precautions to prevent aspiration, intravenous insulin titrated to a serum glucose of less than 180 mg per dL, and frequent blood glucose monitoring is a satisfactory choice.

Ljungqvist O, Nygren J, Soop M, et al. Metabolic perioperative management: novel concepts. *Curr Opin Crit Care*. 2005;11:295–299.

McAnulty GR, Robertshaw HJ, Hall GM. Anaesthetic management of patients with diabetes mellitus. *Br J Anaesth*. 2000;85(1):80–90.

C.3. How should this patient be monitored?

If preoperative evaluation reveals a risk of hemodynamic

instability, cardiac ischemia, or congestive heart failure, added cardiovascular monitoring should be considered, depending on the procedure. Peripheral vascular disease can complicate placement of an arterial catheter but is not a contraindication because in patients who have cardiovascular comorbidities, the benefits of monitoring outweigh the risks.

Frequent glucose monitoring is recommended in cases lasting longer than an hour or when hypoglycemic agents are being used. Serum glucose by finger stick or, ideally, venous or arterial sample should be measured at least every hour when giving intravenous insulin.

In this patient, pulse oximetry, continuous ECG monitoring, end-tidal carbon dioxide and gas analysis, and noninvasive blood pressure monitoring are satisfactory, if no further concerns arise from cardiovascular evaluation or surgical complexity.

McAnulty GR, Robertshaw HJ, Hall GM. Anaesthetic management of patients with diabetes mellitus. *Br J Anaesth*. 2000;85(1):80–90.

C.4. How is hyperglycemia treated intraoperatively?

The high end of a normal range for fasting serum glucose is 110 mg per dL; however, hyperglycemia in inpatients need not be treated until it reaches a higher level.

The one good agent for treating intraoperative hyperglycemia is intravenous insulin. Onset takes minutes, peak effect is achieved in 15 to 30 minutes, and duration of effect is less than an hour, facilitating titration. Insulin may be administered by continuous infusion or as intermittent boluses; the bolus consumes less lead time and eliminates the risk of pump misprogramming or malfunction. Subcutaneous insulin is less ideal for use during general anesthetics or complex procedures because variable peripheral blood flow will alter the uptake and duration of action. Most other therapies for DM2 are not fit for

intraoperative use. Oral agents cannot be easily administered, are not reliably absorbed, and have too long a duration of action to be practical perioperatively. They may be taken on the day of surgery before minor procedures. In this case, sitagliptin should be discontinued to avoid hypoglycemia. Metformin, a biguanide, increases the risk of lactic acidosis during periods of hypoperfusion. Metformin is discontinued for 3 or more days before extensive procedures when a large-volume blood loss is possible.

Smiley DD, Umpierrez GE. Perioperative glucose control in the diabetic or nondiabetic patient. *South Med J*. 2006;99(6):580–589.

C.5. How is hypoglycemic shock recognized and treated intraoperatively?

Hypoglycemia can lead to tissue energy failure and has been associated with hemodynamic collapse and brain injury. Any patient receiving insulin, pramlintide, sitagliptin, or sulfonylureas is at risk for hypoglycemia. Because risk is usually known beforehand, hourly or more frequent monitoring of serum glucose should detect hypoglycemia. If glucose levels are low or decrease rapidly, the fastest treatment is a bolus of intravenous dextrose, 50% solution, administered slowly. In an emergency, one full ampule is the starting dose. In less urgent settings when the serum glucose level is low but not critical, smaller doses can be titrated to serum glucose values.

Dierdorf SF. Anesthesia for patients with diabetes mellitus. *Curr Opin Anaesthesiol*. 2002;15:351–357.

D. Postoperative Management

D.1. How is diabetes controlled in this patient postoperatively?

Unless there is a change in disease status as a consequence of surgery or preoperative care was inadequate, this patient should be transitioned back to her preoperative regimen. Before transitioning, she must recover from the stress response to the surgery. If this were a simple outpatient procedure, such as a cataract extraction, she could return home on her outpatient medication regimen. In this case, however, the effects of tissue injury may not peak for days; diabetes control is thus a dynamic challenge. Regular monitoring of glucose is required (at a minimum, checks should be made every 6 hours).

She is monitored for hyperglycemia, and her nutrition regimen is adjusted to serum glucose measurements. Hourly glucose measurements and insulin infusion can control hyperglycemia. Most patients can be effectively managed with subcutaneous insulin and less frequent measurements. Insulin dose should take into account preoperative requirements, insulin resistance from the stress response, and caloric intake. Many patients receive intravenous dextrose postoperatively; if they are hyperglycemic on this regimen, dextrose is discontinued.

Oral diabetes medications can be reintroduced once the acute stress response begins to wane and the patient is cleared for a normal diet. Resumption of an oral diet can increase the risk of hyperglycemia, so ongoing monitoring is essential.

Smiley DD, Umpierrez GE. Perioperative glucose control in the diabetic or nondiabetic patient. *South Med J*. 2006;99(6):580–589.

D.2. Does diabetes increase perioperative risk?

Because patients with diabetes are at a greater risk of atherosclerosis, infection, autonomic and cardiovascular instability, and metabolic abnormalities than those without diabetes, perioperative risk is higher in this patient population. After surgery, the diabetic patient is monitored for hyperglycemia and hypoglycemia, ischemic complications,

circulatory compromise, and wound and nosocomial infection. As a group, patients with diabetes have an increased risk for complications and poor outcomes from complications.

Lipshutz AK, Gropper MA. Perioperative glycemic control: an evidence-based review. *Anesthesiology*. 2009;110:408–421.

D.3. What are the common postoperative complications to be expected in a diabetic patient?

Hyperglycemia and hypoglycemia, wound infections, and organ ischemia are the most common and worrisome postoperative complications in patients with diabetes. Following myocardial infarction or cerebrovascular accident, hyperglycemia is associated with a worse prognosis.

Smiley DD, Umpierrez GE. Perioperative glucose control in the diabetic or nondiabetic patient. *South Med J*. 2006;99(6):580–589.

D.4. Is it necessary to achieve tight perioperative control of glucose?

In the critical care setting, there is evidence for improved outcomes with tight glycemic control, variably defined as serum glucose between 80 and 120 mg per dL or higher; other evidence has shown no benefit or even harm. Some advocate for tight glycemic control in cardiac and noncardiac surgery; however, the risks of hypoglycemia and data from more recent studies have tempered the enthusiasm for tight glycemic control.

Potential benefits from tight glycemic control include improvement in metabolic, anti-inflammatory, organ, and circulatory function. Unfortunately, there is little evidence to suggest these benefits are substantial perioperatively. Unresolved details include the best time for tight control, the goals of therapy, the effect of nutrition, and the magnitude and factors in the potential for significant hypoglycemia. The patient is transitioned to her preoperative level of control during

recovery, and severe hyperglycemia is prevented by monitoring glucose closely. Glucose levels above 180 mg per dL increase the risk of protein glycation and osmotic diuresis; targeting serum glucose below this value makes physiologic sense.

Gandhi GY, Nuttall GA, Abel MD, et al. Intensive intraoperative insulin therapy versus conventional glucose management during cardiac surgery: a randomized trial. *Ann Intern Med*. 2007;146:233–243.

NICE-SUGAR Study Investigators. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med*. 2009;360:1283–1297.

van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in critically ill patients. *N Engl J Med*. 2001;345(19):1359–1367.

SECTION 6 The Genitourinary System

24 Transurethral Resection of the Prostate and Geriatric Anesthesia

Anuj Malhotra, Vinod Malhotra, and Fun-Sun F. Yao

A 79-year-old man with benign prostatic hypertrophy is scheduled for transurethral resection of the prostate (TURP). His past medical history includes myocardial infarction (MI) 7 months ago requiring drug-eluting coronary stent (DES) placement and an implantable cardioverter-defibrillator (ICD) inserted for episodes of ventricular tachycardia. His current left ventricular ejection fraction is 25%. The patient is taking diuretics, a β-blocker, clopidogrel, aspirin, and an angiotensin-converting enzyme (ACE) inhibitor.

A. Medical Disease and Differential Diagnosis

1. What comorbidities are common in patients undergoing TURP?
2. What are the normal physiologic consequences of aging for the various organ systems?
3. How should drug dosages be adjusted for elderly patients? Should any particular medications be avoided?
4. Does a history of prior MI increase the patient's risk of perioperative reinfarction or stent thrombosis?
5. In patients with a history of recent MI, would you recommend that the surgery be postponed for a certain period?

B. Preoperative Evaluation and Preparation

1. How would you evaluate the patient's cardiac condition? Does he need additional testing?
2. Would you discontinue any antihypertensives or any medications for angina?
3. For a patient with a cardiac implantable electronic device (CIED), what information should you know? What precautions should be taken?
4. What types of coronary stents are available? What is their perioperative relevance?
5. What is the conventional recommendation for dual antiplatelet therapy (DAPT) in a patient with previous percutaneous coronary intervention (PCI) undergoing elective noncardiac surgery?
6. What risk is associated with continuing perioperative antiplatelet therapy? What risk is there with stopping it?
7. How should patients with coronary stents undergoing noncardiac surgery be managed?

C. Intraoperative Management

1. What monitors would you use for this patient?
2. Is there a preferred anesthetic technique for patients undergoing TURP, and why?

3. Does regional anesthesia result in a lower incidence of perioperative mortality than general anesthesia?
4. What intravenous fluid would you use during TURP?
5. Forty minutes after a sensory level of T10 was established with intrathecal anesthesia, and monopolar TURP (M-TURP) resection was initiated with the use of glycine as the bladder irrigating solution, the patient becomes agitated and complains of nausea. Further sedation along with an antiemetic is administered. However, shortly thereafter, the patient becomes very restless, blood pressure rises, and heart rate decreases. The patient becomes cyanotic and obtunded, blood pressure precipitously falls, and pupils are dilated and unresponsive to light. What is the most likely cause of these signs and symptoms, and would these occur during bipolar (B-TURP) or laser TURP (L-TURP) resection?
6. What are the important characteristics of irrigation solutions used during TURP?
7. What is the effect on body temperature of continuous bladder irrigation during TURP?
8. What is the definition of TURP syndrome? What are the signs and symptoms of the syndrome?
9. How does the patient absorb irrigation solution during TURP?
10. What factors increase the incidence of TURP syndrome?
11. What is the effect on cardiopulmonary, renal, and central nervous system (CNS) functions of excessive absorption of irrigation solution during TURP?
12. What causes CNS dysfunction in patients who have undergone M-TURP?
13. How does acute hyponatremia affect the cardiovascular system?
14. What prophylactic measures may reduce the incidence of TURP syndrome?
15. What therapeutic measures are recommended for patients with

TURP syndrome?

16. Is hypertonic saline administration necessary to correct hyponatremia? Explain. What are the risks of rapidly correcting hyponatremia?
17. What are the toxic effects of glycine? Is there an antidote to glycine toxicity? What are the metabolic by-products of glycine?
18. What are the symptoms and clinical course of TURP-induced hyperammonemia?
19. What are the clinical characteristics, causes, and prognosis of TURP-related blindness?
20. What are the causes of excessive bleeding during TURP?
21. What are the causes, signs, symptoms, and treatment of bladder perforation during TURP?
22. What are the causes of hypotension during TURP?

D. Postoperative Management

1. What is the source of postoperative bacteremia in patients who have undergone TURP? What factors increase the incidence of bacteremia?
2. What are the signs of post-TURP septicemia? What preventive measures are generally recommended?
3. Is postoperative hypothermia a risk factor for myocardial ischemia?
4. What is postoperative cognitive dysfunction (POCD)? How does this differ from delirium, and what is the time course to resolution?
5. What are the mechanisms and risk factors for POCD? How would you mitigate the risk of POCD? Does anesthesia type influence development of POCD?

E. Comparing M-TURP, B-TURP, and L-TURP

1. What differentiates M-TURP from B-TURP?
2. Are decreased morbidity and mortality associated more closely

with M-TURP or with B-TURP?

3. What differentiates the technologies for L-TURP?

A. Medical Disease and Differential Diagnosis

A.1. What comorbidities are common in patients undergoing TURP?

TURP patients often are elderly and suffer from cardiac, pulmonary, vascular, and endocrine disorders. The incidence of cardiac disease is 67%; vascular disease, 50%; chronic obstructive pulmonary disease, 29%; and diabetes mellitus, 8%.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North Am*. 2000;18:883–897.

Malhotra V, Malhotra A, Pamnani A. Anesthesia and the renal and genitourinary systems. In: Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1929–1959.

A.2. What are the normal physiologic consequences of aging for the various organ systems?

- CNS changes include decreases in brain size, neuronal density, regional neurotransmitters, and neuroreceptors. Pharmacodynamic sensitivity increases with age for all intravenous agents (e.g., propofol, fentanyl, and midazolam). The minimal alveolar concentration (MAC) of inhalational anesthetics decreases by approximately 6% per decade after age 40 years. Also, a decrease in cholinergic receptor activity may explain the geriatric patient's vulnerability to the anticholinergic side effects of medications such as diphenhydramine, meperidine, and scopolamine.
- In the cardiovascular system, loss of arterial compliance increases afterload. Systolic function remains relatively preserved, but diastolic dysfunction is common, making patients dependent on adequate filling and atrial kick.

Valvular dysfunction and particularly aortic stenosis is common, occurring in >10% of patients older than 75 years.

- Total lung capacity remains unchanged, but residual volume increases, leading to an overall decrease in vital capacity. Closing capacity also increases with age and can exceed functional residual capacity, resulting in atelectasis. Decreased gas exchange and ventilation/perfusion ($\dot{V}/\dot{Q}$) mismatch also occur.
- The glomerular filtration rate (GFR) decreases by 1 mL/min/1.73 m^2 per year starting at 40 years of age, which can slow clearance of renally excreted medications. Creatinine clearance is a good estimate of GFR, whereas urine output is not.
- Hepatic blood flow also decreases, particularly affecting drugs that undergo phase I but not phase II metabolism.
- Lean muscle mass decreases, as does subcutaneous (but not total body) fat, predisposing to temperature dysregulation and hypothermia.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2102–2114.

Nickalls RW, Mapleson WW. Age-related iso-MAC charts for isoflurane, sevoflurane and desflurane in man. *Br J Anaesth*. 2003;91:170–174.

Peters R. Ageing and the brain. *Postgrad Med J*. 2006;82:84–88.

A.3. How should drug dosages be adjusted for elderly patients? Should any particular medications be avoided?

Decreased GFR and decreased hepatic blood flow result in prolonged effect of drugs metabolized and excreted through these pathways. It is important to note that normal creatinine or liver synthetic function alone are not indicative of GFR or hepatic blood flow because the former can reflect decreased muscle mass rather than preserved renal function and the latter is

often preserved despite significant decrease in liver mass with aging.

In general, geriatric patients are more sensitive to the effects of all intravenous and inhalational anesthetics due to age-related physiologic changes in organ systems as discussed aforementioned and in section A.2. Initial doses of intravenous anesthetic agents should be reduced, with a longer interval between repeat doses. It is safer to start with 50% of the regular doses and then titrate to the desired effect. The dose of all inhalational agents should also be reduced by approximately 6% per decade after age 40 years.

In addition, the American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults identifies medications that are likely to cause cognitive issues for elderly patients, many of which are commonly used as part of an anesthetic (**Table 24.1**).

TABLE 24.1 Common Medications in the Perioperative Period with Potential Neurological Effects

Drug	Rationale
Diphenhydramine	Highly anticholinergic; may increase confusion
Hydroxyzine	Highly anticholinergic; may increase confusion
Scopolamine	Highly anticholinergic
Amitriptyline	Highly anticholinergic; sedating
Antipsychotics	Increased risk of stroke and mortality in persons with dementia
Benzodiazepines	Older adults have increased sensitivity and decreased metabolism. Risk of cognitive impairment, delirium, and falls
Metoclopramide	Extrapyramidal side-effects; risk may be increase in older adults
Pethidine	Not effective analgesic; may cause neurotoxicity
Pentazocine	May cause central nervous system adverse events, including confusion and hallucinations
Neuromuscular blocking drugs	Poorly tolerated by older adults, with anticholinergic adverse effects

From American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults. American Geriatrics Society abstracted clinical practice guideline for postoperative delirium in older adults. *J Am Geriatr Soc*. 2015;63(1):142–150. Copyright © 2014 The American Geriatrics Society. Reprinted by permission of John Wiley & Sons, Inc.

Berger M, Schenning KJ, Brown CH IV, et al. Best practices for postoperative brain health: recommendations from the Fifth International Perioperative Neurotoxicity Working Group. *Anesth Analg*. 2018;127:1406–1413.

Nickalls RW, Mapleson WW. Age-related iso-MAC charts for isoflurane, sevoflurane and desflurane in man. *Br J Anaesth*. 2003;91:170–174.

Peters R. Ageing and the brain. *Postgrad Med J*. 2006;82:84–88.

A.4. Does a history of prior MI increase the patient's risk of perioperative reinfarction or stent thrombosis?

Yes, a history of prior MI or ischemic heart disease is considered an intermediate predictor of perioperative cardiac morbidity and is part of the revised cardiac risk index. MI, as indication for initial stent placement also yields a higher risk for subsequent stent thrombosis.

Fleisher LA. The value of preoperative assessment before noncardiac surgery in the era of value-based care. *Circulation*. 2017;136:1769–1771.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130:2215–2245.

Holcomb CN, Hollis RH, Graham LA, et al. Association of coronary stent indication with postoperative outcomes following noncardiac surgery. *JAMA Surg*. 2016;151(5):462–469.

Lee TH, Marcantonio ER, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation*. 1999;100(10);1043–1049.

A.5. In patients with a history of recent MI, would you recommend that the surgery be postponed for a certain period?

An acute MI (<7 days) or a recent MI (>7 days but <30 days) is considered an unstable coronary syndrome requiring additional evaluation and delay of elective noncardiac surgery. It is advocated to wait >60 days after an MI without revascularization before elective surgery is performed. Also see

Chapter 14, section A.7.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130:e278–e333.

B. Preoperative Evaluation and Preparation

B.1. How would you evaluate the patient's cardiac condition? Does he need additional testing?

The American College of Cardiology/American Heart Association guidelines suggest a stepwise approach that takes into account the clinical markers of cardiac risk, surgery risk, and functional capacity. The patient's medical history should focus on information about previous cardiac evaluations and interventions (coronary stent and automatic ICD [AICD] placement). Active cardiac conditions such as unstable coronary syndromes (recent MI or unstable angina), decompensated congestive heart failure (CHF), significant arrhythmias, or severe valvular disease warrant additional work up prior to surgery. If the patient has stable coronary artery disease (CAD), then risk for major adverse cardiac event (MACE) can be determined using combined clinical/surgical risk score. If risk for MACE is low (<1%), no additional information is required. If MACE is elevated, the functional capacity of the patient is best evaluated by the activity history and assessment of metabolic equivalents (METs), with >4 to 10 METs being suggestive of sufficient cardiac reserve. Stress testing may be indicated for patients with poor exercise tolerance or unable to assess METs, if this would affect the choice to proceed with surgery. Electrocardiogram (ECG) is reasonable in a patient with cardiac history undergoing greater than low-risk surgery

but is not required. Assessment of left ventricular function is reserved for cases of active CHF or known history without reassessment within 1 year. Also see Chapter 14, section B.1.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130:e278–e333.

B.2. Would you discontinue any antihypertensives or any medications for angina?

Antianginal agents and β-blockers should be continued perioperatively including the day of surgery to prevent rebound hypertension and tachycardia that may result from sudden withdrawal of these drugs. Patients taking ACE inhibitors or angiotensin II receptor blockers (ARBs) can be predisposed to refractory intraoperative hypotension due to blunting of the sympathetic effect on vascular tone by anesthesia, increasing reliance on the renin–angiotensin–vasopressin system to maintain blood pressure and renal perfusion. It is recommended that these medications be held 24 hours before surgery.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130:e278–e333.

Roshanov PS, Rochwerg B, Patel A, et al. Withholding versus continuing angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers before noncardiac surgery: an analysis of the vascular events in noncardiac surgery patients cohort evaluation prospective cohort. *Anesthesiology*. 2017;126:16–27.

B.3. For a patient with a cardiac implantable electronic device (CIED), what information should you know? What precautions should be taken?

Patients undergoing surgery with a CIED need to have the device interrogated prior to surgery to determine the device's features, settings, pacer function, pacing dependency, baseline rhythm and rate, ICD function, tachyarrhythmia history, effect of magnet, and battery status. Intraoperative management will be determined by risk for electromagnetic interference. If there is risk, pacer function can be programmed to asynchronous mode if pacemaker dependent and the antitachycardia algorithm of the ICD should be turned off (via magnet or programming, depending on settings) and external cardioversion paddles placed. Postoperatively, reprogram to baseline settings if programming changes were made. Also see Chapter 8, section C.

American Society of Anesthesiologists. Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter-defibrillators: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices. *Anesthesiology*. 2011;114:247–261.

B.4. What types of coronary stents are available? What is their perioperative relevance?

Coronary stent placement was introduced in order to reduce the risk of thrombosis, dissection, and restenosis after angioplasty. Two types of coronary stents have been used: bare metal stents (BMS) and DES. DES have been used extensively to reduce the neointimal hyperplastic reaction seen with the use of BMS, which is the main cause of restenosis; however, by delaying endothelialization of coronary stent struts, DES predispose to stent thrombosis if DAPT is stopped early. First-generation DES required 12 months minimum DAPT before cessation or interruption in therapy; however, second-generation DES appears to endothelialize faster and may be safe to stop at 6 months. Also see Chapter 10, section A.5, **Fig. 10.1**).

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130:2215–2245.

Levin GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: an update of the 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention, 2011 ACCF/AHA guideline for coronary artery bypass graft surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease, 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction, 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes, and 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery. *Circulation*. 2016;134:e123–e155.

B.5. What is the conventional recommendation for dual antiplatelet therapy (DAPT) in a patient with previous percutaneous coronary intervention (PCI) undergoing elective noncardiac surgery?

Therapy with thienopyridines (ticlopidine or clopidogrel) and aspirin, DAPT, is recommended after PCI. However, due to increased risk for bleeding, discontinuation is often required prior to surgery. DAPT is recommended for 2 to 4 weeks after dilatation without stenting (angioplasty); elective surgery should be postponed for 2 to 4 weeks. After BMS, antiplatelet therapy for 4 to 6 weeks is recommended; elective surgery should be postponed for 4 to 6 weeks, minimum 30 days. After the implantation of newer generation DES, at least 6 months of antiplatelet therapy is required, although if risk of delaying surgery would outweigh stent thrombosis, consideration can be given to proceeding at 3 months. In patients with an indication for PCI and a projected need for surgery within the next 6 months, a balloon angioplasty or BMS may be considered. Daily

aspirin should be continued during the perioperative period and DAPT should be resumed as soon as possible postoperatively. Also see Chapter 14, section A.8 and **Figure 14.1**.

Levin GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: an update of the 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention, 2011 ACCF/AHA guideline for coronary artery bypass graft surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease, 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction, 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes, and 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery. *Circulation*. 2016;134:e123–e155.

B.6. What risk is associated with continuing perioperative antiplatelet therapy? What risk is there with stopping it?

In meta-analysis of perioperative aspirin withdrawal versus low-dose aspirin, the low-dose group's relative risk of bleeding increased by a factor of 1.5, but there was no increase in bleeding complications or in perioperative mortality, with the possible exceptions of intracranial surgery and prostatectomy. Studies with ticlopidine or clopidogrel demonstrate a small increased risk of major perioperative bleeding with DAPT (0.4% to 1%). The risk of stopping antiplatelet therapy is stent thrombosis with resulting acute MI and a high mortality rate, so whether bleeding risks outweigh the benefit of protection from stent thrombosis must be considered.

Burger W, Chemnitius JM, Kneissl GD, et al. Low-dose aspirin for secondary cardiovascular prevention—cardiovascular risks after its perioperative withdrawal versus bleeding risks with its continuation—review and meta-analysis. *J Intern Med*. 2005;257(5):399–414.

Oscarsson A, Gupta A, Fredrikson M, et al. To continue or discontinue aspirin

in the perioperative period: a randomized, controlled clinical trial. *Br J Anaesth*. 2010;104:305–312.

B.7. How should patients with coronary stents undergoing noncardiac surgery be managed?

The preoperative evaluation of patients with coronary stents should include information regarding the date of stent placement, the coronary anatomy, the type of coronary stent, and the antiplatelet strategy. Multidisciplinary discussions regarding how the risk of bleeding for the particular surgery compares with the risk of coronary stent thrombosis are strongly encouraged. When possible, continuing double antiplatelet therapy is recommended in patients with DES for surgery with minor or intermediate risk of perioperative bleeding. Discussion between the anesthesiologist, the surgeon, and the treating cardiologist is recommended.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130:2215–2245.

Levin GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: an update of the 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention, 2011 ACCF/AHA guideline for coronary artery bypass graft surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease, 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction, 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes, and 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery. *Circulation*. 2016;134:e123–e155.

C. Intraoperative Management

C.1. What monitors would you use for this patient?

The following monitors would be used for this patient:

- American Society of Anesthesiologists standard monitors, including multiple-lead ST-segment analysis
- Temperature
- Consider invasive arterial blood pressure.

C.2. Is there a preferred anesthetic technique for patients undergoing TURP, and why?

The choice of anesthetic technique should be guided by the requirements of the surgical procedure, coexisting diseases, need to prevent postoperative complications, and patient preferences.

Regional anesthesia has advantages for patients undergoing M-TURP for the following reasons:

- It allows monitoring of the patient's mentation, thereby facilitating early detection of signs of TURP syndrome.
- It can allow for earlier detection of prostate capsular tears or bladder perforation via patient reports of peritoneal or diaphragmatic (referred shoulder) pain.
- It promotes vasodilation and peripheral pooling of blood, thereby reducing the severity of circulatory overloading.
- It reduces blood loss by lowering arterial and venous blood pressure during surgery.
- However, less emphasis is placed on regional anesthesia for TURP now because of the increased use of bipolar electrode and laser resection surgical techniques.
- Regional anesthesia may not be a safe option in an anticoagulated patient.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1929–1959.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North Am*. 2000;18:883–897.

O'Donnell AM, Foo ITH. Anaesthesia for transurethral resection of the

prostrate. *Contin Educ Anaesth Crit Care Pain*. 2009;9(3):92–96.

C.3. Does regional anesthesia result in a lower incidence of perioperative mortality than general anesthesia?

Although spinal anesthesia offers distinct advantages over general anesthesia for TURP surgery, mortality and many markers of patient outcome are similar for both groups, in large part because the safety of the procedure itself has advanced. The 30-day mortality rate associated with TURP has steadily declined from 2.5% in 1962 to current estimates of 0.2% to 0.8%. Mortality rates are similar in patients receiving regional anesthesia or general anesthesia. Increased morbidity is more associated with surgical and patient factors than anesthesia type and has been found in patients with resections exceeding 90 minutes, gland size greater than 45 g, acute urinary retention, and age older than 80 years. The incidence of postoperative complications, specifically MI, pulmonary embolism, cerebrovascular accidents, transient ischemic attacks, renal failure, hepatic insufficiency, and the need for prolonged ventilation is similar in patients receiving regional anesthesia and those receiving general anesthesia. With the increased use of L-TURP resection surgical techniques, even less emphasis has been placed on regional anesthesia as the preferred anesthetic technique given minimal absorption of irrigating fluid.

Gainsburg DM, Bryson EO, Frost EAM, eds. *Anesthesia for Urologic Surgery*. New York: Springer; 2014:35–51.

Hanson RA, Zornow MH, Conlin MJ, et al. Laser resection of the prostate: implications for anesthesia. *Anesth Analg*. 2007;105:475–479.

Hawary A, Mukhtar K, Sinclair A, et al. Transurethral resection of the prostate syndrome: almost gone but not forgotten. *J Endourol*. 2009;23:2013–2020.

Malhotra V, Malhotra A, Pamnani A. Anesthesia and the renal and genitourinary systems. In: Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1929–1959.

C.4. What intravenous fluid would you use during

TURP?

Because dilutional hyponatremia commonly occurs in patients undergoing M-TURP, the intravenous fluid of choice perioperatively is normal saline that contains sodium, 154 mEq per L. Circulatory overloading from absorbed irrigant is common in patients undergoing M-TURP or B-TURP (but not L-TURP); therefore, the amount of intravenous fluid administered during surgery should be carefully monitored.

Gainsburg DM, Bryson EO, Frost EAM, eds. *Anesthesia for Urologic Surgery*. New York: Springer; 2014:35–51.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1929–1959.

C.5. Forty minutes after a sensory level of T10 was established with intrathecal anesthesia, and monopolar TURP (M-TURP) resection was initiated with the use of glycine as the bladder irrigating solution, the patient becomes agitated and complains of nausea. Further sedation along with an antiemetic is administered. However, shortly thereafter, the patient becomes very restless, blood pressure rises, and heart rate decreases. The patient becomes cyanotic and obtunded, blood pressure precipitously falls, and pupils are dilated and unresponsive to light. What is the most likely cause of these signs and symptoms, and would these occur during bipolar (B-TURP) or laser TURP (L-TURP) resection?

Restlessness and incoherence during TURP are particularly ominous signs of TURP syndrome. These are caused by pulmonary edema, hypoxemia, and cerebral edema. These signs must not be misinterpreted as signs of inadequate anesthesia. The administration of sedatives or general anesthesia in the

presence of TURP syndrome has been associated with severe complications including death. In B-TURP and L-TURP, normal saline can be used as the bladder irrigating solution and hyponatremia is not expected. In B-TURP, absorption of the intravascular bladder irrigating solution can still occur via the prostatic venous sinuses, resulting in circulatory overload. This is not expected in L-TURP because the treatment zone is rapidly coagulated.

Chen Q, Zhang L, Fan QL, et al. Bipolar transurethral resection in saline vs traditional monopolar resection of the prostate: results of a randomized trial with a 2-year follow-up. *BJU Int*. 2010;106(9):1339–1343.

Geavlete B, Multescu R, Dragutescu M, et al. Transurethral resection (TUR) in saline plasma vaporization of the prostate vs standard TUR of the prostate: 'the better choice' in benign prostatic hyperplasia? *BJU Int*. 2010;106(11):1695–1699.

O'Hara J. Anesthesia for select urologic procedures. In: *ASA Refresher Courses in Anesthesiology*. 2011;39(1):115–119.

C.6. What are the important characteristics of irrigation solutions used during TURP?

Ideal TURP irrigation solutions would be either isotonic or nearly isotonic, electrically inert, nontoxic, and transparent. Electrolyte-containing solutions such as normal saline are avoided in M-TURP because they can conduct electrical current to surrounding tissues and cause burns. Instead, solutions with nontoxic solutes are used for M-TURP; however, the need for transparency necessitates a hypotonic solution. If intravascular hypotonic bladder irrigating solution is absorbed, absorption can lead to hyponatremia, hypoosmolality, and, in severe cases, hemolysis. These complications are avoided when normal saline is used with B-TURP and L-TURP resection.

Over the years, a number of irrigation solutions have been introduced. The most commonly used solution for M-TURP is glycine (1.2% and 1.5%). Mannitol (3%), glucose (2.5% to 4%),

Cytal (a mixture of sorbitol 2.7% and mannitol 0.54%), and urea (1%) solutions are also occasionally used.

Gainsburg DM, Bryson EO, Frost EAM, eds. *Anesthesia for Urologic Surgery*. New York: Springer; 2014:35–51.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg*. 1997;84:438–446.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North Am*. 2000;18:883–897.

C.7. What is the effect on body temperature of continuous bladder irrigation during TURP?

Several liters of irrigation solution pass through the bladder during TURP. This can reduce body temperature at the rate of 1°C per hour (**Fig. 24.1**). Approximately half of patients undergoing TURP become hypothermic and shiver at the conclusion of surgery.

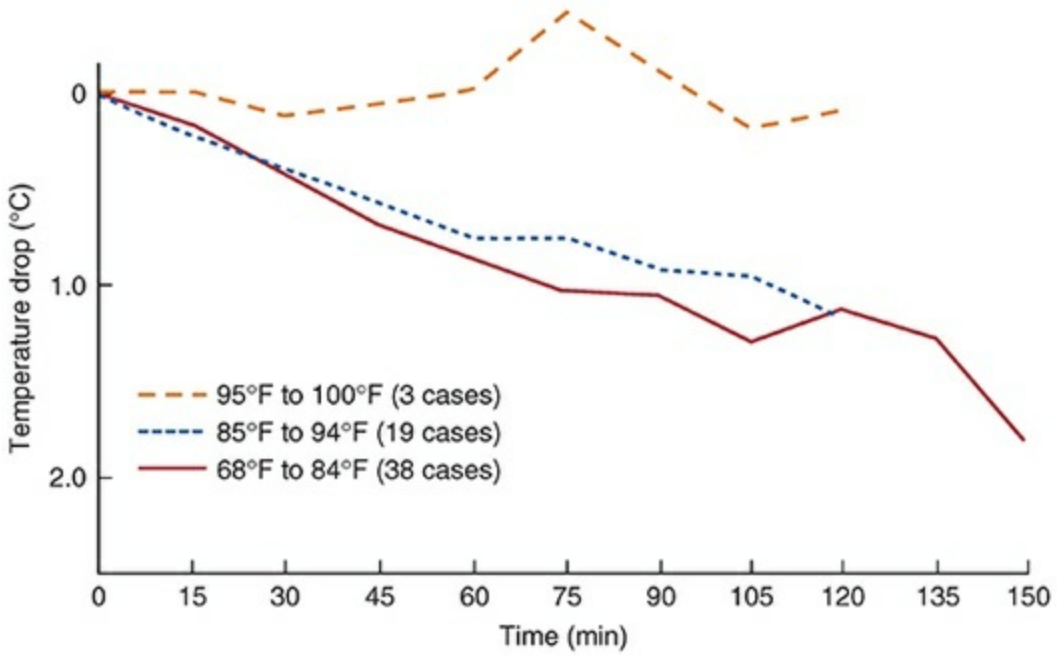

FIGURE 24.1. The decrease in body temperature during TURP is related to the temperature of the irrigating solution and to the duration of surgery. (*Modified with permission from Allen TD.*

Body temperature changes during prostatic resection as related to the temperature of the irrigating solution. J Urol. *1973;110[4]:433–535*.)

Gainsburg DM, Bryson EO, Frost EAM, eds. *Anesthesia for Urologic Surgery*. New York: Springer; 2014:35–51.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North Am*. 2000;18:883–897.

C.8. What is the definition of TURP syndrome? What are the signs and symptoms of the syndrome?

Rapid absorption of a large-volume, hypotonic bladder irrigation solution during TURP can lead to TURP syndrome. TURP syndrome is characterized by intravascular volume shifts and plasma-solute (osmolarity) effects. The signs and symptoms of TURP syndrome are as follows:

Cardiopulmonary

- Hypertension
- Bradycardia
- Dysrhythmia
- Respiratory distress
- Cyanosis
- Hypotension
- Shock
- Death

Hematologic and Renal

- Hyperglycinemia
- Hyperammonemia
- Hyponatremia
- Hypoosmolality
- Hemolysis/anemia
- Acute renal failure
- Death

Central Nervous System

- Nausea/vomiting
- Confusion/restlessness
- Blindness
- Twitches/seizures
- Lethargy/paralysis
- Dilated/nonreactive pupils
- Coma
- Death

TURP syndrome can occur as early as 15 minutes after surgery has started and as late as 24 hours after surgery. Patient complaints of dizziness, headache, nausea, chest or throat tightness, and shortness of breath are often early clinical signs. Then the patient becomes restless, confused, and nauseated. Some patients complain of abdominal pain. The blood pressure often rises (both systolic and diastolic), and the heart rate decreases (Fig. 24.2). If not treated promptly, the patient becomes cyanotic and hypotensive and ultimately sustains cardiac arrest.

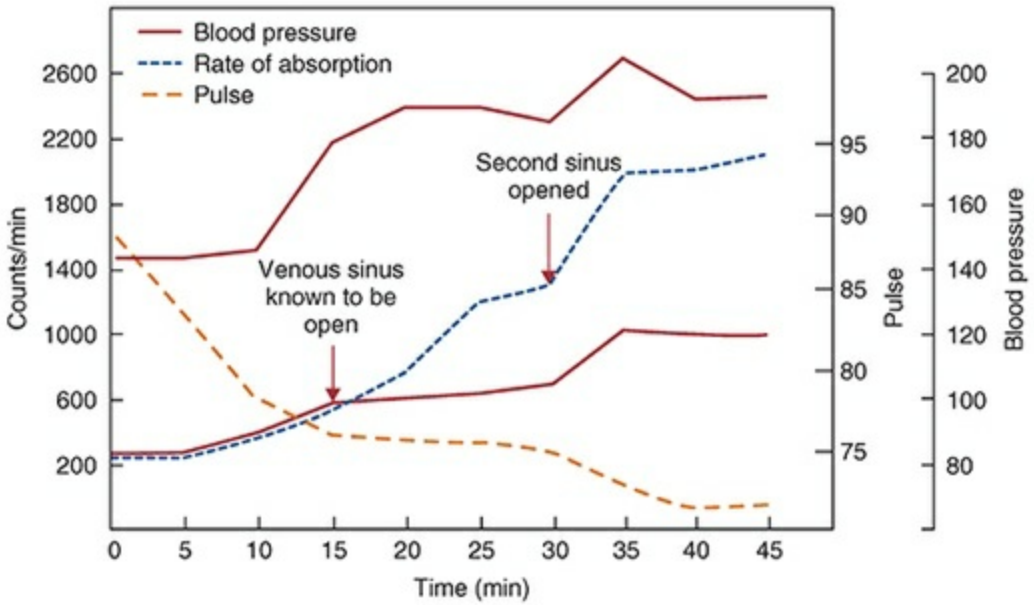

FIGURE 24.2. The blood pressure, heart rate, and absorption rate of radioactively tagged

irrigation solution during TURP. (*Modified with permission from Taylor RO, Maxson ES, Carter FH, et al. Volumetric gravimetric and radioisotopic determination of fluid transfer in transurethral prostatectomy.* J Urol. *1958;79[3]:490–499*.)

Occasionally, TURP syndrome manifests as neurologic signs. The patient becomes lethargic and then unconscious, and pupils dilate, reacting sluggishly to light. These signs may be followed by short episodes of tonic–clonic seizures and then coma lasting from minutes to hours.

If the patient is under general anesthesia, the presenting signs of TURP syndrome are typically a rise and then a fall in blood pressure, decreasing oxygen saturation, and severe refractory bradycardia. The ECG may show nodal rhythm, ST-segment changes, U waves, and widening of the QRS complex. Recovery from general anesthesia is delayed.

Gainsburg DM, Bryson EO, Frost EAM, eds. *Anesthesia for Urologic Surgery*. New York: Springer; 2014:35–51.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg*. 1997;84:438–446.

C.9. How does the patient absorb irrigation solution during TURP?

The bladder irrigation solution enters the bloodstream directly through open prostatic venous sinuses created during monopolar and bipolar resection techniques, particularly if the prostatic capsule is violated during surgery.

If the complication of bladder perforation occurs, significant accumulation of irrigating fluid in the intraperitoneal or retroperitoneal space can occur regardless of technique, resulting in significant intravascular absorption.

Gainsburg DM, Bryson EO, Frost EAM, eds. *Anesthesia for Urologic*

Surgery. New York: Springer; 2014:35–51.

Geavlete B, Multescu R, Dragutescu M, et al. Transurethral resection (TUR) in saline plasma vaporization of the prostate vs standard TUR of the prostate: 'the better choice' in benign prostatic hyperplasia? *BJU Int*. 2010;106(11):1695–1699.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1929–1959.

C.10. What factors increase the incidence of TURP syndrome?

TURP syndrome is more likely to occur if the prostatic gland is atypically large, the prostatic capsule is violated during surgery, or the hydrostatic pressure of the irrigation solution is excessively high. Large prostatic glands have rich venous networks that promote intravascular absorption of irrigation solution. The violation of the prostatic capsule during surgery promotes entry of irrigation solution into the periprostatic and retroperitoneal spaces. The hydrostatic pressure of the irrigation solution is an important determinant of the rate at which the patient will absorb the solution. This pressure depends primarily on the height of the irrigation solution pole. When the height of the pole exceeds 60 cm (approximately 2 ft), the absorption of irrigation solution is greatly enhanced. Also, an excessively distended bladder during surgery facilitates absorption.

Gainsburg DM, Bryson EO, Frost EAM, eds. *Anesthesia for Urologic Surgery*. New York: Springer; 2014:35–51.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg*. 1997;84:438–446.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1929–1959.

C.11. What is the effect on cardiopulmonary, renal, and central nervous system (CNS) functions of excessive absorption of irrigation solution during TURP?

Excessive absorption of irrigation solution during TURP causes hypervolemia and hypertension with bradycardia and may induce angina and pulmonary edema (**Fig. 24.3**). It may also have an adverse effect on renal function. An inverse relation has been observed between the amount of irrigation solution absorbed during surgery and postoperative urinary output.

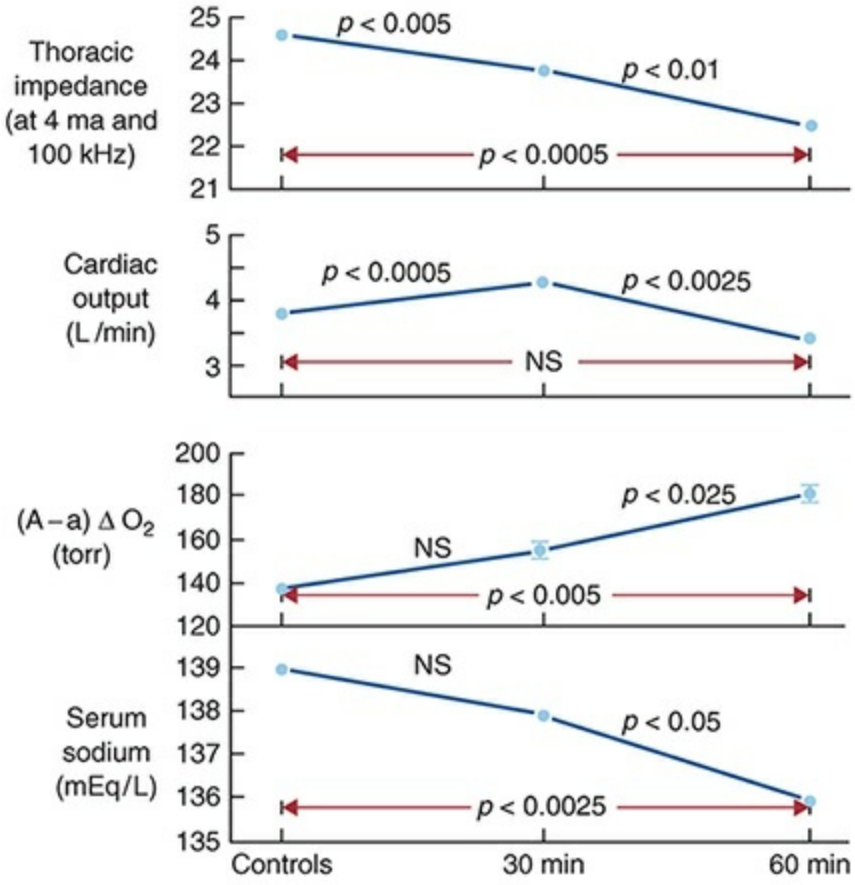

FIGURE 24.3. Mean changes in thoracic impedance, cardiac output, alveolar–arterial oxygen tension difference, and serum sodium level during TURP. NS, nonsignificant. (*Modified with permission from Casthely P, Ramanathan S, Chalon J, et al. Decreases in electric thoracic impedance during transurethral resection of the prostate: an index of early water intoxication.* J Urol. *1981;125[3]:347–349.*)

Some patients with TURP syndrome exhibit neurologic signs resulting from water intoxication if a hypotonic irrigating solution is used. They assume a decerebrate posture, exhibit clonus and positive Babinski reflex, and eventually convulse and

lapse into coma. Examination of the eyes reveals papilledema and dilated and sluggishly reacting pupils. The electroencephalogram shows low voltage bilaterally. The patients may remain in a coma from a few hours to several days.

Gainsburg DM, Bryson EO, Frost EAM, eds. *Anesthesia for Urologic Surgery*. New York: Springer; 2014:35–51.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. *Anesth Analg*. 1997;84:438–446.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1929–1959.

C.12. What causes CNS dysfunction in patients who have undergone M-TURP?

The physiologic derangement of CNS function in TURP syndrome is not hyponatremia but acute hypoosmolality, which is predictable because the blood–brain barrier is essentially impermeable to sodium but freely permeable to water, leading to cerebral edema. The primary factor governing the manifestation of symptoms is the rate at which the serum sodium level falls rather than the total fall itself; the faster the fall in serum sodium level, the greater the incidence of neurologic symptoms. However, under 120 mEq per L, all patients are symptomatic. Cerebral edema caused by acute hypoosmolality can increase intracranial pressure, which results in bradycardia and hypertension by the Cushing reflex. The rise in intracranial pressure is directly correlated to the gain in body weight during TURP.

Fujiwara A, Nakahira J, Sawai T, et al. Prediction of clinical manifestations of transurethral resection syndrome by preoperative ultrasonographic estimation of prostate weight. *BMC Urol*. 2014;14:67.

Gainsburg DM, Bryson EO, Frost EAM, eds. *Anesthesia for Urologic Surgery*. New York: Springer; 2014:35–51.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a

review of the pathophysiology and management. *Anesth Analg*. 1997;84:438–446.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1929–1959.

C.13. How does acute hyponatremia affect the cardiovascular system?

When serum sodium level falls to less than 120 mEq per L, signs of cardiovascular depression can occur. A decrease of less than 115 mEq per L causes bradycardia, widening of the QRS complex, ST-segment elevation, ventricular ectopic beats, and T-wave inversion. Patients with a serum sodium level of less than 110 mEq per L can develop respiratory and cardiac arrest.

Gainsburg DM, Bryson EO, Frost EAM, eds. *Anesthesia for Urologic Surgery*. New York: Springer; 2014:35–51.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1929–1959.

C.14. What prophylactic measures may reduce the incidence of TURP syndrome?

The most important preventive measure during surgery is preservation of the prostatic capsule. Another preventive measure is restriction of the hydrostatic pressure of the irrigation solution to 60 cm H_2O. This can be accomplished by limiting the height of the irrigation pole to 60 cm (approximately 2 ft) above patient level. Also, the bladder should not be allowed to overdistend and the duration of surgery should be restricted.

Serial serum sodium and osmolality are advisable in order to detect a decreasing trend in M-TURP. If clinical signs of TURP syndrome present, the surgeon should be informed and therapeutic measures immediately instituted. If serum sodium level approaches 120 mEq per L, surgery should be terminated as soon as possible.

Intravenous fluids should be cautiously administered during

M-TURP and B-TURP. A microdrip is recommended particularly for patients with cardiac or renal disease. If regional anesthesia causes hypotension, a small dose of a vasoconstrictor is recommended to raise the blood pressure rather than rapid infusion of intravenous fluids.

Gainsburg DM, Bryson EO, Frost EAM, eds. *Anesthesia for Urologic Surgery*. New York: Springer; 2014:35–51.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020.

C.15. What therapeutic measures are recommended for patients with TURP syndrome?

When symptoms of TURP syndrome appear, the following therapeutic measures are recommended:

- Terminate surgery as soon as possible.
- Administer furosemide, 20 to 40 mg intravenously. Although furosemide results in natriuresis, this effect is negligible relative to the desired acute diuresis and volume offloading of free water.
- Administer oxygen by nasal cannula or face mask to maintain oxygen saturation and consider intubation.
- Obtain arterial blood gas, serum osmolality, and sodium analysis.
- If the serum sodium level is abnormally low and clinical signs of hyponatremia are evident, intravenous administration of hypertonic saline (3% to 5%) may be recommended. The hypertonic solution should be given at a rate no faster than 100 mL per hour. In most cases, no more than 300 mL of hypertonic saline is needed to correct the hyponatremia.
- If the patient develops seizures, a short-acting anticonvulsant such as diazepam (5 to 20 mg) or midazolam (2 to 10 mg) can be administered intravenously. If these drugs do not arrest the seizures, a barbiturate or phenytoin can be added.

- If pulmonary edema or hypotension develops, invasive hemodynamic monitoring is recommended. This will serve as a guide for pharmacologic support and fluid administration.
- If significant blood loss is suspected, the administration of packed red blood cells should be considered. In general, intravenous fluids should be administered cautiously because of the propensity of these patients to develop pulmonary edema.

Gainsburg DM, Bryson EO, Frost EAM, eds. *Anesthesia for Urologic Surgery*. New York: Springer; 2014:35–51.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020.

C.16. Is hypertonic saline administration necessary to correct hyponatremia? Explain. What are the risks of rapidly correcting hyponatremia?

The administration of hypertonic saline to correct hyponatremia is not always necessary and sometimes can be detrimental. Unless the patient develops severe clinical signs of hyponatremia, hypertonic saline administration is not recommended. Spontaneous or induced diuresis usually corrects the hyponatremia within a few hours.

Patients who have undergone TURP often sustain circulatory overloading during surgery; consequently, hypertonic saline administration in these patients can induce pulmonary edema. In addition, rapid administration of hypertonic saline has been associated with central pontine myelinolysis (osmotic demyelination syndrome)—a poorly understood and fatal neurologic complication.

To reduce the hazards of hypertonic saline administration, serum osmolarity should be monitored and corrected aggressively only until symptoms substantially subside and then hyponatremia should be corrected at a rate no faster than 1.5

mEq/L/hr.

O'Donnell AM, Foo ITH. Anaesthesia for transurethral resection of the prostrate. *Contin Educ Anaesth Crit Care Pain*. 2009;9(3):92–96.

Sterns RH, Riggs JE, Schochet SS Jr. Osmotic demyelination syndrome following correction of hyponatremia. *N Engl J Med*. 1986;314:1535–1542.

C.17. What are the toxic effects of glycine? Is there an antidote to glycine toxicity? What are the metabolic by-products of glycine?

Glycine is an inhibitory neurotransmitter similar to γ-aminobutyric acid in the spinal cord and brain. When absorbed by the patient in large amounts, glycine has direct toxic effects on the heart and retina. In patients who have undergone M-TURP with glycine absorption, it has been shown to cause an average decrease of 17.5% in cardiac output. In animal studies, the administration of the amino acid arginine reversed the myocardial depressing effect of glycine. The mechanism by which glycine depresses cardiac function and the mechanism by which arginine protects the heart is unknown.

Hyperglycinemia may cause transient visual disturbance (blindness) during TURP. However, glycine toxicity in patients who have undergone TURP is uncommon, probably because most of the absorbed glycine is retained in the periprostatic and retroperitoneal spaces, where access to the circulation is limited.

The most common metabolites of glycine are ammonia and glyoxylic and oxalic acids (**Fig. 24.4**). In some patients, excessive absorption of glycine during TURP leads to hyperammonemia. Hyperoxaluria could compromise renal function in patients with coexisting renal disease, which is often present in elderly patients undergoing TURP.

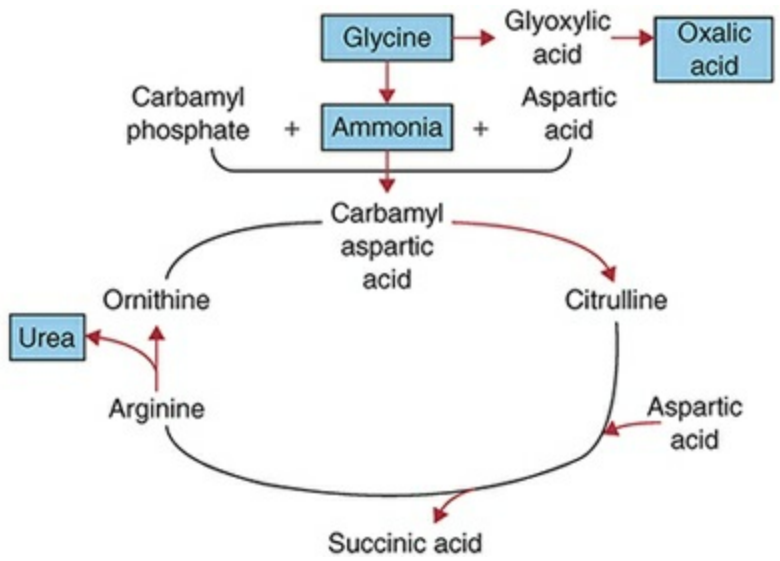

FIGURE 24.4. Metabolic pathways of glycine. (*Modified from McGilvery RW, Goldstein GW.* Biochemistry: A Functional Approach. *3rd ed. Philadelphia, PA: WB Saunders; 1983:584. Copyright © 1983 Elsevier. With permission.*)

Gainsburg DM, Bryson EO, Frost EAM, eds. *Anesthesia for Urologic Surgery*. New York: Springer; 2014:35–51.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North Am*. 2000;18:883–897.

Ovassapian A, Joshi CW, Brunner EA. Visual disturbances: an unusual symptom of transurethral prostatic resection reaction. *Anesthesiology*. 1982;57:332–334.

C.18. What are the symptoms and clinical course of TURP-induced hyperammonemia?

The signs and symptoms of hyperammonemia usually appear within 1 hour of surgery. Typically, the patient becomes nauseated, vomits, and then becomes comatose. Blood ammonia level can rise to more than 500 mmol per L. The patient remains comatose for 10 to 12 hours and eventually awakens when ammonia blood level decreases to less than 150 mmol per L. The hyperammonemia tends to linger postoperatively, probably because glycine absorption from the periprostatic space continues after surgery.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North Am*. 2000;18:883–897.

Roesch RP, Stoelting RK, Lingeman JE, et al. Ammonia toxicity resulting from glycine absorption during a transurethral resection of the prostate. *Anesthesiology*. 1983;58:577–579.

C.19. What are the clinical characteristics, causes, and prognosis of TURP-related blindness?

Transient blindness is one of the more alarming complications of TURP. The patient complains of blurred vision and of seeing halos around objects. This can occur either during surgery or later in the recovery room. Although it is sometimes accompanied by other TURP-related complications, blindness can occur as an isolated symptom. Examination of the eyes reveals dilated and unresponsive pupils. Postoperatively, TURP-related blindness gradually recedes and eyesight returns to normal within 8 to 48 hours of surgery.

The cause of TURP-related blindness is unclear. The intraocular pressure and optic discs remain normal. In the past, edema of the cerebral optical cortex was suspected; however, the clinical signs of TURP-related blindness are consistent with retinal rather than cortical dysfunction. Unlike cortical blindness, TURP-related blindness allows perception of light and the blink reflex is preserved. TURP-related blindness is most likely caused by a toxic effect of glycine on the retina. This theory is supported by the fact that glycine is a known inhibitory neurotransmitter. In animals, glycine has been shown to inhibit neuronal visual pathways. Also, the severity of TURP-related blindness is directly related to glycine blood level. Postoperatively, vision gradually improves as the glycine blood level declines.

Gainsburg DM, Bryson EO, Frost EAM, eds. *Anesthesia for Urologic Surgery*. New York: Springer; 2014:35–51.

Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a

review of the pathophysiology and management. *Anesth Analg*. 1997;84:438–446.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1929–1959.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North Am*. 2000;18:883–897.

C.20. What are the causes of excessive bleeding during TURP?

Patients undergoing TURP commonly bleed perioperatively, with 2.5% of patients undergoing M-TURP requiring transfusion. One possible cause is dilutional thrombocytopenia resulting from excessive absorption of irrigation solution. Another possible cause is local release of fibrinolytic agents (plasminogen and urokinase) from the mucosa of the lower urinary tract. During and immediately after TURP, these agents cause local fibrinolysis and promote bleeding from the raw surfaces of the prostatic gland. The existence of a local fibrinolytic mechanism is supported by the observation that prophylactic administration of ε-aminocaproic acid (an antifibrinolytic agent) reduces bleeding from the prostatic bed.

Systemic coagulopathy can also occur during TURP. The coagulopathy is caused by disseminated intravascular coagulation (DIC) rather than by primary fibrinolysis. DIC is triggered during TURP by prostatic particles rich in thromboplastin that enter the bloodstream during surgery. Characteristically, the platelet count and fibrinogen blood level are abnormally low. At autopsy, multiple microthrombi are observed in various parts of the body. The high level of fibrin-degradation products found in the blood of these patients is caused by secondary fibrinolysis, which commonly accompanies DIC.

Gainsburg DM, Bryson EO, Frost EAM, eds. *Anesthesia for Urologic Surgery*. New York: Springer; 2014:35–51.

Gropper MA, Cohen NH, Eriksson LA, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1929–1959.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North Am*. 2000;18:883–897.

C.21. What are the causes, signs, symptoms, and treatment of bladder perforation during TURP?

The incidence of bladder perforation during TURP is approximately 1% and stems from trauma by surgical instrumentation, overdistention of the bladder, and, rarely, explosion of traces of hydrogen gas inside the bladder.

An early sign of bladder perforation is a sudden decrease in the return of irrigation solution from the bladder. This sign often goes unnoticed until a significant amount of irrigation solution accumulates in the abdomen, causing abdominal distress. Other clinical signs are hypotension, followed by hypertension and nausea. Reflex-type movements of the limbs have been observed under both general and regional anesthesia. When the perforation is intraperitoneal, symptoms develop faster and include severe shoulder pain caused by diaphragmatic irritation.

Diagnosis of bladder perforation is confirmed by cystourethrography. Treatment is immediate suprapubic cystotomy.

Gainsburg DM, Bryson EO, Frost EAM, eds. *Anesthesia for Urologic Surgery*. New York: Springer; 2014:35–51.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1929–1959.

Hansen RI, Iversen P. Bladder explosion during uninterrupted transurethral resection of the prostate. A case report and an experimental model. *Scand J Urol Nephrol*. 1979;13:211–212.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North Am*. 2000;18:883–897.

C.22. What are the causes of hypotension during TURP?

The more common causes of hypotension during TURP are

circulatory overloading with resulting CHF, MI or myocardial ischemia, severe anemia resulting from blood loss, severe hyponatremia, and bacteremia.

Gainsburg DM, Bryson EO, Frost EAM, eds. *Anesthesia for Urologic Surgery*. New York: Springer; 2014:35–51.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1929–1959.

D. Postoperative Management

D.1. What is the source of postoperative bacteremia in patients who have undergone TURP? What factors increase the incidence of bacteremia?

The prostatic gland often harbors large amounts of bacteria. TURP facilitates the entry of these bacteria into the bloodstream by opening of venous sinuses, leading to postoperative bacteremia. Approximately 30% of patients undergoing TURP have infected urine preoperatively, and half of them have transient bacteremia postoperatively, although most are asymptomatic; 6% to 7%, however, will develop signs of sepsis.

Surgical disruption of the prostatic venous sinuses and excessive hydrostatic pressure of the irrigation solution facilitate the entry of bacteria into the bloodstream. Also, a preoperative indwelling catheter promotes bacterial growth in the urethra.

Gainsburg DM, Bryson EO, Frost EAM, eds. *Anesthesia for Urologic Surgery*. New York: Springer; 2014:35–51.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1929–1959.

D.2. What are the signs of post-TURP septicemia? What preventive measures are generally recommended?

The signs of septicemia usually appear postoperatively in the postanesthesia care unit (PACU). They include fever, chills, low

blood pressure, and tachycardia. Symptoms may be related to bacterial endotoxins, in which case they are self-limited, or direct bloodstream seeding with bacteria.

Antibiotics administered prophylactically before TURP do not sterilize the urine because they do not easily penetrate the prostatic gland. Nevertheless, the preoperative administration of antibiotics is strongly recommended.

If sepsis is suspected postoperatively in a patient who has undergone TURP, broad-spectrum antibiotics should be started immediately without waiting for blood culture results.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1929–1959.

Malhotra V. Transurethral resection of prostate. *Anesthesiol Clin North Am*. 2000;18:883–897.

D.3. Is postoperative hypothermia a risk factor for myocardial ischemia?

Yes. Unexpected hypothermia and shivering is associated with a significantly higher incidence of postoperative demand myocardial ischemia. Therefore, it is important to maintain normothermia during the perioperative period, particularly in an elderly population at higher risk for hypothermia due to decreased subcutaneous fat. Also see Chapter 14, section D.4.

Frank SM, Beattie C, Christopherson R, et al. Unintentional hypothermia is associated with postoperative myocardial ischemia. The Perioperative Ischemia Randomized Anesthesia Trial Study Group. *Anesthesiology*. 1993;78:468–476.

D.4. What is postoperative cognitive dysfunction (POCD)? How does this differ from delirium, and what is the time course to resolution?

POCD is a syndrome defined by worsening cognitive performance postoperatively compared to perioperative baseline. The deficit is present in multiple domains and presents days to

weeks after surgery, highly correlated with age. POCD usually resolves within months; however, time course varies and sustained deficits have been reported.

Postoperative delirium, by contrast, manifests as acute fluctuation in orientation shortly following emergence.

However, for clinical purposes, a multispecialty working group recommends that "perioperative neurocognitive disorders" (PND) be used as an overarching term for cognitive impairment identified in the preoperative or postoperative period. This includes cognitive decline diagnosed before operation (described as neurocognitive disorder); any form of acute event (postoperative delirium) and cognitive decline diagnosed up to 30 days after the procedure (delayed neurocognitive recovery) and up to 12 months (postoperative neurocognitive disorder).

Evered LA, Silbert BS. Postoperative cognitive dysfunction and noncardiac surgery. *Anesth Analg*. 2018;127:496–505.

Evered L, Silbert B, Knopman DS, et al. Recommendations for the nomenclature of cognitive change associated with anaesthesia and surgery—2018. *Br J Anaesth*. 2018;121:1005–1012.

D.5. What are the mechanisms and risk factors for POCD? How would you mitigate the risk of POCD? Does anesthesia type influence development of POCD?

The proposed mechanisms include a preexisting neuroinflammation or neurodegeneration, which primes the brain to react more strongly to the systemic inflammatory response to the surgical procedure itself, resulting in accelerated progression of neuroinflammation and neurodegeneration with delay in neurocognitive recovery. Progression or eventual resolution of POCD may be impacted by several intraoperative and postoperative factors.

Preoperative risk factors include preexisting cognitive impairment, older age, and lower educational achievement. Intraoperative risk factors include major, prolonged, or emergency surgical procedures, as well as selection and dosing of certain anesthetic and adjunct agents, and possibly depth of general anesthesia.

The recommended strategies to mitigate the risk of POCD include the following:

- Avoid use of benzodiazepines, opioids (particularly meperidine), anticholinergics (particularly scopolamine), diphenhydramine, metoclopramide, and agents that may cause serotonin syndrome.
- Use raw or processed electroencephalography (EEG) or other neuromonitoring techniques, when available as a supplemental guide to manage intraoperative dosing of anesthetic agents.
- Avoid hypotension and hypoxemia.
- Avoid hyperventilation because cerebral blood flow decreases by 2% to 4% for each mmHg decrease in $PaCO_2$. Prolonged $PaCO_2$ below 30 mmHg may result in cerebral ischemia and possibly POCD.
- Evidence suggests that postoperative administration of dexmedetomidine may decrease the incidence of delirium, although results are inconsistent for intraoperative administration, and there is scant evidence for other types of POCD.
- Inadequate postoperative pain control is associated with increased incidence of delirium. A multimodal approach could be employed to reduce the risk of opioid-related side effects.
- In a severely agitated PACU patient, after treatment of reversible causes and redirection and reorientation have failed, administration of a small dose of haloperidol (e.g., 0.5

to 2 mg) is reasonable; this dose may be repeated (up to approximately 5 mg total dose). However, prophylactic haloperidol is not recommended to prevent delirium.

Neuraxial or regional anesthesia with either light or deep sedation does not consistently decrease the incidence of postoperative neurocognitive disorders compared with general anesthesia. When general anesthesia is selected, neither a total intravenous anesthesia (TIVA) technique nor an inhalation-based anesthetic technique affects the incidence of postoperative delirium in adult patient.

Small prospective studies have compared spinal anesthesia with intravenous sedation to general anesthesia in elderly TURP patients, showing no difference in perioperative mental function between the groups at 30 days.

Berger M, Nadler JW, Browndyke J, et al. Postoperative cognitive dysfunction: minding the gaps in our knowledge of a common postoperative complication in the elderly. *Anesthesiol Clin*. 2015;33(3):517–550.

Berger M, Schenning KJ, Brown CH IV, et al. Best practices for postoperative brain health: recommendations from the Fifth International Perioperative Neurotoxicity Working Group. *Anesth Analg*. 2018;127:1406–1413.

Chung FF, Chung A, Meier RH, et al. Comparison of perioperative mental function after general anaesthesia and spinal anaesthesia with intravenous sedation. *Can J Anaesth*. 1989;36:382–387.

Cole DJ, Kharasch ED. Postoperative brain function: toward a better understanding and the American Society of Anesthesiologists Perioperative Brain Health Initiative. *Anesthesiology*. 2018;129:861–863.

Evered LA, Silbert BS. Postoperative cognitive dysfunction and noncardiac surgery. *Anesth Analg*. 2018;127:496–505.

Silbert BS, Evered LA, Scott DA. Incidence of postoperative cognitive dysfunction after general or spinal anaesthesia for extracorporeal shock wave lithotripsy. *Br J Anaesth*. 2014;113:784–791.

E. Comparing M-TURP, B-TURP, and L-TURP

E.1. What differentiates M-TURP from B-TURP?

M-TURP uses high-energy cautery, which allows a fast cutting technique of prostatic tissue with minimal coagulation in the process. The body is the conduit of the energy dispersed from the monopolar electrode to complete the electrical circuit to a large-surface skin grounding pad placed on the patient. It also requires the use of an electrolyte-free bladder irrigating fluid. In B-TURP, the electrical circuit is completely contained within the resectoscope. This prevents energy from traveling through the body. Instead, the energy remains confined to the site of prostatic resection and is returned via the second limb of the bipolar resectoscope. With the bipolar electrode, less bleeding occurs at the prostatic tissue site and normal saline can be used as the bladder irrigating fluid.

Gainsburg DM, Bryson EO, Frost EAM, eds. *Anesthesia for Urologic Surgery*. New York: Springer; 2014:35–51.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020.

Issa MM. Technological advances in transurethral resection of the prostate: bipolar versus monopolar TURP. *J Endourol*. 2008;22:1587–1595.

E.2. Are decreased morbidity and mortality associated more closely with M-TURP or with B-TURP?

In a meta-analysis that reviewed the safety of M-TURP versus B-TURP in a small number of TURP patients (1,802), a significant benefit was reported in the bipolar group in overall complication rate, need for transfusion, and the absence of TURP syndrome. Subsequent randomized controlled trials have confirmed this morbidity benefit.

Chen Q, Zhang L, Fan QL, et al. Bipolar transurethral resection in saline vs traditional monopolar resection of the prostate: results of a randomized trial with a 2-year follow-up. *BJU Int*. 2010;106(9):1339–1343.

Issa MM. Technological advances in transurethral resection of the prostate: bipolar versus monopolar TURP. *J Endourol*. 2008;22:1587–1595.

Reich O, Gratzke C, Bachmann A, et al. Morbidity, mortality, and early

outcome of transurethral resection of the prostrate: a prospective multicenter evaluation of 10,654 patients. *J Urol*. 2008;180:246–249.

E.3. What differentiates the technologies for L-TURP?

L-TURP delivers light energy to coagulate or vaporize prostatic tissue. Holmium laser enucleation of the prostate (HoLEP), in particular, has been suggested as the new gold standard for surgical treatment of benign prostate hypertrophy (BPH). Prostatic tissue is vaporized, and the resulting heat dissipation coagulates small to medium blood vessels. HoLEP can be used safely on patients with larger prostatic glands with similar outcomes as patients undergoing open prostatectomy, and compared to traditional M-TURP, HoLEP demonstrates lower transfusion rates, catheterization time, and shorter hospital stays. Photoselective vaporization and bipolar plasma vaporization have shown similar benefits.

There are five advantages of L-TURP: (1) It uses normal saline as the irrigating bladder solution; (2) it minimizes the absorption of irrigating fluid; (3) it minimizes or altogether eliminates TURP syndrome; (4) it produces significantly less bleeding, which allows the procedure to be performed on an anticoagulated patient if needed; and (5) it de-emphasizes regional anesthesia as the preferred anesthetic technique.

Gainsburg DM, Bryson EO, Frost EAM, eds. *Anesthesia for Urologic Surgery*. New York: Springer; 2014:35–51.

Geavlete B, Multescu R, Dragutescu M, et al. Transurethral resection (TUR) in saline plasma vaporization of the prostate vs standard TUR of the prostate: 'the better choice' in benign prostatic hyperplasia? *BJU Int*. 2010;106(11):1695–1699.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020.

Michalak J, Tzou D, Funk J. HoLEP: the gold standard for the surgical management of BPH in the 21(st) century. *Am J Clin Exp Urol*. 2015;3:36–42.

25 Kidney Transplant

Christine Lennon and Fun-Sun F. Yao

A 50-year-old man with rapid onset of end-stage renal disease (ESRD) prefers not to start hemodialysis. He would like to receive an organ transplant from a living related donor, but other options include a deceased donor or a paired donor exchange program.

A. Medical Disease and Differential Diagnosis

1. What are the causes of chronic renal disease that can progress to renal failure?
2. How is chronic kidney disease (CKD) diagnosed?
3. What are the indications for dialysis?
4. What are the common clinical manifestations of ESRD?
5. What electrolyte imbalances occur in patients with impaired renal function, and how are they treated?
6. How is metabolic acidosis managed in chronic renal failure?
7. Are patients with renal disease at increased risk of cardiovascular disease?
8. When is the best time to receive a kidney transplant?
9. How are immunosuppressive drugs managed in kidney transplant recipients?
10. How are kidneys allocated to recipients on the waiting list in the United States?

11. What is donation after cardiac death (DCD)?
12. What is a living donor transplant program?
13. What is a paired donor exchange transplant program?
14. What are some barriers to receiving a kidney transplant?
15. What surgical techniques are available for donor nephrectomy (DN)?
16. How is a donor kidney preserved?
17. Describe the operative procedure of kidney transplantation.

B. Preoperative Evaluation and Preparation

1. What preoperative workup would you order for a recipient?
2. How does the presence of obesity affect the outcome of a transplanted kidney?
3. How are routine medications and immunosuppressive medications managed in the perioperative period?

C. Intraoperative Management

1. Are a central venous pressure (CVP) monitoring line, an arterial line, and a pulmonary artery catheter required for the transplant procedure?
2. What type of intravenous fluid should be used during surgery?
3. How would you conduct the anesthesia induction?
4. Is succinylcholine contraindicated in renal failure patients?
5. How are the nondepolarizing muscle relaxants affected by renal failure?
6. How would you maintain anesthesia during the case?
7. What are the effects of inhalation anesthetics on renal blood flow (RBF), glomerular filtration (GFR), and urine output?
8. What are the potential nephrotoxic effects of inhalation anesthetics? What are the nephrotoxic metabolites of inhalation anesthetics?
9. How does renal failure affect the pharmacology of opioids?

D. Postoperative Management

1. How is the diagnosis of transplant rejection made?
2. What are immunosuppressive agents, and how do they affect anesthetic care?

A. Medical Disease and Differential Diagnosis

A.1. What are the causes of chronic renal disease that can progress to renal failure?

The most common etiologies of renal disease leading to kidney transplant are the following:

- Diabetes
- Hypertension
- Glomerular diseases
- Polycystic kidney disease
- Vascular diseases (e.g., systemic lupus erythematosus)
- Congenital and metabolic diseases
- Tubular and interstitial diseases
- Neoplasms
- Retransplant and graft failure

CKD has many potential causes that differ among the world's populations. In developed countries, age, hypertension, cardiovascular disease, diabetes, increased body mass index (BMI), and smoking are predominantly associated with CKD. In the developing world, unique causes of kidney failure include infections due to bacteria, viruses, and parasites.

The global increase in CKD parallels the obesity epidemic. Obesity has been associated with a secondary focal segmental glomerulosclerosis, which is referred to as obesity-related glomerulopathy (ORG). The accumulation of lipid in the cellular structure of the kidney is associated with structural and functional changes.

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de Vries AP, Ruggenenti P, Ruan XZ, et al. Fatty kidney: emerging role of

ectopic lipid in obesity-related renal disease. *Lancet Diabetes Endocrinol*. 2014;2(5):417–426.

Hart A, Smith JM, Skeans MA, et al. OPTN/SRTR 2017 annual data report: kidney. *Am J Transplant*. 2019;19(suppl 2):19–123.

A.2. How is chronic kidney disease (CKD) diagnosed?

CKD is defined as an abnormality of kidney structure or function that is present for more than 3 months, with implications for health. It is not dependent on the etiology leading to deteriorated kidney function.

The criteria for CKD include any of the following present for more than 3 months:

- Albuminuria
- Urine sediment abnormalities
- Electrolyte and other abnormalities due to tubular disorders
- Abnormalities detected by histology
- Structural abnormalities detected by imaging
- History of kidney transplantation
- GFR less than 60 mL/min/1.73 m^2

GFR and the progression of CKD may be estimated using several formulas, one of the most common in the United States being the Modification of Diet in Renal Disease (MDRD) formula. ESRD is established when GFR is less than 15 mL/min/1.73 m^2.

GFR, in mL/min/1.73 m^2 = 175 × $(SCr)^{-1.154}$ × $(age)^{-0.203}$ × (0.742 if female) × (1.21 if black)

SCr is the serum creatinine (milligrams per deciliter). Among individuals with established CKD, progression is based on estimation of GFR and level of albuminuria.

Kidney Disease: Improving Global Outcomes. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl*. 2013;3(1):1–150.

National Kidney Foundation. KDOQI clinical practice guideline for hemodialysis adequacy: 2015 update. *Am J Kidney Dis*. 2015;66(5):884–930.

A.3. What are the indications for dialysis?

The decision about when to start dialysis is complex and patient specific and generally depends on the estimated GFR, the rate of decline of the GFR, and the presence of ESRD-related signs and symptoms. Recent data indicate that mortality may be higher when dialysis is initiated early, with no significant benefit in terms of quality of life. It is generally recommended that dialysis be initiated in patients with GFR between 5 and 15 mL/min/1.73 m^2 and concomitant signs and symptoms that could be due to ESRD, and in all patients with GFR <5 mL/min/1.73 m^2 regardless of the presence of additional signs or symptoms.

Patients with uremic symptoms (e.g., encephalopathy, pericarditis, and pleuritis) should be started on dialysis even if GFR is not at critically low levels. Other indications for dialysis in CKD include refractory volume overload; refractory acidosis, hyperkalemia, or hyperphosphatemia; declining nutritional status; fatigue and malaise; and mild cognitive impairment.

Cooper BA, Branley P, Bulfone L, et al. A randomized, controlled trial of early versus late initiation of dialysis. *N Engl J Med*. 2010;363(7):609–619.

National Kidney Foundation. KDOQI clinical practice guideline for hemodialysis adequacy: 2015 update. *Am J Kidney Dis*. 2015;66(5):884–930.

A.4. What are the common clinical manifestations of ESRD?

The common problems related to ESRD are the following:

- Electrolytes: volume expansion, hyponatremia, hyperkalemia, metabolic acidosis, hyperuricemia, hyperphosphatemia, hypocalcemia
- Gastrointestinal: gastroparesis, nausea, vomiting, pancreatitis, anorexia, uremic gastroenteritis, peptic ulcer disease, gastrointestinal bleeding
- Cardiovascular: accelerated atherosclerosis, systemic hypertension, left ventricular hypertrophy, congestive heart

failure, pulmonary edema, cardiomyopathy, pericarditis, hyperdynamic circulation

- Hematologic: anemia, B- and T-cell dysfunction, qualitative platelet dysfunction, bleeding diathesis
- Musculoskeletal: muscle weakness, uremic osteodystrophy (osteomalacia, osteosclerosis, osteitis fibrosa cystica)
- Neurologic: encephalopathy, loss of memory, seizures, peripheral neuropathy, autonomic dysfunction (postural hypotension), myoclonus, asterixis, dialysis disequilibrium (dehydration, weakness, nausea and vomiting, hypotension, and occasionally convulsion and coma)
- Endocrine: vitamin D deficiency, secondary hyperparathyroidism, carbohydrate intolerance, hypertriglyceridemia

Pain is extremely common in ESRD and can result from renal and nonrenal etiologies. In a prospective study of 205 hemodialysis patients, musculoskeletal pain was most common (63.1%), followed by dialysis-associated pain (13.6%), peripheral neuropathy (12.6%), and peripheral vascular disease claudication pain (9.7%). Polycystic kidney disease can cause chronic abdominal pain. Fentanyl and methadone are considered the safest opioids for use in patients with ESRD. Secondary hyperparathyroidism often results in bone pain.

O'Connor NR, Corcoran AM. End-stage renal disease: symptom management and advance care planning. *Am Fam Physician*. 2012;85(7):705–710.

A.5. What electrolyte imbalances occur in patients with impaired renal function, and how are they treated?

Chronic renal insufficiency and ESRD are associated with abnormalities in sodium (Na), potassium, calcium, and magnesium balance as well as metabolic acidosis.

Na and water (H_2O) balance are closely related. The kidney has its own inherent circadian rhythm involved in the

transcription genes for renal Na excretion and blood pressure control. This function is impaired in renal disease. In patients with chronic renal failure, the total body content of Na and H_2O may be increased. This can be due to glomerular disease promoting Na retention or excessive ingestion of Na leading to extracellular fluid (ECF) expansion. The ECF expansion and hyperosmolarity contributes to hypertension. Nonanuric patients may be treated with loop diuretics and salt restriction.

The renal mechanisms for conserving Na and H_2O are impaired in ESRD. Urine in nonoliguric patients is isosthenuric. This means the usual indices of detecting prerenal azotemia (high urine osmolality, low urine Na, and low fractional excretion of sodium [FE_{Na}]) are not applicable in such patients. If additional fluid loss (vomiting, fever) is imposed, they may become severely hypovolemic, necessitating careful rehydration with normal saline.

Hyperkalemia rarely occurs in patients with a GFR greater than 25 mL/min/1.73 m^2 in the absence of an endogenous or exogenous potassium load. Patients with GFR less than 25 mL/min/1.73 m^2 may be chronically hyperkalemic. Severe hyperkalemia increases cardiac and skeletal muscle excitability. The earliest changes begin with levels above 6.5 mEq per L. The electrocardiogram (ECG) shows peaked T waves, flattened P waves, lengthened PR interval, disappearance of P waves, and a widened QRS complex that can progress to a “sine wave,” ventricular asystole, or ventricular fibrillation. Muscle weakness can cause respiratory failure. Membrane excitability is more dependent on the rate of increase in potassium than on potassium concentration per se. The treatment of hyperkalemia includes a combination of insulin, glucose, loop diuretics (nonanuric), sodium bicarbonate, calcium, and magnesium (**Table 25.1**). The anesthesiologist may also institute

hyperventilation in mechanically ventilated patients. Hemodialysis or peritoneal dialysis is the definitive treatment for severe hyperkalemia.

TABLE 25.1 Drug Treatment for Hyperkalemia

Drug	Dose
Calcium chloride	5 mL of 10% solution IV over 2 min (monitor for bradycardia)
Calcium gluconate	10 mL of 10% solution IV over 2 min (monitor for bradycardia)
Insulin	5–10 units regular insulin with 1–2 amps $D_{50}W$ IV bolus
Sodium bicarbonate	1 mEq/kg slow IV push or continuous drip; not to exceed 50–100 mEq
β-Agonists (albuterol)	2.5 mg mixed with 3 mL isotonic saline through nebulizer every 20 min as tolerated
Diuretic (furosemide)	20–40 mg IV push
Magnesium	1–2 g IV over 30–60 sec; repeat every 5–15 min as required or 3–10 mg/min IV infusion

$D_{50}W$, 50% dextrose in water; IV, intravenous.

Magnesium imbalance can accompany chronic renal failure. High blood magnesium levels cause dose-dependent neuromuscular toxicity and increased sensitivity to depolarizing and nondepolarizing neuromuscular blockers. Bradycardia, hypotension, and heart block are due to the calcium channel blocking effects of magnesium. The acute toxicity can be antagonized by intravenous infusion of calcium. Conversely, decreased dietary intake and impaired intestinal absorption can lead to hypomagnesemia. Magnesium deficiency has been related to progression of atherosclerosis and low parathyroid hormone (PTH) levels.

Phosphate retention occurs when GFR begins to decline. Retained phosphate promotes secondary hyperparathyroidism by lowering ionized plasma calcium levels, decreasing renal formation of calcitriol (1,25-dihydroxyvitamin D), and stimulating PTH gene expression.

Ionized and protein-bound calcium levels are lower in uremic

patients. This is the result of hyperphosphatemia and reduced gastrointestinal absorption secondary to the decreased production of vitamin D.

Kanbay M, Goldsmith D, Uyar ME, et al. Magnesium in chronic kidney disease: challenges and opportunities. *Blood Purif*. 2010;29(3):280–292.

Kovesdy CP. Management of hyperkalaemia in chronic kidney disease. *Nat Rev Nephrol*. 2014;10(11):653–662.

Malberti F. Hyperphosphataemia: treatment options. *Drugs*. 2013;73(7):673–688.

Nikolaeva S, Pradervand S, Centeno G, et al. The circadian clock modulates renal sodium handling. *J Am Soc Nephrol*. 2012;23(6):1019–1026.

A.6. How is metabolic acidosis managed in chronic renal failure?

A mild-to-moderate acidosis is commonly noted when the GFR decreases to less than 20% to 25% of normal. The decreased renal mass results in decreased production and excretion of proton load. The plasma bicarbonate concentration ranges between 12 and 22 mEq per L, and blood pH remains greater than 7.20. This does not routinely require correction. It may gradually evolve into a high anion gap acidosis when the GFR is below 20 mL/min/1.73 m^2. Some patients with ESRD maintain close to normal acid–base parameters even when renal function is severely compromised. However, when exposed to an increased dietary acid load, these patients may have decreased ability to increase bicarbonate generation.

The correction of acidosis by oral sodium bicarbonate or a diet rich in fruits and vegetables can attenuate rate of decline of renal function.

Goraya N, Wesson DE. Does correction of metabolic acidosis slow chronic kidney disease progression? *Curr Opin Nephrol Hypertens*. 2013;22(2):193–197.

Loniewski I. Combining a fruit and vegetable diet with sodium bicarbonate supplementation seems the best dietary option for chronic kidney disease

patients. *Kidney Int*. 2012;82(8):937.

A.7. Are patients with renal disease at increased risk of cardiovascular disease?

ESRD is associated with an increased incidence and prevalence of a wide range of cardiovascular morbidities including hypertension, coronary artery disease, stroke, congestive heart failure, atrial fibrillation, sudden cardiac death, pulmonary hypertension, and valvular heart disease.

Extensive vascular calcification contributes to early-onset cardiovascular disease and cardiovascular mortality. In addition to traditional cardiovascular risks, risk factors specific to CKD such as phosphate retention, hypercalcemia, history of dialysis, high-dose vitamin D therapy, and deficiency of calcification inhibitors promote arterial calcification. There is no specific therapy to reverse vascular calcification, but statin therapy is associated with decreased cardiovascular death. Additional measures such as reduction of calcium phosphate load, using non–calcium-containing phosphate binders, and moderate doses of active vitamin D may attenuate arterial hardening.

The rate of sudden cardiac death increases as the stage of CKD increases and could be responsible for 60% of cardiac deaths in patients undergoing dialysis. The uremic load results in cardiac fibrosis and in left ventricular systolic and diastolic dysfunction. The occurrence of conduction abnormalities and arrhythmias is exacerbated by electrolyte shifts, diabetes, and autonomic neuropathy. Cardioverter-defibrillator implantation decreases the risk of sudden death in patients with CKD.

Hypertension has been reported to occur in 85% to 95% of patients with CKD (stages 3 to 5). The relationship between hypertension and CKD is cyclic in nature. Uncontrolled hypertension is a risk factor for developing CKD and leads to a more rapid progression of CKD. In turn, renal disease

exacerbates uncontrolled hypertension due to volume expansion and increased systemic vascular resistance. An imbalanced autonomic system results in an exaggerated sympathetic drive with a loss of vagal tone. Autonomic neuropathy creates a setting for silent myocardial ischemia.

Correction of the uremic state and improved GFR after kidney transplant may decrease the incidence and severity of cardiovascular complications.

Botdorf J, Chaudhary K, Whaley-Connell A. Hypertension in cardiovascular and kidney disease. *Cardiorenal Med*. 2011;1:183–192.

Disthabanchong S. Vascular calcification in chronic kidney disease: pathogenesis and clinical implication. *World J Nephrol*. 2012;1(2):43–53.

Glicklich D, Vohra P. Cardiovascular risk assessment before and after kidney transplantation. *Cardiol Rev*. 2014;22(4):153–162.

Shamseddin MK, Parfrey PS. Sudden cardiac death in chronic kidney disease: epidemiology and prevention. *Nat Rev Nephrol*. 2011;7(3):145–154.

A.8. When is the best time to receive a kidney transplant?

In general, a patient is a candidate for a kidney transplant if the estimated GFR (eGFR) is 20 mL/min/1.73 m^2 or less, and renal function has irreversibly deteriorated to the point that a transplant or dialysis will be inevitable. Studies show that survival of a transplanted kidney is incrementally worse if the recipient has been on long-term dialysis. The best outcomes are seen for patients who are preemptively transplanted before dialysis is initiated. Therefore, if it is obvious the patient will eventually require dialysis and a living donor is available now, transplant is practical and cost-effective option.

Patients who are potentially interested in a transplant and with no known contraindications should be referred to a transplantation program early, when the eGFR is around 30 mL/min/1.73 m^2. Preparation for a transplant candidate can take several months, involving thorough medical evaluation and optimization of cardiac and pulmonary status.

Link DK, Saxena R. The right patient, the right treatment, the right access and the right time. *Adv Chronic Kidney Dis*. 2014;21(4):360–364.

Taal MW, Chertow GM, Marsden PA, et al, eds. *Brenner and Rector's The Kidney*. 9th ed. Philadelphia, PA: Saunders; 2012:2495–2514.

A.9. How are immunosuppressive drugs managed in kidney transplant recipients?

In order to decrease the incidence of graft rejection, several regimens of immunosuppressive agents have been devised. Centers throughout the world may use different combinations of these drugs, but the central purpose is to prevent acute and chronic T-cell alloimmune rejection. The regimens are separated into an induction phase and a long-term maintenance phase. Four classes of immunosuppressive medications are used: corticosteroids, calcineurin inhibitors (CNIs) (cyclosporine and tacrolimus), antimetabolites (mycophenolate mofetil, mycophenolate sodium, and azathioprine), and the target-of-rapamycin (TOR) inhibitor (sirolimus). The maintenance phase involves a combination of two or three of these drugs, each from a separate class.

Immunosuppressant therapy is started in the immediate preoperative period. In the intraoperative period, induction therapy is targeted to eliminate lymphoid cells that may cause acute rejection of the graft. An induction agent may be withheld if immediate graft function occurs from a living donor kidney. After surgery, maintenance therapy is initiated and continued for the lifetime of the recipient. Although lifelong immunosuppression helps prevent rejection of the allograft, it also increases the risk of malignancy and infectious diseases. The regimens may not prevent the slow deterioration associated with chronic graft rejection.

In an effort to reduce the long-term toxicities of immunosuppressant drugs, corticosteroid- and CNI-sparing protocols have become popular in managing kidney transplant

patients. This is because the long-term use of steroids contributes to cardiovascular disease and/or infectious disease complications.

CNIs prevent acute rejection but are associated with reduced long-term allograft function. Protocols with agents such as mycophenolate mofetil, mycophenolate sodium, sirolimus, everolimus, and belatacept allow discontinuation of CNI within 6 months or avoid the CNIs.

Helal I, Chan L. Steroid and calcineurin inhibitor-sparing protocols in kidney transplantation. *Transplant Proc*. 2011;43(2):472–477.

A.10. How are kidneys allocated to recipients on the waiting list in the United States?

A national allocation policy for deceased-donor kidneys was established in 1987 by the United Network for Organ Sharing (UNOS) and the Organ Procurement and Transplant Network (OPTN). In 2014, the kidney allocation system (KAS) was extensively revised in order to increase utilization of available kidneys, reduce regional variability in access to transplantation, and improve outcomes for individual kidneys that are transplanted.

Adult patients may be registered on the waiting list after the diagnosis of irreversible kidney disease is made and GFR ≤20 mL/min/1.73 m^2. The estimated posttransplant survival (EPTS) is a measure used to estimate the number of years of potential benefit from a kidney transplant and is calculated for all candidates on the waiting list using candidate age, time on dialysis, presence or absence of diabetes, and prior history of solid organ transplant. A combination of a candidate's EPTS score and the time spent on the waiting list is used to determine their ranked priority on the waiting list. Additional priority is given to candidates with rare blood types and high immune system sensitivity because these patients have fewer

opportunities for a transplant.

The kidney donor risk index (KDRI) is a measure that provides information about the quality of a donor kidney graft based on how long it is estimated to function after transplant. The KDRI is calculated using donor age, ethnicity, creatinine, history of hypertension or diabetes, cause of death, height, weight, hepatitis C virus (HCV) status, and whether the kidney was donated after circulatory death. Kidneys with the highest KDRI score (i.e., the shortest predicted lifespan) must be offered over a wider geographic area in order to increase the utilization of donated kidneys. Transplant programs must have informed consent from potential recipients to receive a kidney with a KDRI score >85%.

Hart A, Smith JM, Skeans MA, et al. OPTN/SRTR 2017 annual data report: kidney. *Am J Transplant*. 2019;19(suppl 2):19–123.

A.11. What is donation after cardiac death (DCD)?

DCD has opened new perspectives in the donor pool. It refers to kidney donation from patients with brain injuries who do not meet the criteria for brain death and who experience cardiopulmonary arrest after withdrawal of ventilatory support. This criterion does increase the number of organs available, but DCD kidneys do have a greater than fivefold increase in the incidence of delayed graft function and a higher primary nonfunction rate compared to donation after brain death. DCD kidneys also have a higher rate of discard and retrieval-associated injury. Long-term graft function is equivalent between brain death and cardiac death donors. Renal preservation fluid is delivered either with rapid laparotomy and direct aortic cannulation or using an intra-aortic catheter placed via the femoral artery. Rapid laparotomy is associated with lower kidney discard rate, shorter warm ischemia times, and higher graft survival rates. Newer preservation strategies using

extracorporeal membrane oxygenation (ECMO) are under study to develop uniform guidelines for procurement.

Akoh JA. Kidney donation after cardiac death. *World J Nephrol*. 2012;1(3):79–91.

Morrissey PE, Monaco AP. Donation after circulatory death: current practices, ongoing challenges, and potential improvements. *Transplantation*. 2014;97(3):258–264.

Neyrinck A, Van Raemdonck D, Monbaliu D. Donation after circulatory death: current status. *Curr Opin Anaesthesiol*. 2013;26(3):382–390.

A.12. What is a living donor transplant program?

A living donor transplant program allows recipient and donor surgery to be scheduled simultaneously. It offers the advantage of minimal organ preservation time. The total ischemia time from removal of the kidney from the donor to the restoration of blood flow in the recipient can be less than 1 hour. A short preservation time allows immediate graft function, high-volume urine output, and initiation of creatinine clearance.

A large number of recipients have preformed antibodies to potential living donors. These antibodies are the result of exposure to foreign antigens by blood transfusions, prior transplantation, or pregnancy. As a result, the recipients have positive crossmatches against living donor tissue antigens. There are preoperative measures that can facilitate the transplant to occur. One such regimen involves the combination of plasmapheresis and low-dose intravenous immunoglobulin with or without rituximab (a B-cell depleter) administered to a positive crossmatch and/or highly sensitized recipient. The living donor transplant is conducted when the crossmatch converts to negative. The recipient usually has to undergo additional plasmapheresis treatments and immunoglobulin infusions postoperatively.

Jin MK, Cho JH, Kwon O, et al. Successful kidney transplantation after

desensitization using plasmapheresis, low-dose intravenous immunoglobulin, and rituximab in highly sensitized patients: a single-center experience. *Transplant Proc*. 2012;44(1):200–203.

Tong A, Chapman JR, Wong G, et al. Living kidney donor assessment: challenges, uncertainties and controversies among transplant nephrologists and surgeons. *Am J Transplant*. 2013;13(11):2912–2923.

A.13. What is a paired donor exchange transplant program?

This program is sometimes referred to as a "kidney swap." For example, one incompatible donor–candidate pair is matched to another pair with a complementary incompatibility, such that the donor from one pair gives an organ to a compatible candidate in the other pair and vice versa. Each kidney paired donation (KPD) has developed its own features to accommodate local needs. Reasons for participating in KPD include blood group incompatibility, sensitization of the recipient against the donor, the potential for improvement in transplant quality (e.g., age difference or graft size), and tissue compatibility. Sophisticated algorithms allow simultaneous two-way, three-way, or four-way exchanges or nonsimultaneous chains of transplants over the course of months.

There are many benefits to a paired donor exchange program:

- It expands the pool of donors.
- By using ABO-compatible but nonidentical donors, transplants can be performed at individual centers without requiring large sharing networks.
- Type O recipients with incompatible donors are likely to be the primary beneficiary of exchange programs.
- These programs reflect a paradigm shift for live donation, converting a private resource (the donor) to a shared one.
- Both donors and recipients are more willing to participate if their intended recipient, or donor is enthusiastic about participating.

Chkhotua A. Paired kidney donation: outcomes, limitations, and future perspectives. *Transplant Proc*. 2012;44(6)1790–1792.

Mierzejewska B, Durlik M, Lisik W, et al. Current approaches in national kidney paired donation programs. *Ann Transplant*. 2013;18:112–124.

A.14. What are some barriers to receiving a kidney transplant?

Absolute contraindications to kidney transplant include active infections, active malignancy, active substance abuse, reversible renal failure, uncontrolled psychiatric disease, documented active and ongoing treatment nonadherence, and a significantly shortened life expectancy. Recipient age alone is not a contraindication to transplant. However, in order to be an acceptable candidate to receive a transplant, patients should have an estimated life expectancy longer than the anticipated waiting time for a kidney. A living donor transplant is often the best option for an older patient.

Recipient with HIV infection is not a contraindication to acquiring a kidney. The U.S. Congress passed a law called the HIV Organ Policy Equity (HOPE) Act. This law ended a federal ban on transplantation of organs from deceased HIV-infected donors to HIV-infected recipients. The new policy will expand the number of donor organs available for transplantation into HIV-positive patients. The potential recipient should be clinically stable on highly active antiretroviral therapy (HAART), with an undetectable viral load, and a CD4 count ≥200 cells per μL.

Because the incidence of obesity has increased in the general population, more obese patients are referred for kidney transplantation. Obese patients have increased risk for delayed graft failure. Diet and/or bariatric surgery are beneficial for patients with a BMI of 40 kg per m^2 or more prior to transplant. Improvements in postoperative management have resulted in similar graft survival and mortality in obese patients compared

to nonobese patients.

Many patients on dialysis are infected with hepatitis B and/or hepatitis C. Currently, chronic hepatitis B is treated with interferon α-2a or interferon α-2b and lamivudine. Antiviral treatment with interferon is contraindicated after transplantation due to the risk of rejection, so treatment is recommended before transplant. Unlike interferon, lamivudine is a safe and effective antiviral hepatitis B virus (HBV) treatment both before and after renal transplantation. New treatment strategies with oral nucleotide NS5B polymerase inhibitors (sofosbuvir) are revolutionizing therapy for HCV. A recipient infected with HCV may accept an organ from an HCV-positive donor. Established HBV or HCV with cirrhosis and active viral infection is a relative contraindication to renal transplant.

Bahde R, Vowinkel T, Unser J, et al. Prognostic factors for kidney allograft survival in the Eurotransplant Senior Program. *Ann Transplant*. 2014;19:201–209.

Burra P, Rodríguez-Castro KI, Marchini F, et al. Hepatitis C virus infection in end-stage renal disease and kidney transplantation. *Transpl Int*. 2014;27(9):877–891.

Malani PN. New law allows organ transplants from deceased HIV-infected donors to HIV-infected recipients. *JAMA*. 2013;310(23):2492–2493.

Nicoletto BB, Fonseca NK, Manfro RC, et al. Effects of obesity on kidney transplantation outcomes: a systematic review and meta-analysis. *Transplantation*. 2014;98(2):167–176.

A.15. What surgical techniques are available for donor nephrectomy (DN)?

The standard techniques for DN are open surgery, laparoscopic, and hand-assisted laparoscopic DN. Laparoscopic living-DN (LLDN) has increased in popularity. In some centers, it has replaced open DN as the standard technique. Laparoscopic DN results in less blood loss, reduced operative time, and shorter hospital stay than open DN. Hand-assisted laparoscopic DN has

the potential to decrease warm ischemia time for renal allografts. Donors managed laparoscopically have fewer complications, significantly less wound-related morbidity, and less delayed graft function than patients who undergo open DN.

Robotic nephrectomy offers several advantages compared to standard laparoscopic approaches. In particular, a robotic system restores the three-dimensional vision lost in the laparoscopic approach and enhances the ability of the surgeon to perform complex tasks.

Laparoendoscopic single-site surgery (LESS) uses one extraction site to place all ports to minimize the invasiveness of the planned procedure. A hybrid technique uses one periumbilical access and extraction site and an additional 2-mm needlescopic port. A robot can be used to aid in the surgery.

Caso JR. Minimally invasive donor nephrectomy: innovations. *Curr Urol Rep*. 2014;15(1):378.

Giacomoni A, Di Sandro S, Lauterio A, et al. Evolution of robotic nephrectomy for living donation: from hand-assisted to totally robotic technique. *Int J Med Robot*. 2014;10(3):286–293.

A.16. How is a donor kidney preserved?

Currently, static cold storage and hypothermic pulsatile machine perfusion are the two methods used to preserve donor kidneys. The benefit of one method over the other remains debated.

In static cold storage, the kidney is flushed, cooled with one of several cold preservation solutions, and transported on ice. In hypothermic machine perfusion, after an initial washout of blood, the kidney is connected to a perfusion device, and a solution is pumped continuously through the organ at temperatures between 1°C and 10°C until the moment of graft placement.

Preservation solutions are agents that do not readily permeate the cell membrane and have an electrolyte composition similar

to the intracellular environment (low sodium, high potassium), thus preventing loss of cellular potassium. The organ-preserving cold storage interval is called cold ischemia time (CIT). It extends from the initiation of cold preservation of donor organs to restoration of warm circulation in the organ recipient. In general, kidneys with a CIT over 24 hours or more are susceptible to delayed graft function. Delayed graft function means a requirement for dialysis in the first week after receiving a transplant.

As more suboptimal donor kidneys are used, machine perfusion has regained clinical interest. Hypothermic machine perfusion reduces delayed graft function compared with static cold. There is no difference in primary nonfunction, acute rejection, long-term renal function, or patient survival between the two methods.

Kidneys from living donors are easier to handle. The organ is flushed with preservation solution or iced Ringer's lactate solution containing heparin and mannitol. The ischemic time during implantation is usually 20 to 30 minutes because the transplant operation takes place immediately. Some practices place the living donor kidney in a pulsatile preservation machine that maintains organ viability for longer periods of time. The influence of improved immunosuppression, lower CIT have contributed to the recent improvements in graft function and survival.

Bathini V, McGregor T, McAlister VC, et al. Renal perfusion pump vs cold storage for donation after cardiac death kidneys: a systematic review. *J Urol*. 2013;189(6):2214–2220.

O'Callaghan JM, Morgan RD, Knight SR, et al. Systematic review and meta-analysis of hypothermic machine perfusion versus static cold storage of kidney allografts on transplant outcomes. *Br J Surg*. 2013;100(8):991–1001.

A.17. Describe the operative procedure of kidney transplantation.

Prior to the induction of anesthesia, a large-bore peripheral intravenous line (18- or 16-gauge) is required. Following induction of anesthesia, a triple-lumen central line may be placed either via the internal jugular or subclavian route. A Foley catheter is placed in the bladder, and the bladder is irrigated with an antibiotic solution. Fluids are infused liberally through the central line and intravenous line. An arterial line may also be placed depending on the patient's underlying clinical status.

A kidney is harvested from a living donor using a left-flank laparoscopic approach. Harvesting of the left kidney is favored because the left renal vein is longer. New surgical techniques allow preservation of longer arterial length on the harvested kidney. Longer vessel preservation facilitates a right kidney donation.

The donor kidney is placed in either the right or left iliac fossa. The right kidney is usually placed in the left groin and vice versa. The renal artery of the donor kidney is connected to the external or internal iliac artery in the recipient. The renal vein of the donor kidney is connected to the external iliac vein in the recipient. Occasionally, a donor kidney has multiple renal arteries. This is addressed using primary or secondary anastomosis. A multiple-artery donor kidney has a longer operative and ischemic time than a kidney with a single artery. In the event that the recipient weighs less than 20 kg, the kidney is placed intra-abdominally posterior to the right colon. Urinary continuity is restored by placing the distal ureter into the bladder through a tunnel without opening the bladder.

In deceased donor kidney transplant, prior to the release of the arterial clamp and following completion of the anastomosis, an intra-arterial injection of verapamil or papaverine may be given by direct push into the renal artery to prevent arterial vasospasm.

In dual kidney transplantation, two kidneys from a donor are placed into one recipient. It is a reflection of donor shortage and reluctance to discard potentially functional organs. Such kidneys have usually been refused for single kidney transplantation. The criteria extends to very old (>60 years) or very young (<3 years) donors. The kidneys are transplanted en bloc. The donor aorta and vena cava are anastomosed to the external iliac artery and vein of the recipient. A dual kidney transplant procedure is of longer duration and involves more third spacing, greater volume requirements, and blood loss.

Chedid MF, Muthu C, Nyberg SL, et al. Living donor kidney transplantation using laparoscopically procured multiple renal artery kidneys and right kidneys. *J Am Coll Surg*. 2013;217(1):144–152.

Laftavi MR, Stephan R, Feng L, et al. Dual kidney transplants from very old or very young donors: long-term outcomes and complications. *Transplant Proc*. 2011;43(2):507–511.

B. Preoperative Evaluation and Preparation

B.1. What preoperative workup would you order for a recipient?

The transplant recipient should receive a thorough, multidisciplinary workup prior to being listed as a candidate on the wait-list. This workup should include routine tests such as ECG, chest radiograph, complete blood counts, serum electrolytes and glucose, blood urea nitrogen and creatinine concentration, coagulation tests, and liver function tests.

Because cardiac disease is prevalent in this patient population and cardiac events are the leading cause of posttransplant mortality, a thorough cardiac evaluation is recommended. In addition to adhering to the established 2014 American College of Cardiology/American Heart Association (ACC/AHA) guidelines on perioperative cardiovascular evaluation of patients

undergoing noncardiac surgery, additional testing may be considered in pretransplant patients. Specifically, noninvasive stress testing may be considered in kidney transplantation candidates with no active cardiac conditions based on the presence of multiple coronary artery disease risk factors regardless of functional status. Relevant risk factors among transplantation candidates include diabetes mellitus, prior cardiovascular disease, more than 1 year on dialysis, left ventricular hypertrophy, age greater than 60 years, smoking, hypertension, and dyslipidemia. Additionally, there is some recent evidence that the coronary artery calcium score (CACS), which is a noninvasive diagnostic test for advanced coronary artery disease performed by nonenhanced computed tomography with minimal radiation, may be useful as a primary risk stratification tool in this patient population. Medical treatment or intervention for coronary artery disease is recommended when indicated by the cardiologist.

Routine dialysis should be avoided in the 24 hours prior to transplantation because it may increase the risk of delayed graft function. (This recommendation is different than for dialysis-dependent patients undergoing nontransplant surgery, for whom dialysis in the 24 hours prior to surgery is generally recommended.) If dialysis needs to be done within 24 hours of the operation, it is best to avoid overzealous ultrafiltration as expanded filling pressures are desired, and intravascular volume depletion may result in severe hypotension during or after anesthetic induction.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;64(22):e77–e137.

Lentine KL, Costa SP, Weir MR, et al. Cardiac disease evaluation and management among kidney and liver transplantation candidates: a scientific

statement from the American Heart Association and the American College of Cardiology Foundation. *J Am Coll Cardiol*. 2012;60:434–480.

Winther S, Bøttcher M, Jørgensen HS, et al. Coronary calcium score may replace cardiovascular risk factors as primary risk stratification tool before kidney transplantation. *Transplantation*. 2016;100(10):2177–2187.

B.2. How does the presence of obesity affect the outcome of a transplanted kidney?

The benefit of renal transplantation in obese patients is controversial, with many centers setting upper limits on BMI in consideration for listing patients for transplant. High BMI at transplant is associated with increased risk of wound and surgical site infections, delayed graft function, acute rejection episodes, and graft loss. Prospective evaluations of the impact of targeted risk modification such as dietary changes and monitored exercise programs are being investigated at this time. Bariatric surgery is both safe and effective in patients with CKD and ESRD. A sleeve gastrectomy improves eligibility for transplant based on BMI and does not affect postoperative immunosuppressant dosing regimens. All patients presenting for kidney transplant should be considered to have full stomachs regardless of the period of preoperative fasting.

Lentine KL, Delos Santos R, Axelrod D, et al. Obesity and kidney transplant candidates: how big is too big for transplantation? *Am J Nephrol*. 2012;36(6):575–586.

Pham PT, Danovitch GM, Pham PC. Kidney transplantation in the obese transplant candidates: to transplant or not to transplant? *Semin Dial*. 2013;26(5):568–577.

B.3. How are routine medications and immunosuppressive medications managed in the perioperative period?

Patients awaiting transplant often have comorbidities such as hypertension and diabetes. Antihypertensive drugs should be continued until the time of surgery. There are no rigorous

studies in the transplant population regarding the protective value of β-blockers. It is recommended that β-blockade be continued to reduce the risk of myocardial infarction. Medications such as angiotensin-converting enzyme inhibitor (ACE-I) and angiotensin II receptor blocker (ARB) should be omitted because of the risk of severe and refractory intraoperative hypotension. In spite of careful antihypertensive therapy, patient hemodynamics may still remain labile during induction, laryngoscopy, intubation, and extubation.

Oral hypoglycemic agents should be held on the morning of surgery. An insulin sliding scale can be used to manage patients on insulin. The sliding scale may be used intraoperatively if high blood glucose levels are measured. Antibiotic prophylaxis for infectious complications includes a first-generation cephalosporin (cefazolin 2 g intravenously), or if penicillin-allergic, an alternative such as vancomycin (1 g intravenously).

Anxiolytics should be titrated carefully because these patients may have increased sensitivity to premedication drugs. For example, diazepam is highly bound to albumin, but with decreased albumin levels, the effect of the drug is increased. Midazolam is water soluble, less affected by albumin levels, and useful prior to induction.

Prior to entering the operating room, patients are given intravenous corticosteroids and an immunosuppressive agent. Diphenhydramine and acetaminophen should be given before the rabbit antithymocyte globulin (Thymoglobulin) is infused intraoperatively. Under specific circumstances, basiliximab (Simulect) is substituted for Thymoglobulin. This is typically done if the patient has history of reaction to Thymoglobulin, has significantly decreased cardiac function, or is a perfect match to the donor kidney. No prophylactic premedication is required with basiliximab. Rituximab and plasmapheresis followed by intravenous immunoglobulin are incorporated into the regimens

of those patients with a positive crossmatch. A steroid-sparing regimen includes intraoperative methylprednisolone, which is tapered over 4 days. Patients go home taking only tacrolimus (Prograf) and mycophenolate mofetil (CellCept). In the steroid protocol, patients are continued on prednisone.

Spiro MD, Eilers H. Intraoperative care of the transplant patient. *Anesthesiol Clin*. 2013;31(4):705–721.

C. Intraoperative Management

C.1. Are a central venous pressure (CVP) monitoring line, an arterial line, and a pulmonary artery catheter required for the transplant procedure?

Measuring the CVP is not an absolute requirement; however, ensuring adequate hydration is an important part of the anesthetic management in renal transplant. Most patients will have undergone hemodialysis within 48 hours of surgery and may have intravascular volume depletion as a result. To decrease the incidence of postoperative acute tubular necrosis (ATN), a liberal hydration policy is employed intraoperatively. Although the utility of the CVP to guide fluid resuscitation is the subject of some debate, studies have shown that hydration guided by CVP monitoring can maintain stable hemodynamics and promote diuresis in kidney transplant recipients. The systolic blood pressure is maintained between 130 and 160 mmHg (or close to the individual patient's baseline blood pressure), and the CVP is maintained between 12 and 14 mmHg. Maintaining adequate CVP is especially important in pediatric recipients because reperfusion of an adult-size kidney graft may divert a significant amount of their own blood volume. CVP may decline 1 to 2 hours after revascularization despite aggressive fluid management in the operating room. The decline

in CVP is similar in recipients of both cadaveric and living related donor kidneys. It may decline 25% to 50% below the CVP measured in the operating room at reperfusion of the transplanted kidney. The reason for the decline is not clear but may be multifactorial such as redistribution of fluids, changes in vascular permeability, or increased nitric oxide levels. Increased hydration likely works to counteract this mechanism by atrial distension and the subsequent release of atrial natriuretic peptide and increased renal perfusion. Postoperatively, the patient should receive an equal amount of fluid to replace their urine output. If a central venous line is not placed, large-bore peripheral IV access or a large-bore central access via a midline catheter should be established.

An arterial line is not absolutely required for the transplant procedure. It should be placed if a patient has an advanced comorbid condition that requires close monitoring of blood pressure or acid–base status. Oftentimes, placement of an intra-arterial line is difficult because many recipients have poor arterial access secondary to diabetes, peripheral vascular disease, arteriovenous fistulas, and shunts. Major swings in blood pressure may occur, with hypotension (49.6%) being more likely than hypertension (26.8%). Administration of induction drugs and maintenance agents should be titrated carefully. The main utility of instantaneous blood pressure reading is toward the end of the procedure. Hypotension may occur after unclamping of the iliac vessels and/or from partial systemic absorption of the vasodilator (verapamil or papaverine) injected by the surgeon into the graft vessels. Hypotension must be avoided during this period because it can lead to delayed graft function and/or renal vein thrombosis.

A pulmonary artery catheter is not routinely placed for kidney transplantation. Patients with severe comorbid conditions, such as symptomatic coronary artery disease, left ventricular

dysfunction, congestive heart failure, valvular heart disease, or severe chronic obstructive pulmonary disease, can be monitored precisely with a pulmonary artery catheter. A transesophageal echocardiography can help determine if hypotension is caused by hypovolemia or myocardial dysfunction.

Othman MM, Ismael AZ, Hammouda GE. The impact of timing of maximal crystalloid hydration on early graft function during kidney transplantation. *Anesth Analg*. 2010;110(5):1440–1446.

Trzebicki J, Flakiewicz E, Nowakowski P, et al. Is external jugular venous pressure a good predictor of volume status in kidney graft recipients? *Transplant Proc*. 2009;41(8):3033–3035.

C.2. What type of intravenous fluid should be used during surgery?

Traditionally, the administration of normal saline and normal saline–based fluids (5% albumin) has been the standard of care for fluid management in patients undergoing renal transplant surgery. This practice is primarily based on avoidance of potassium-containing fluids, which could theoretically contribute to intraoperative hyperkalemia. However, several recent studies suggest a higher risk of acidosis and hyperkalemia when using normal saline solutions versus balanced saline solutions such as lactated Ringer's or Plasma-Lyte, and no difference in clinical outcomes. Therefore, many transplant centers have made the switch to administering balanced, potassium-containing solutions. The typical fluid requirement for a 70-kg adult is about 3,000 to 4,000 mL. In addition, 500 mL of 5% albumin is given.

The recipient's blood is usually typed and screened, but blood loss is minimal, so transfusion is unlikely. The anesthesiologist should attempt to maintain a systolic blood pressure in the normal-to-high range of 130 to 160 mmHg, and CVP between 10 and 14 cm H_2O.

The intravenous administration of adequate volumes of fluid is associated with earlier onset of graft function, lower postoperative serum creatinine, higher postoperative creatinine clearance, reduced incidence of delayed graft function, and improved graft survival.

O'Malley CMN, Frumento RJ, Hardy MA, et al. A randomized, double-blind comparison of lactated Ringer's solution and 0.9% NaCl during renal transplantation. *Anesth Analg*. 2005;100(5):1518–1524.

Othman MM, Ismael AZ, Hammouda GE. The impact of timing of maximal crystalloid hydration on early graft function during kidney transplantation. *Anesth Analg*. 2010;110(5):1440–1446.

Weinberg L, Harris L, Bellomo R, et al. Effects of intraoperative and early postoperative normal saline or Plasma-Lyte 148® on hyperkalaemia in deceased donor renal transplantation: a double-blind randomized trial. *Br J Anaesth*. 2017;119(4):606–615.

C.3. How would you conduct the anesthesia induction?

The circumstances for renal transplant can vary between a scheduled or emergent procedure. Living donor transplants are scheduled surgical cases. Patients receiving cadaver kidneys may learn of the surgical procedure under short notice. Standard anesthesia monitors are required prior to induction. A central venous line and/or arterial line are usually placed after induction.

The induction of general anesthesia and intubation of the trachea can be safely accomplished with several of the commonly used drugs. The induction drugs should be given slowly to minimize the chance of drug-induced hypotension. Regardless of blood volume status, these patients often respond to induction of anesthesia as if they were hypovolemic. The sympathetic nervous system response may be attenuated by antihypertensive therapy or diabetic autonomic neuropathy. A blunted sympathetic response impairs compensatory peripheral vasoconstriction. In addition, the central nervous system (CNS)

may exhibit an increased sensitivity to the induction drugs. Low serum protein and albumin levels can increase the level of unbound drug crossing the blood–brain barrier into CNS receptors. Uremia can also disrupt the blood–brain barrier. The dose of induction agent may need to be adjusted based on volume status, acidic pH, and comorbidities. Propofol or etomidate can be used in routine circumstances. A reduced induction dose of propofol may be considered because lower plasma protein levels and postdialysis hypovolemia can exaggerate its cardiac depressant effects. Ketamine pharmacokinetics are not significantly altered by renal disease, but its hypertensive effects make it undesirable in patients with underlying hypertension. Etomidate is well tolerated and preserves hemodynamic stability.

Large fluctuations in blood pressure and heart rate may occur in patients with preexisting hypertension during intubation. Underlying coronary artery disease should be carefully considered. Opioids can blunt the response to laryngoscopy. Fentanyl can be used in moderate doses, but there is a small risk of hypotension after induction and lack of stimulation. Remifentanil is also effective for heart rate control. A short-acting β-blocker such as esmolol (0.5 to 1.0 mg per kg) can blunt the response to intubation.

A number of neuromuscular blocking agents can be used to facilitate tracheal intubation. Patients with uremia and diabetes may have gastroparesis. Pretreatment with a clear, nonparticulate antacid such as 30 mL of sodium citrate raises gastric pH. A rapid sequence induction with cricoid pressure using either succinylcholine or rocuronium may be required to prevent reflux and aspiration. Succinylcholine can be used safely because potassium release is not exaggerated in patients with chronic renal failure. If the preoperative potassium is in the high normal range or if there is underlying metabolic acidosis,

the additional increase of 0.5 to 1.0 mEq per L should be considered. When choosing a nondepolarizing agent for maintenance, it is better to use ones that are independent of renal clearance mechanisms (cisatracurium, atracurium).

Schmid S, Jungwirth B. Anaesthesia for renal transplant surgery: an update. *Eur J Anaesthesiol*. 2012;29(12)552–558.

C.4. Is succinylcholine contraindicated in renal failure patients?

Normally, succinylcholine causes an increase in serum potassium of 0.5 to 1.0 mEq per L within 3 to 5 minutes after intravenous administration and lasts less than 10 to 15 minutes. Succinylcholine can be used safely in patients with chronic renal failure if the potassium concentration is less than 5.5 mEq per L and repeated doses are avoided. Potassium flux after administration of succinylcholine in patients with renal failure does not differ from normal patients. Plasma cholinesterase activity has been reported to be below normal in more than 20% of ESRD patients whether they are receiving any form of dialysis. Values are rarely so low that they cause a prolonged block.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1929–1956.

C.5. How are the nondepolarizing muscle relaxants affected by renal failure?

Table 25.2 notes the commonly used nondepolarizing agents and how they are affected by renal failure. The prolonged duration of action to nondepolarizing agents is primarily due to slow renal clearance. Cisatracurium mainly undergo Hofmann elimination that is not altered in patients with CKD. Renal failure may delay clearance of laudanosine, the principal metabolite of cisatracurium. Laudanosine does not have effect at

the neuromuscular junction but at high plasma levels may act as a CNS stimulant. The long-acting muscle relaxant such as pancuronium is not suitable for use because the kidneys excrete most of the drug and its metabolite. The prolonged effect of a nondepolarizing agent may not be apparent after a single small dose. After a small dose, the termination of action is by redistribution rather than elimination. It is only after a single large dose, repeated dosing, or prolonged infusion that the increased elimination half-life becomes clinically apparent. It has also been shown that there are large differences in pharmacokinetics with renal failure patients receiving rocuronium. Maintenance doses for patients with decreased renal function should be smaller, and the interval between doses should be increased. Monitoring of neuromuscular blockade with a nerve stimulator is recommended.

TABLE 25.2 Pharmacokinetics of Neuromuscular Blocking Agents in Normal versus Anephric Patients

Drug	Renal Excretion (%)	Normal $T_{1/2}$ (min)	Anephric $T_{1/2}$ (min)
Pancuronium	85	132	258
Rocuronium	10	42	58
Vecuronium	40–50	54	84
Atracurium	10–40	18	24
Cisatracurium	16	34	No effect
Mivacurium	<5	1.8	3.6
Succinylcholine	<25	1	1

$T_{1/2}$, half life.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1929–1956.

Staals LM, de Boer HD, van Egmond J, et al. Reversal of rocuronium-induced neuromuscular block by sugammadex is independent of renal perfusion in anesthetized cats. *J Anesth*. 2011;25(2):241–246.

Staals LM, Snoeck MM, Driessen JJ, et al. Reduced clearance of rocuronium

and sugammadex in patients with severe to end-stage renal failure: a pharmacokinetic study. *Br J Anaesth*. 2010;104(1):31–39.

C.6. How would you maintain anesthesia during the case?

General anesthesia is the preferred technique for kidney transplantation. Volatile agents, opioids, and a muscle relaxant are required to provide optimal operating conditions.

The choice of inhaled anesthetic includes desflurane and isoflurane. Sevoflurane may be avoided because the metabolism of sevoflurane has been implicated in renal toxicity due to production of fluoride and compound A. Desflurane and isoflurane do not have any nephrotoxic potential secondary to fluoride accumulation.

Opioids such as fentanyl, sufentanil, alfentanil, and remifentanil can be used during the procedure. Morphine and meperidine have metabolites that depend on renal clearance and can accumulate. A muscle relaxant that is not dependent on renal clearance such as cisatracurium should be used.

Hypotension may occur after unclamping the iliac vessels and reperfusion of the graft. It is important to maintain the blood pressure because renal function is critically dependent on adequate perfusion. It is critical that the patient is adequately hydrated throughout surgery in preparation for reperfusion of the graft. Close monitoring of the CVP and lightening the level of anesthesia during hemodynamic instability can prevent hypotension. Vasopressors with α-agonist action should be avoided because they can comprise blood flow to the transplanted organ. Additional fluid may be required to maintain blood pressure and replace urine output. Furosemide or mannitol can enhance urine output. Loop diuretics block the Na/K channels in the thin ascending loop of Henle. This prevents reabsorption of electrolytes in this part of the nephron. The high-osmolar fluid then prevents reabsorption of water in the distal tubule. A large volume of fluid with high electrolyte content is

excreted. Mannitol is freely filtered in the glomerulus but not reabsorbed. It causes osmotic expansion of urine volume.

The estimated blood loss during the case ranges between 200 and 500 mL. In some cases, greater blood loss may require transfusion of packed red blood cells. Packed red blood cells should be cytomegalovirus negative. At the end of surgery, patients can be given reversal agents and extubated promptly. Patients are then transferred to the postanesthesia care unit (PACU) for continued monitoring of urine output and electrolytes.

Morris P, Knechtle SJ. *Kidney Transplantation: Principles and Practice*. 7th ed. Philadelphia, PA: Saunders Elsevier; 2014.

Spiro MD, Eilers H. Intraoperative care of the transplant patient. *Anesthesiol Clin*. 2013;31(4):705–721.

C.7. What are the effects of inhalation anesthetics on renal blood flow (RBF), glomerular filtration (GFR), and urine output?

All volatile anesthetics produce a dose-related transient and reversible decrease in RBF, GFR, urine output, and the urinary excretion of sodium. This is primarily in response to a decline in systemic blood pressure and cardiac output. Reduced RBF, loss of renal autoregulation, and neurohumoral and neuroendocrine factors also contribute. Specific differences among the agents on renal function are to be noted. Desflurane and sevoflurane are two most frequently used inhalational anesthetics. Desflurane has demonstrated better hepatic and renal function tests after surgery when compared to sevoflurane.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1929–1956.

Ko JS, Gwak MS, Choi SJ, et al. The effects of desflurane and sevoflurane on hepatic and renal functions after right hepatectomy in living donors. *Transpl Int*. 2010;23(7):736–744.

C.8. What are the potential nephrotoxic effects of inhalation anesthetics? What are the nephrotoxic metabolites of inhalation anesthetics?

Fluoride-induced nephrotoxicity is a potential hazard following metabolism of volatile anesthetics. Desflurane (0.02%), isoflurane (0.2%), enflurane (2%), sevoflurane (2% to 3%), and halothane (12% to 20%) are metabolized in the body (rule of 2). When serum inorganic fluoride reaches 50 to 80 mmol per L, subclinical renal toxicity (laboratory abnormalities) occurs. Clinical nephrotoxicity usually becomes apparent when the serum fluoride level is more than 80 mmol per L. The high-output renal failure is dose related and characterized by vasopressin-resistant polyuria, hypernatremia, serum hyperosmolarity, increased serum urea nitrogen, and inorganic fluoride concentration. Despite the potential for relatively high plasma levels of fluoride after long exposure to newer anesthetics, the minimal amount of sevoflurane and enflurane renal defluorination may explain the relative absence of serious renal concentrating defects with these anesthetics. Although the conventional measurements of renal function (blood urea nitrogen, creatinine) are not altered, evidence shows transient impairment of renal concentrating ability and renal tubular injury in patients receiving sevoflurane or enflurane. Nevertheless, it has not been confirmed whether administration of sevoflurane in patients with preexisting renal disease could further deteriorate renal function. Fluoride levels after isoflurane and halothane increase by 3 to 5 μM per L and 1 to 2 μM per L, respectively. These agents do not pose a risk for nephrotoxicity. Desflurane is resistant to biodegradation because fluorine is the only halogen in the desflurane molecule. Mean inorganic fluoride concentration after 1 minimum alveolar concentration (MAC) hour exposure to desflurane is less than 1 μmol per L.

Prolonged exposure to desflurane (7.0 MAC hours) has been associated with normal renal function in patients without renal disease. Neither desflurane nor isoflurane lead to a deterioration of creatinine clearance in patients with preexisting renal impairment.

Sodium or barium hydroxide lime absorbents react with sevoflurane, resulting in a by-product called *compound A*. The nephrotoxic potential of compound A has been noted in animals and is inconclusive in human studies. The concentrations that occur in humans are far below the nephrotoxic levels in animals. A fresh gas flow of 1 L per minute or higher is recommended to minimize the accumulation of compound A in the breathing circuit. Low-flow sevoflurane (1 L per minute) has been used on many occasions with no effect on renal function. Carbon dioxide absorbents that contain calcium hydroxide and calcium chloride do not result in compound A formation when exposed to sevoflurane. The U.S. Food and Drug Administration (FDA) recommends the use of sevoflurane with fresh gas flow rates at least 1 L per minute for exposures up to 1 hour and at least 2 L per minute for exposures greater than 1 hour. Nevertheless, it is important to note that other countries have not recommended such limitations on the clinical use of sevoflurane and problems have not been noted.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:438–439, 1356.

Frink EJ Jr, Malan TP Jr, Isner RJ, et al. Renal concentrating function with prolonged sevoflurane or enflurane anesthesia in volunteers. *Anesthesiology*. 1994;80:1019–1025.

Gentz BA, Malan TP Jr. Renal toxicity with sevoflurane: a storm in a teacup? *Drugs*. 2001;61:2155–2162.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier; 2012:338.

Litz RJ, Hübler M, Lorenz W, et al. Renal responses to desflurane and isoflurane in patients with renal insufficiency. *Anesthesiology*. 2002;97:1133–

1136.

C.9. How does renal failure affect the pharmacology of opioids?

The effect of renal failure on individual opioids varies, so one must consider the effect of renal failure on drug metabolites as well as the parent compound.

Morphine is metabolized in the liver to morphine-6-glucuronide (M6G) (10%), morphine-3-glucuronide (M3G) (55%), and normorphine (4%), all of which are excreted by the kidneys, along with about 10% of the parent compound, in subjects with normal renal function. M6G has been reported to mediate CNS and respiratory depression when it accumulates in renal failure.

Meperidine is metabolized in the liver to normeperidine, also excreted by the kidneys. Accumulation of this metabolite may lead to excitatory CNS effects such as convulsions.

Fentanyl is metabolized by the liver, with only 7% excreted unchanged in the urine. Fentanyl is suitable for use during surgery and is safe in the short term. There are reports of the parent compound accumulating during renal failure, but clinical experience is that there are no adverse effects. However, if being used long term in renal failure patients, the pharmacodynamic effects should be monitored carefully.

Alfentanil metabolism occurs by inducible cytochrome c enzymes in the liver, making it suitable for renal failure patients. The clearance and half-life of sufentanil and alfentanil are not significantly different in patients with reduced renal function.

Remifentanil is metabolized by blood and tissue esterases. The principle metabolite of remifentanil (GR90291) is eliminated by the kidney. The reduced renal elimination of this metabolite is not of clinical significance because the potency is 1 in 4,000 of the parent compound.

Nayak-Rao S. Achieving effective pain relief in patients with chronic kidney disease: a review of analgesics in renal failure. *J Nephrol*. 2011;24(1):35–40.

Niscola P, Scaramucci L, Vischini G, et al. The use of major analgesics in patients with renal dysfunction. *Curr Drug Targets*. 2010;11(6):752–758.

D. Postoperative Management

D.1. How is the diagnosis of transplant rejection made?

There are various forms of rejection such as hyperacute, accelerated acute, acute, and chronic. Acute rejection is the most common, but less common with immunosuppressive agents. It is usually seen within days to a few months posttransplant. The diagnosis is made with a renal biopsy. In patients with prolonged delayed graft function, surveillance biopsies can detect or exclude acute rejection episodes. The process is associated with systemic symptoms such as fever, chills, malaise, and arthralgias. However, with current immunosuppressive drugs, most acute rejection episodes are generally asymptomatic. Laboratory data note a rapid increase in creatinine of 10% to 25% over baseline with or without a decrease in urine output.

Nankivell BJ, Alexander SI. Rejection of the kidney allograft. *N Engl J Med*. 2010;363:1451–1462.

D.2. What are immunosuppressive agents, and how do they affect anesthetic care?

Induction drugs are antirejection medicines used at the time of transplant. The patient is then placed on maintenance drugs for the long term.

There are generally four classes of maintenance drugs:

- Calcineurin inhibitors: tacrolimus, belatacept, cyclosporine
- Antiproliferative agents: mycophenolate mofetil, mycophenolate sodium, azathioprine
- TOR inhibitors: sirolimus, everolimus

- Steroids: prednisone

Some of the side effects of immunosuppressive agents may be encountered if a posttransplant patient presents for other surgeries and are pertinent to anesthetic care:

- Calcineurin inhibitors: nephrotoxicity, hypertension, hyperchloremic acidosis, hyperkalemia, hypomagnesemia, hypocalcemia, glucose intolerance, coarse tremor, dysesthesia, headache, seizure, prolonged QT interval, hypercoagulability, acute microvascular disease (similar to thrombotic thrombocytopenic purpura)
- Mycophenolate mofetil: nausea, vomiting, cytopenia (leukopenia, anemia, thrombocytopenia), leukocytosis
- TOR inhibitors: mucocutaneous ulceration, hypokalemia, hypomagnesemia, impaired wound healing, interstitial pneumonia, cytopenia
- Azathioprine: cytopenia, hepatitis

Halleck F, Friedersdorff F, Fuller TF, et al. New perspectives of immunosuppression. *Transplant Proc*. 2013;45(3)1224–1231.

Laftavi MR, Sharma R, Feng L, et al. Induction therapy in renal transplant recipients: a review. *Immunol Invest*. 2014;43(8):790–806.

26 Robotic-Assisted Laparoscopic Surgery

Judith Weingram

A 72-year-old man with biopsy-proven carcinoma of the prostate had a prostate-specific antigen (PSA) of 22 ng per mL but negative pelvic computed tomography (CT) and bone scans. He weighed 120 kg. Despite hypertension, a 50 pack-year smoking history, and recent surgery for retinal detachments, he was vigorous and active. He chose to be treated surgically.

A. Medical Disease and Differential Diagnosis

1. What is the incidence of carcinoma of the prostate?
2. How is prostate cancer diagnosed?
3. How is prostate cancer treated?
4. Define laparoscopy.
5. Describe the development of robotic-assisted laparoscopy.
6. What are the advantages and disadvantages of minimally invasive surgery over open surgery?
7. What are the contraindications to laparoscopic or robotic-assisted laparoscopic surgery? Is pregnancy a contraindication to robotic surgery?
8. What other specialties commonly perform robotic surgery?
9. Why is carbon dioxide (CO_2) the gas of choice for robotic

laparoscopy? What are its disadvantages?

10. How much endogenous CO_2 is produced at basal level and at maximal exercise?
11. How much CO_2 is stored in the body? Where is it stored? Of what significance is this to laparoscopy?
12. Describe the diffusion and solubility properties of CO_2 and their significance in laparoscopy.
13. Is CO_2 soluble in water or plasma? Is it soluble in blood? Why?

B. Preoperative Evaluation and Preparation

1. What do you want to know about this patient's history and physical condition that may affect whether or not you clear him for robotic surgery?
2. What factors increase this patient's risk of pulmonary complications?
3. What laboratory tests should be performed preoperatively?
4. What specific information should the patient be given about robotic surgery before obtaining informed consent?
5. What additional procedures should be done before surgery?
6. What are the three major forces that uniquely alter the patient's physiology during robotic laparoscopy?

C. Intraoperative Management

1. What is the anesthetic technique of choice for robotic-assisted laparoscopy? Why?
2. Can a laryngeal mask airway (LMA) be used?
3. What anesthetic agents or adjuvant drugs are recommended for laparoscopy? Are any anesthetic agents contraindicated?
4. Should nitrous oxide (N_2O) be used during laparoscopy? What are the pros and cons? Does N_2O cause bowel distention during laparoscopy? Does N_2O cause nausea and vomiting after laparoscopy?

5. Can laparoscopy be performed under local or regional anesthesia?
6. What monitors and devices would you apply to the patient? Why?
7. How is the patient to be positioned? What special precautions are required for robotic laparoscopy?
8. How will you ventilate the patient? What are the respiratory and circulatory effects of the Trendelenburg position during laparoscopy?
9. What techniques are available for initial access to the peritoneal cavity? What anesthetic problems can arise during insufflation?
10. What intravenous (IV) solution and how much fluid volume do you plan to infuse?
11. Under what circumstances should laparoscopy be converted to laparotomy?
12. What is the arterial to end-tidal CO_2 gradient ($PaCO_2$–$EtCO_2$) in the normal awake patient? What is the cause of the gradient? Does the gradient change during laparoscopy? Why?
13. Is an arterial line necessary? Why? Does end-tidal CO_2 tension accurately reflect arterial CO_2 tension? Under what circumstances may the $EtCO_2$ exceed the $PaCO_2$? Why?
14. What are the possible causes of hypercarbia?
15. What factors play a role in the unusually rapid and marked elevation of CO_2 that is sometimes seen in laparoscopy?
16. How rapidly does the $PaCO_2$ rise in the apneic patient (endogenous CO_2)? How rapidly does the $PaCO_2$ rise if 5% CO_2 gas is inhaled (exogenous)? How rapidly can the CO_2 rise during laparoscopy? What factors explain the differences?
17. What is the net effect of pneumoperitoneum, hypercarbia, and steep Trendelenburg on the cardiovascular system?
18. What is the net effect of pneumoperitoneum, hypercarbia, and

steep Trendelenburg on the respiratory system?

19. What is the net effect of pneumoperitoneum, hypercarbia, and steep Trendelenburg on the central nervous system?
20. What are the neuroendocrine changes that occur during laparoscopy?
21. What is the net effect of pneumoperitoneum, hypercarbia, and steep Trendelenburg on the renal system?
22. What is the net effect of pneumoperitoneum, hypercarbia, and steep Trendelenburg on the bowel and gastrointestinal system?
23. How would you recognize a CO_2 embolism during laparoscopy? How does this differ from an air embolism? Why should N_2O be discontinued during suspected embolization? Will N_2O increase the size of CO_2 emboli?
24. What is the mechanism of increase in shunting resulting from embolization?
25. How is a gas embolism (CO_2 or air) treated?
26. What are the causes of pneumothorax or pneumomediastinum during laparoscopy? How would you diagnose it? How would you treat it?
27. How would you decide when to extubate?

D. Postoperative Management

1. What are some of the unique complications of laparoscopy?
2. In the postanesthesia care unit (PACU), our patient complains of numbness and weakness of the lower extremities after 6 hours of anesthesia for robotic prostatectomy. What tests will you order? When would you remove the Foley catheter and arterial line? Under what circumstances would you order a chest x-ray film?
3. What is the incidence of postoperative nausea and vomiting?

A. Medical Disease and Differential Diagnosis

A.1. What is the incidence of carcinoma of the prostate?

Carcinoma of the prostate is the most frequently diagnosed nonskin cancer in American men. The Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute estimated that in 2018, there were 165,000 new cases of prostate cancer (or 9.5% of all new cancer cases) and more than 29,000 deaths from prostate cancer (or 4.8% of all cancer deaths). Based on their data from 2013 to 2015, approximately 11.2% of men will be diagnosed with prostate cancer at some point in their lifetime.

Undetected microscopic prostate cancer cells are believed to be present in 30% to 40% of men older than the age of 50 years and in 75% of men older than the age of 75 years, but it is estimated that only approximately 8% of these men will develop clinically significant disease. It has been stated that more men die *with* prostate cancer than *from* it. Therefore, it is not yet known whether early detection of subclinical disease, much of which may have remained clinically insignificant, will improve survival.

Carcinoma of the prostate is rare in Asian men, whereas African-American men have about twice the incidence as white American men.

American Cancer Society. *Cancer Facts & Figures 2014*. Atlanta, GA: American Cancer Society; 2008.

Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. *CA Cancer J Clin*. 2018;68(1):7–30.

A.2. How is prostate cancer diagnosed?

The most reliable methods for diagnosis include a digital rectal examination plus the serum PSA level. Palpation of a tumor or indurated area and finding an elevated PSA should be followed by prostatic needle biopsies under transrectal ultrasound guidance and/or magnetic resonance imaging (MRI) and new

genetic biomarkers.

Litwin MS, Tan HJ. The diagnosis and treatment of prostate cancer: a review. *JAMA* 2017;317:2532–2542.

Qaseem A, Barry MJ, Denberg TD, et al. Screening for prostate cancer: a guidance statement from the Clinical Guidelines Committee of the American College of Physicians. *Ann Intern Med*. 2013;158:761–769.

A.3. How is prostate cancer treated?

Treatment choices vary not only with the stage of the disease but also with the patient's age and life expectancy, associated medical conditions, and lifestyle. In patients with localized disease, treatment choices include "watchful waiting," brachytherapy (in which radioactive seeds are implanted in the prostate gland), radiation (including external beam, intensity-modulated radiation therapy, stereotactic therapy, proton beam therapy, etc.), cryosurgery, vaccine therapy, and other nonsurgical treatments. Surgical options include the traditional open radical prostatectomy performed through either a retropubic (lower abdominal) or perineal incision or laparoscopic radical prostatectomy, which can be hand-assisted or robot-assisted.

A patient with nonlocalized disease may choose to be treated with radiation, hormones, chemotherapy, other nonsurgical options, or even to have no treatment.

Coelho RF, Rocco B, Patel MB, et al. Retropubic, laparoscopic, and robot-assisted radical prostatectomy: a critical review of outcomes reported by high-volume centers. *J Endourol*. 2010;24:2003–2015.

D'Alonzo RC, Gan TJ, Moul JW, et al. A retrospective comparison of anesthetic management of robot-assisted laparoscopic radical prostatectomy versus radical retropubic prostatectomy. *J Clin Anesth*. 2009;21(5):322–328.

Lim SK, Kim KH, Shin TY, et al. Current status of robot-assisted laparoscopic radical prostatectomy: how does it compare with other surgical approaches? *Int J Urol*. 2013;20:271–284.

A.4. Define laparoscopy.

Laparoscopy (or peritoneoscopy) is a “minimally invasive” procedure allowing endoscopic access to the peritoneal cavity after insufflation of a gas (CO_2) to create space between the anterior abdominal wall and the viscera. The space is necessary for the safe manipulation of instruments and organs. Laparoscopic surgery can also be extraperitoneal. It can also be gasless with abdominal wall retraction, and more recently, it may be hand-assisted or robotically assisted.

A.5. Describe the development of robotic-assisted laparoscopy.

The era of open incisions in which surgeons could directly see, touch, and manipulate organs was superseded by minimally invasive surgery in which tiny cameras and laparoscopes could be inserted through small ports in the patient’s body. However, conventional laparoscopy is limited by poor depth perception (visualization on a two-dimensional monitor) and the use of long, straight instruments that limit mobility and dexterity.

Robotic devices were initially designed by National Aeronautics and Space Administration (NASA) for the purpose of performing tasks outside the space shuttle while being controlled remotely from inside the spacecraft or from earth. This technology was adapted for surgery as the da Vinci computer-assisted robotic system.

The surgeon sits at a remote control console near the patient and operating room table and views the operative field as a high-resolution magnified three-dimensional image transmitted from a video camera. By using hand-and-finger control devices, the surgeon can precisely manipulate the mechanical arms of the robot to achieve wrist-like motion. Foot pedals also allow the surgeon to more precisely control the robot, camera, and cautery.

Awad H, Walker CM, Shaikh M, et al. Anesthetic considerations for robotic prostatectomy: a review of the literature. *J Clin Anesth*. 2012;24:494–504.

A.6. What are the advantages and disadvantages of minimally invasive surgery over open surgery?

The advantages include the cosmetic results of small non–muscle-splitting incisions, decreased blood loss, less postoperative pain and ileus, shorter hospitalization and convalescence, and ultimately lower cost. Postoperative respiratory muscle function returns to normal more quickly than in open surgery, especially in laparoscopic cholecystectomy and other upper abdominal procedures. Wound complications such as infection and dehiscence are less frequent, and host defense mechanisms may be greater in laparoscopic than in open surgery.

The disadvantages include the long learning curve for the surgeon (most complications occur during the first 10 laparoscopies), the narrowed two-dimensional visual field on video in conventional laparoscopy, the need for general anesthesia with muscle paralysis, and the potentially longer operative duration.

Robotic-assisted laparoscopy, by virtue of its high-resolution three-dimensional visualization and greater precision, offers a greater likelihood of nerve sparing in prostatectomy and, therefore, retention of continence and potency. The disadvantages of the robot include added operative time, the high cost (in millions of dollars) of equipment purchase and maintenance, and the need for a permanently dedicated operating room location for this heavy and bulky equipment.

Soto E, Lo Y, Friedman K, et al. Total laparoscopic hysterectomy versus da Vinci robotic hysterectomy: is using the robot beneficial? *J Gynecol Oncol*. 2011;22:253–259.

Wilson T, Torrey R. Open versus robotic-assisted radical prostatectomy: which is better? *Curr Opin Urol*. 2011;21(3):200–205.

A.7. What are the contraindications to laparoscopic or robotic-assisted laparoscopic surgery? Is pregnancy a contraindication to robotic surgery?

Increasing experience with the laparoscopic technique has made most contraindications relative rather than absolute. However, it is probably best to avoid or to use extreme caution in patients with a coagulopathy, a diaphragmatic hernia, severe cardiovascular or pulmonary disease (including bullae), morbid obesity, increased intracranial pressure or space-occupying masses, a retinal detachment, acute glaucoma, impending renal shutdown, a history of extensive surgery or adhesions, sickle cell disease (because sickle crisis may be precipitated by acidosis), peritonitis, a large intra-abdominal mass, a tumor of the abdominal wall, or hypovolemic shock. Patients with shunts (e.g., ventriculoperitoneal) are at risk for gas emboli, shunt obstruction, and intracranial hypertension, all of which may occur during laparoscopy and may require intracranial pressure monitoring and ventricular drainage if laparoscopic surgery is necessary. In summary, most of the contraindications concern patients who are unable to tolerate extremes of position, pneumoperitoneum, and/or hypercarbia.

Pregnancy is no longer considered a contraindication to robotic surgery. In order to preserve fetal and maternal well-being and to prevent premature labor, the anesthesiologist must weigh the effects of hypercarbia, pneumoperitoneum and extreme positions on the parturient who may present with increased blood volume, increased cardiac output, decreased systemic vascular resistance (SVR), hypercoagulability, the supine hypotensive syndrome, increased respiratory minute volume, decreased residual volume, decreased functional residual capacity (FRC), increased oxygen consumption, mild hypocapnia, increased risk of aspiration, and decreased

anesthetic requirement. This combination of factors tends to promote hypercarbia and hypoxemia. However, extreme hyperventilation may result in decreased uteroplacental perfusion. Arterial blood gas monitoring has been suggested to detect fetal acidosis because capnography may not reveal a large arterial to end-tidal difference in CO_2. In all cases, preoperative and postoperative fetal and uterine monitoring is essential.

Chohan L, Kilpatrick CC. Laparoscopy in pregnancy: a literature review. *Clin Obstet Gynecol*. 2009;52(4):557–569.

Ravaoherisoa J, Meyer P, Afriat R, et al. Laparoscopic surgery in a patient with ventriculoperitoneal shunt: monitoring of shunt function with transcranial Doppler. *Br J Anaesth*. 2004;92(3):434–437.

Steinbrook RA, Bhavani-Shankar K. Hemodynamics during laparoscopic surgery in pregnancy. *Anesth Analg*. 2001;93:1570–1571.

A.8. What other specialties commonly perform robotic surgery?

Robotic procedures in urology have become standard, especially for prostatectomy, uncomplicated adrenalectomy, and nephrectomy including live donor nephrectomy. Robotic gynecologic surgery includes tubal surgery (sterilization, treatment of ectopic pregnancy, etc.), cystectomies, hysterectomies, various ablations (endometriosis), and so on. Robotic surgery is performed in pregnancy and also in pediatrics.

Robotic general surgery includes cholecystectomy, hernia repair, antireflux procedures, splenectomy, appendectomy, bowel surgery including bariatric procedures, and various other upper and lower abdominal procedures.

Thoracoscopic, cardiovascular, and neurosurgical intracranial surgery, using modified laparoscopic instruments without the need for gas insufflation, are some of the more recent areas of endoscopic surgery. Lumbar discectomies and other types of

spinal surgery also have been done laparoscopically through an anterior approach. Even autopsies have been attempted laparoscopically. The list continues to grow.

Muñoz CJ, Nguyen HT, Houck CS. Robotic surgery and anesthesia for pediatric urologic procedures. *Curr Opin Anaesthesiol*. 2016;29(3):337–344.

Rodrigues ES, Lynch JJ, Suri RM, et al. Robotic mitral valve repair: a review of anesthetic management of the first 200 patients. *J Cardiothorac Vasc Anesth*. 2014;28(1):64–68.

A.9. Why is carbon dioxide (CO_2) the gas of choice for robotic laparoscopy? What are its disadvantages?

CO_2 is the insufflating gas of choice because it is nonflammable, does not support combustion, readily diffuses across membranes, is rapidly removed in the lungs, and is highly soluble because of rapid buffering in whole blood. The risk of CO_2 embolization is small. As much as 200 mL of CO_2 injected directly into a peripheral vein may not be lethal, whereas only 20 mL of air may prove to be so. In addition, CO_2 levels in blood and expired air can easily be measured, and its elimination can be facilitated by increasing ventilation. As long as oxygen requirements are met, a high concentration of blood CO_2 can be tolerated. Also, medical grade CO_2 is readily available and inexpensive.

It is for these reasons that the following gases are unsatisfactory for pneumoperitoneum: N_2O (does not cause pain intra-abdominally but does not suppress combustion); oxygen (flammable); helium, air, and nitrogen (each has no hemodynamic or acid–base sequelae but can cause gas emboli); and argon (adverse effect on hepatic blood flow, emboli).

It should be emphasized, however, that CO_2 plays a dual role in the body, and it is not inert. Under normal circumstances, it is an intrinsic waste product of metabolism. During laparoscopic

surgery, it acts as an extrinsic drug often present in quantities far larger than the body is physiologically capable of generating even with the most extreme exercise or hypermetabolic state.

The disadvantages mainly stem from the fact that CO_2 is not inert, and it has contradictory roles as an endogenous chemical and as an exogenous foreign substance. Changes in its concentration and tensions have enormous biochemical and physiologic consequences. Changes at the local tissue level are often at odds with the overall systemic effect. It causes direct peritoneal irritation and pain during laparoscopy under local anesthesia because it transiently forms carbonic acid when in contact with the moist peritoneum. In addition, CO_2 is not very soluble in the absence of red blood cells, and therefore, it can remain in gaseous form intraperitoneally (subhepatic) after laparoscopy, causing referred shoulder pain. Hypercarbia and respiratory acidosis occur when the buffering capacity of blood is temporarily exceeded. In addition, CO_2 exerts widespread local and systemic effects that may manifest overall as hypertension, tachycardia, cerebral vasodilation, hypercarbia, and respiratory acidosis.

Malhotra V, ed. *Anesthesia for Renal and Genito-Urologic Surgery*. New York: McGraw-Hill; 1996:157.

Menes T, Spivak H. Laparoscopy: searching for the proper insufflation gas. *Surg Endosc*. 2000;14(11):1050–1056.

Tsereteli Z, Terry ML, Bowers SP, et al. Prospective randomized clinical trial comparing nitrous oxide and carbon dioxide pneumoperitoneum for laparoscopic surgery. *J Am Coll Surg*. 2002;195(2):173–180.

A.10. How much endogenous CO_2 is produced at basal level and at maximal exercise?

CO_2 and water are the major end products of aerobic metabolism in the mitochondria of the cells. Carbonic acid, the major acid produced in the body, is uniquely volatile, and

therefore, it must be eliminated mainly by the lungs. (Other acids are eliminated by the kidney.)

At basal rate, an average adult manufactures approximately 200 mL of CO_2 per minute (while consuming 250 mL of oxygen) or 12 L of CO_2 (35 g) per hour. At maximal metabolic rate, it is estimated that the body can produce, transport, and excrete 90 to 100 L per hour, an 800% increase over the basal rate.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:151–169.

A.11. How much CO_2 is stored in the body? Where is it stored? Of what significance is this to laparoscopy?

The body contains approximately 120 L of stored CO_2, most of it in the form of carbonate ion in bone. (This is approximately 100 times the amount of stored oxygen.) CO_2 in the blood is in equilibrium with CO_2 in different tissues. The rate of uptake and distribution of CO_2 from the blood (where it exists as bicarbonate ion) depends on the perfusion and storage capacity of those different tissues. The well-perfused tissues, including brain, kidneys, and blood, come to rapid equilibrium. The medium-perfused compartment consists mainly of resting skeletal muscle. The slowly perfused compartment, mainly fat and bone (where it exists as the carbonate ion), has the largest CO_2 storage capacity. In contrast to rapidly changing oxygen levels, CO_2 levels reach equilibrium more slowly.

These storage sites serve to buffer and stabilize blood CO_2 levels because they provide a place for excess CO_2 to "park" until ventilation can catch up and restore equilibrium. The increase in CO_2 storage during laparoscopy is illustrated clinically by the decelerating rate of rise in Et_{CO_2} despite

continuing insufflation. Blood or end-tidal CO_2 levels increase rapidly at first and plateau between 15 and 35 minutes despite continuing low flow insufflation. At constant ventilation, CO_2 levels increase but not as much as if no simultaneous storage processes were occurring. But if ventilation is increased to keep CO_2 constant, then the increase needed is only approximately 40% of the predicted volume of ventilation because of the drain off of CO_2 into the storage sites.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:151–169.

Seed RF, Shakespeare TF, Muldoon MJ. Carbon dioxide homeostasis during anaesthesia for laparoscopy. *Anaesthesia*. 1970;25:223–231.

A.12. Describe the diffusion and solubility properties of CO_2 and their significance in laparoscopy.

Diffusion describes the process by which gases travel from an area of higher partial pressure to one of lower partial pressure. For a gaseous environment, Graham law states that the rate of diffusion of a gas is inversely proportional to the square root of its density (i.e., the smaller the molecule, the more easily it will diffuse).

When that same gas molecule arrives at an aqueous membrane (e.g., a gas–liquid interface), the solubility of that gas in water now becomes the major factor in determining its diffusing capacity (as shown in **Table 26.1**). The water solubility of CO_2 is 24 times that of oxygen, whereas the diffusion capacity of CO_2 is 20.5 times that of oxygen. The capacity of a gas to diffuse across an aqueous membrane is directly proportional to its solubility in water and inversely proportional to its molecular weight. However, the actual movement of that gas across the aqueous membrane depends not only on its diffusing capacity but also more importantly on the

pressure gradient across that membrane (**Table 26.1**).

TABLE 26.1 Influence of Physical Properties on the Diffusion of Gas through a Gas–Liquid Interface

Gas	Molecular Weight	Density Relative to O_2	Solubility Relative to O_2	Water Diffusion Capacity Relative to O_2
O_2	32	1.0	1.0	1.0
N_2	28	0.88	0.515	0.55
CO_2	44	1.37	24.0	20.5
N_2O	44	1.37	16.3	14.0
He	4	0.125	0.37	1.05

CO_2, carbon dioxide; He, helium; N_2, dinitrogen; N_2O; nitrous oxide; O_2, oxygen.

The fate of CO_2 gas insufflated into the peritoneal cavity is the same that would occur in any other closed but distensible cavity. The pressure obtained within the cavity varies directly with the volume of gas insufflated and indirectly with the compliance of the closed cavity.

Therefore, the ability of CO_2 to move from the closed peritoneal cavity to the lungs for excretion is dependent on its intrinsic diffusion and solubility properties, the rate of continuing CO_2 insufflation, the surface area of the cavity, and the partial pressure difference across membranes.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:151–169.

McHoney M, Corizia L, Eaton S, et al. Carbon dioxide elimination during laparoscopy in children is age dependent. *J Pediatr Surg*. 2003;38:105–110.

A.13. Is CO_2 soluble in water or plasma? Is it soluble in blood? Why?

CO_2 is relatively insoluble in plasma, interstitial fluid, and water. (Think of the rapid escape of gas from a freshly opened

carbonated soft drink.) The solubility of CO_2 in water at 37°C (98.6°F) is only 0.03 mmol/L/mmHg. This must be contrasted to the very high solubility of CO_2 in whole blood. This extremely important distinction exists because of a zinc-containing enzyme, carbonic anhydrase, that exists within the erythrocyte but not at all in plasma.

$$H_2O + CO_2 \xrightarrow{\text{carbonic anhydrase}} H_2CO_3 \rightarrow H^+ + HCO_3^-$$

In the equation shown, carbonic anhydrase catalyzes the left side of the equation (i.e., the hydration of CO_2 to $H_2CO_3^-$). Once formed, carbonic acid is unstable and immediately dissociates into H^+ and HCO_3^-. It is estimated that without carbonic anhydrase, it would take 200 seconds at 38°C (100.4°F) for the previous reaction to come to 10% equilibrium. Because blood travels through the pulmonary capillaries in less than 1 second, carbonic anhydrase speeds up the reaction by a factor of 7,500 times.

Carbonic anhydrase, therefore, allows the insufflated CO_2 gas to be dissolved and carried as bicarbonate in the blood. The process is reversed in the lungs, and the reconstituted CO_2 gas is removed by respiration.

Christian G, Greene NM. Blood carbonic anhydrase activity in anesthetized man. *Anesthesiology*. 1962;23: 179–186.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:151–169.

B. Preoperative Evaluation and Preparation

B.1. What do you want to know about this patient's history and physical condition that may affect whether or not you clear him for robotic surgery?

All patient comorbidities must be evaluated to ensure optimal pharmacologic management preoperatively. Because of this patient's advanced age, it is best to form one's own observations of his mental and physical condition. Is he confused, short of breath, kyphoscoliotic, and so forth? A glimpse at where and how this patient's body weight is distributed means more than just knowing that he weighs 120 kg. Ask about smoking, wheezing, any change in exercise tolerance, cough, recent upper respiratory infection, or change in medications. Perform your usual preoperative evaluation and obtain any consultations that may be informative. Consult with the surgeon regarding the need for appropriate preoperative antibiotics. Does he need pulmonary function tests or an echocardiogram or cardiac stress test? Is he as "well-tuned" as he can be? Find out when his retinal detachments were repaired and if intraocular gas was used.

Efron DT, Bender JS. Laparoscopic surgery in older adults. *J Am Geriatr Soc*. 2001;49:658–663.

B.2. What factors increase this patient's risk of pulmonary complications?

- *The robotic procedure itself*. The steep Trendelenburg position and the increased intraperitoneal volumes and pressures in a paralyzed, mechanically ventilated patient cause respiratory dysfunction. Insufflation pressures should not exceed 12 to 15 mmHg. Lower pressures are especially advantageous in American Society of Anesthesiologists (ASA) class III and IV patients with diminished cardiopulmonary reserve. In addition, an increased CO_2 load might call for respiratory minute volumes that are so large that further cardiopulmonary compromise occurs. In addition, the robotic procedure itself, including docking and undocking, adds additional immobile time under anesthesia.

- *Age.* Pulmonary function declines with age, especially in a patient older than age 70 years.
- *Smoking/chronic obstructive pulmonary disease (COPD).* Smokers have increased tracheobronchial secretions with decreased ciliary transport function. They may already have significant pulmonary dysfunction, which may be manifested by diminished exercise tolerance. The forced vital capacity may be diminished in restrictive pulmonary disease, whereas the forced expired volume in 1 second is likely to be decreased in obstructive pulmonary disease.
- *Obesity.* Obesity compounds the problems of immobility and increased intra-abdominal pressure in the Trendelenburg position, possibly for many hours. Excessive weight and pressure on the diaphragm and lung bases can lead to marked ventilation and perfusion abnormalities, difficulty in inserting trocars, upward displacement of the carina (leading to possible endobronchial intubation), barotrauma, and so forth.
- *Overhydration*. Patients often experience oliguria during laparoscopy. This may be interpreted as insufficient hydration, and a relative overhydration with IV fluids may ensue. Unless frank pulmonary edema occurs, this cause of mild or moderate respiratory distress in the PACU may not be recognized without a chest x-ray film.

Kendall AP, Bhatt S, Oh TE. Pulmonary consequences of carbon dioxide insufflation for laparoscopic cholecystectomies. *Anaesthesia*. 1995;50:286–289.

B.3. What laboratory tests should be performed preoperatively?

Basic tests should include complete blood count, urinalysis, clotting functions, electrocardiogram (ECG), and blood typing and screening. In addition, baseline electrolytes, chemistries, and renal function tests (blood urea nitrogen, creatinine) should

be obtained because of the possibility of oliguria during a long laparoscopy. Baseline pulmonary function tests, arterial blood gas measurement, and oxygen saturation values while breathing room air would be helpful in this patient. Markedly abnormal values might suggest the need for bronchodilators, antibiotics, postural drainage, and a delay in surgery until pulmonary function is optimal for this particular patient. Baseline chest films are necessary not only to rule out active disease but also for postoperative comparison of acute changes such as subcutaneous or mediastinal emphysema, pneumothorax, or interstitial or pulmonary edema. The presence of bullae on preoperative chest x-ray films may represent a contraindication to laparoscopic surgery because of the accompanying large tidal volumes and high intrathoracic pressures.

In patients with cardiac issues, echocardiogram, stress test, and cardiology clearance may be advisable.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2236–2250.

B.4. What specific information should the patient be given about robotic surgery before obtaining informed consent?

In addition to the usual general complications of the planned surgery and anesthesia, the patient must also be told of the complications unique to robotic laparoscopy, and consent for possible open laparotomy must be obtained. Emergency laparotomy may be required in the event of complications such as hemorrhage, organ perforation, or anatomic or technical difficulties.

B.5. What additional procedures should be done before surgery?

Although the surgery is described as minimally invasive, the

patient must be ready for maximally invasive surgery if necessary. Therefore, the patient must comply with preoperative orders regarding the following:

- Diet—clear liquids may be ingested up to 2 hours before procedures requiring general anesthesia, regional anesthesia, or procedural sedation and anesthesia. A light meal may be ingested for up to 6 hours before elective procedures requiring anesthesia. Additional fasting time, up to 8 hours or more, may be needed in cases of patient intake of fried foods, fatty foods, or meat.
- A complete bowel preparation is necessary.
- Preoperative antibiotics, as per surgeon

American Society of Anesthesiologists. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists Task Force on preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration. *Anesthesiology*. 2017;126:376–393.

B.6. What are the three major forces that uniquely alter the patient's physiology during robotic laparoscopy?

- *Pneumoperitoneum* and problems related to the creation, maintenance, and consequences of the increase in intra-abdominal pressure and volume
- CO_2, including its chemical and physical properties and its local and systemic effects
- Extremes of patient *positioning* on the operating table, which in this case will be steep Trendelenburg with total immobility and inaccessibility to the patient's limbs.

It is vital that the anesthesiologist have a thorough understanding of the physiologic consequences of changes in these three forces. Separately or in combination, they have profound effects on the patient's hemodynamic, respiratory, and metabolic functions. The early gynecologic laparoscopies were

usually brief, and they were performed on young, healthy women who tolerated these physiologic trespasses with nearly insignificant changes. These same three forces, however, may produce significant physiologic changes in long, complex procedures in older, sicker patients who may be less able to compensate.

Henny CP, Hofland J. Laparoscopic surgery: pitfalls due to anesthesia, positioning, and pneumoperitoneum. *Surg Endosc*. 2005;19(9):1163–1171.

O'Malley C, Cunningham AJ. Physiologic changes during laparoscopy. *Anesthesiol Clin North Am*. 2001;19(1):1–19.

Ost MC, Tan BJ, Lee BR. Urological laparoscopy: basic physiological considerations and immunological consequences. *J Urol*. 2005;174(4 pt 1):1183–1188.

Sosa RE, Weingram J. Physiologic considerations in laparoscopic surgery. *J Endourol*. 1992;6:285–287.

C. Intraoperative Management

C.1. What is the anesthetic technique of choice for robotic-assisted laparoscopy? Why?

The technique of choice for robotic-assisted laparoscopy is general anesthesia with a cuffed endotracheal tube and controlled positive pressure ventilation because of the following reasons:

- The duration of the procedure may be long.
- The Trendelenburg position may cause respiratory compromise and dyspnea in the awake or in the spontaneously breathing patient with abdominal contents under pressure. The obese patient may be especially uncomfortable in this position.
- A nasogastric or orogastric tube, which may be difficult to insert in a conscious patient, is necessary to decompress the stomach and minimize the risk of aspiration or perforation by

trocars. CO_2, as well as N_2O, diffuses into the stomach.

- However, perhaps the most important reason relates to muscle relaxation. Muscle relaxation and paralysis are absolutely necessary because the increase in intra-abdominal pressure and splinting of the diaphragm make spontaneous breathing difficult. It provides a quieter surgical field and better surgical exposure. "Bucking" increases negative pressure in the chest, which increases the risk of pneumothorax or gas dissection. Coughing can further increase pressure in the abdomen and cause movement of, and perforation by, intra-abdominal instruments. Any movement of the patient while robotic instruments are docked may lead to devastating injuries. Moreover, muscle relaxation is necessary to control and augment ventilation to compensate for the hypercarbia and respiratory acidosis that result from absorption of CO_2.

Whalley DG, Berrigan MJ. Anesthesia for radical prostatectomy, cystectomy, nephrectomy, pheochromocytoma, and laparoscopic procedures. *Anesthesiol Clin North Am*. 2000;18(4):899–917.

C.2. Can a laryngeal mask airway (LMA) be used?

Although successful use of the LMA has been reported by several British groups for very brief laparoscopic procedures in healthy patients, its use is contraindicated in robotic procedures. The LMA does not provide stable airway control or protect against aspiration. It also limits the ability to apply positive pressure ventilation and interferes with the use of an orogastric tube.

Bapat PP, Verghese C. Laryngeal mask airway and the incidence of regurgitation during gynecological laparoscopies. *Anesth Analg*. 1997;85:139–143.

C.3. What anesthetic agents or adjuvant drugs are recommended for laparoscopy? Are any anesthetic

agents contraindicated?

Almost any combination that provides amnesia, analgesia, and paralysis is suitable.

Use of an antiemetic is recommended to counteract the nausea that results from peritoneal stimulation and bowel distention (secondary to diffusion of CO_2 into the bowel). Small doses of the antiemetic droperidol had been used effectively because it potentiated sedation; was long acting; could be given early in the procedure; and as an α-blocker, helped counteract the hypertensive effects of systemic CO_2. Other antiemetics include the serotonin ($5\text{-}HT_3$) receptor antagonists, ondansetron, and dolasetron. These may be combined with dexamethasone.

Propofol also has an HT_3 antiemetic effect. However, a propofol-based maintenance anesthetic, when combined with neuromuscular block, may not adequately prevent patient awareness. A bispectral index (BIS) monitor may be helpful in that situation.

A vagolytic drug should be at hand because acute stretching of the peritoneum may cause reflex bradycardia. This is more likely to occur in young women than in older adults.

Halothane, although no longer current, was known to cause arrhythmias in the presence of hypercarbia. Hypnotics and sedatives should be used cautiously in older adults because their duration may be prolonged.

Scuderi PE, D'Angelo R, Harris L, et al. Small-dose propofol by continuous infusion does not prevent postoperative vomiting in females undergoing outpatient laparoscopy. *Anesth Analg*. 1997;84:71–75.

Seed RF, Shakespeare TF, Muldoon MJ. Carbon dioxide homeostasis during anaesthesia for laparoscopy. *Anaesthesia*. 1970;25:223–231.

C.4. Should nitrous oxide (N_2O) be used during laparoscopy? What are the pros and cons? Does N_2O

cause bowel distention during laparoscopy? Does N_2O cause nausea and vomiting after laparoscopy?

The use of N_2O in laparoscopy has been considered controversial because of its effects on bowel distention during surgery and nausea and vomiting postoperatively.

In examining the issue of bowel distention with N_2O, note that the diffusion capacity of N_2O is approximately 14 times that of oxygen and 28 times that of nitrogen (see **Table 26.1**). Therefore, in a closed space that contains air, N_2O enters faster than N_2 can leave, thereby increasing the size of the closed space. If the walls of that space cannot expand, then the pressure within that space will rise. It has been shown that the volume of an enclosed intestinal air pocket can be doubled by the inhalation of 70% N_2O for 2 hours and tripled in 4 hours. When N_2O is limited to 50%, pocket volume increases no more than 50%. A much more rapid increase in gas volume occurs in the pleural space, where volume was shown to double in 10 minutes, triple in 45 minutes, and quadruple in 2 hours. The faster rate of pleural gas expansion as compared to bowel gas expansion may in part be due to the greater blood flow to the pleura and possibly due to direct diffusion of N_2O from the alveoli adjacent to the pleura.

However, during laparoscopy, we are concerned about CO_2 pockets and not air pockets. N_2O, which has a diffusion capacity almost as great as CO_2, will diffuse from the bloodstream into the intraperitoneal pocket of 100% CO_2 at a rate determined by its solubility in water, its diffusing capacity through an aqueous membrane, and its pressure gradients (as discussed in section A.12). Similarly, CO_2 will leave the peritoneal cavity according to its pressure gradients and solubility and diffusion characteristics. Eventually, the amount of N_2O found in the

peritoneal cavity can be significant, and theoretically, it can form an ignition hazard. However, Hunter et al. state that it is necessary for methane or hydrogen to occupy at least 5.5% of the gas volume for N_2O to support combustion, a condition that does not naturally occur.

In the situation of an air pocket in the bowel, it is well known that N_2O will diffuse in according to its gradients, thereby enlarging the pocket. However, even in the absence of N_2O, CO_2 also will diffuse into this pocket and expand it in a manner that is clinically indistinguishable from N_2O.

N_2O is often blamed for a distended bowel during laparoscopy; however, CO_2 is equally capable of diffusing into and distending the bowel. In a double-blinded study of bowel distention in patients undergoing laparoscopic cholecystectomy with either isoflurane 70%-N_2O-oxygen or isoflurane-air-oxygen, the surgeon was able to identify the use of N_2O correctly only 44% of the time. In addition, postoperative nausea and vomiting was independent of the use of N_2O because the incidence was similar in both groups. Another study found no difference in the incidence of postoperative nausea and vomiting between groups receiving propofol-air-oxygen or propofol-N_2O-oxygen in gynecologic laparoscopy. In fact, the propofol-N_2O-oxygen group had the advantages of significantly more rapid emergence, using 30% less propofol, additional analgesia, and less risk of awareness.

Because of these issues, it is recommended that N_2O, if used at all, be limited to not more than 50% of the inspired mixture. Alternatively, a mixture of 75% air and 25% oxygen (fraction of inspired oxygen [F_{IO_2}] = 40%) may be a wiser choice.

Arellano RJ, Pole ML, Rafuse SE, et al. Omission of nitrous oxide from a propofol-based anesthetic does not affect the recovery of women undergoing

outpatient gynecologic surgery. *Anesthesiology*. 2000;93(2):332–339.

Diemunsch PA, Torp KD, Van Dorsselaer T, et al. Nitrous oxide fraction in the carbon dioxide pneumoperitoneum during laparoscopy under general inhaled anesthesia in pigs. *Anesth Analg*. 2000;90:951–953.

Diemunsch PA, Van Dorsselaer T, Torp KD, et al. Calibrated pneumoperitoneal venting to prevent N_2O accumulation in the CO_2 pneumoperitoneum during laparoscopy with inhaled anesthesia: an experimental study in pigs. *Anesth Analg*. 2002;94:1014–1018.

Eger EI II, Saidman LJ. Hazards of nitrous oxide anesthesia in bowel obstruction and pneumothorax. *Anesthesiology*. 1965;26:61–66.

Hunter JG, Staheli J, Oddsdotti M, et al. Nitrous oxide pneumoperitoneum revisited. Is there a risk of combustion? *Surg Endosc*. 1995;9:501–504.

Munson ES. Transfer of nitrous oxide into body air cavities. *Br J Anaesth*. 1974;46:202–209.

Sukhani R, Lurie J, Jabamoni R. Propofol for ambulatory gynecologic laparoscopy: does omission of nitrous oxide alter postoperative emetic sequelae and recovery? *Anesth Analg*. 1994;78:831–835.

C.5. Can laparoscopy be performed under local or regional anesthesia?

Yes. Although unsuitable for robotic procedures, the use of local or regional anesthesia for very brief diagnostic laparoscopic procedures has been reported. However, under local anesthesia, CO_2 may cause pain intraperitoneally, which is referred to the shoulder. It is for this reason that N_2O, which is nonirritating to the peritoneum, had been used as the insufflating gas without cautery. However, rapid peritoneal distention causes nausea that may be exacerbated without a nasogastric tube. Because of patient discomfort, the surgeon may obtain suboptimal visualization of the surgical field. Also, the possibility of having to open the abdomen, although unlikely, speaks against local anesthesia.

Regional anesthesia can be used for laparoscopy. However, it too has serious drawbacks. It requires a high level of sensory block, possibly causing dyspnea in the Trendelenburg position. A nasogastric tube may not be tolerated. Hyperventilation in

response to hypercarbia may cause too much movement in the surgical field, and spontaneous ventilation may be inadequate to compensate for hypercarbia in the Trendelenburg position.

Regional anesthesia may also be combined with general anesthesia. Because the systemic response to hypercarbia is mediated primarily through sympathetic stimulation, the sympathetic denervation resulting from high regional anesthesia will result in hypotension and decreased cardiac output rather than the hypertension and increased cardiac output usually seen with general anesthesia.

Use of IV analgesics or propofol during regional anesthesia may result in respiratory depression or obstruction, especially in steep Trendelenburg position. Hypoxia in the presence of hypercarbia may have serious cardiovascular consequences.

Collins LM, Vaghadia H. Regional anesthesia for laparoscopy. *Anesthesiol Clin North Am*. 2001;19(1):43–55.

Vaghadia H, Solylo MA, Henderson CL, et al. Selective spinal anesthesia for outpatient laparoscopy. II: epinephrine and spinal cord function. *Can J Anaesth*. 2001;48:261–266.

C.6. What monitors and devices would you apply to the patient? Why?

The usual intraoperative monitors, including standard five-lead ECG with ST trending; systemic blood pressure (BP) using automated oscillometry; pulse oximetry; capnography; a nerve stimulator; and indicators of inspired oxygen fraction, minute ventilation, and peak airway pressures are necessary. An esophageal probe may be used for both temperature monitoring (optimal at the distal esophagus) and for breath, heart, and murmur sound monitoring (at heart level). Body temperature should be maintained with a forced warm air heating blanket, warmed IV fluids, or other means. (For robotic procedures, the warming blanket may be placed under the patient.) Rarely,

central venous pressure (CVP), pulmonary artery pressure, pulmonary artery occlusion pressure (PAOP), and cardiac output may be measured in patients with severe cardiac or pulmonary abnormalities. A BIS monitor may be used. Other possibilities include Doppler, transesophageal echocardiography, and noninvasive assessment of cardiac output by thoracic bioimpedance or thoracic ultrasound. An arterial line is suggested for longer, more complex procedures in sicker (ASA classes III and IV) patients. All monitors must be placed and checked before the patient becomes secured to the table and inaccessible as the robot is docked.

Intermittent sequential compression antiembolic stockings should be applied. Shoulder braces or adhesive taping are used for support in the Trendelenburg position. After induction, a nasogastric or orogastric tube and a Foley catheter are inserted for decompression of stomach and bladder. Use of an orogastric tube is not optional. In addition to the danger of regurgitation from the increased abdominal pressure, there are reports of stomach perforation by trocars. The orogastric tube should not be clamped after initial placement, and intermittent suctioning should continue because CO_2 gas continues to diffuse into the stomach and distend it.

In addition to mechanical monitoring, visual and tactile monitoring should be attempted if the position of the robotic arms allow it. Skin color, skin turgor, and capillary refill should be monitored because they can change abruptly. The head, neck, and upper chest may assume a purplish color in the dependent position, especially during hypercarbia. The upper chest wall may not be accessible to check for subcutaneous emphysema. The cornea and conjunctiva should be checked periodically for edema, especially in the Trendelenburg position, and also whenever oliguria occurs because the extent of the edema may influence your decision on when to extubate.

It is important to maintain accurate data on the volume of fluids infused, and the patient's hourly or half-hourly urine output, along with observations on its color and concentration. Despite adequate hydration, oliguria frequently occurs during pneumoperitoneum, especially at intra-abdominal pressures approaching or exceeding 15 mmHg. The acute increase in intra-abdominal pressure is transmitted to the kidneys and is believed to cause shunting from the cortex to the medulla of the kidney, resulting in a decreased urine output. Diuresis usually occurs rapidly on release of intra-abdominal pressure.

Jacobs VR, Morrison JE Jr, Mettler L, et al. Measurement of CO_2 hypothermia during laparoscopy and pelviscopy: how cold it gets and how to prevent it? *J Am Assoc Gynecol Laparosc*. 1999;6:289–295.

Ogunnaike BO, Jones SB, Jones DB, et al. Anesthetic considerations for bariatric surgery. *Anesth Analg*. 2002;95(6):1793–1805.

Tournadre JP, Chassard D, Berrada KR, et al. Effect of pneumoperitoneum and Trendelenburg position on gastro-oesophageal reflux and lower oesophageal sphincter pressure. *Br J Anaesth*. 1996;76:130–132.

C.7. How is the patient to be positioned? What special precautions are required for robotic laparoscopy?

In pyeloplasties, the side to be worked on is usually elevated, enabling gravity to assist in separating the organs and allowing blood to pool away from the operative field. For other laparoscopies, the patient may be supine; in the Trendelenburg position for urology; in dorsal lithotomy for gynecology; in the head-up position for upper gastrointestinal and biliary tract surgery; and in the lateral decubitus position for thoracoscopy, nephrectomy, and adrenalectomy. For standard conventional laparoscopy, you may or may not be able to keep one or both arms out on boards.

Robotically assisted laparoscopies require careful attention to detail before the robot is docked because no movement of any kind should be possible afterward. Thus, it is especially

important to check that any IV or arterial lines as well as BP cuff, ECG leads, and pulse oximeter are functioning properly after the arms have been carefully padded and tucked at the patient's sides. This must be done before the patient is lowered into Trendelenburg position. Once the robot is locked into position, you will no longer have access to check the arms or look under the drapes. It is a good idea to cut off the clamps on the IV tubing that may press into the patient's skin while the arms are tightly tucked.

Next, after satisfactory general endotracheal anesthesia has been obtained, the surgeons must secure the patient's position on the table so that he does not slide when placed in extreme Trendelenburg position. One technique is to place towels or sponges across the patient's chest, followed by crisscrossing of wide adhesive tape reaching from one side of the table and patient's chest to the opposite shoulder and opposite side of the table. This X formation is designed to secure the patient to the table. While the surgeons are applying the tape, it is recommended that you put your hand under the chest sponge to ensure that the tape is not tight enough to restrict chest expansion. Other techniques such as padded shoulder braces may be used instead of tape, but the incidence of brachial plexus injury is higher with these.

With the knees flexed in padded leg holders, the patient is now carefully lowered into steep Trendelenburg position. Robotic laparoscopy frequently requires steeper Trendelenburg positioning than conventional laparoscopy, resulting in a greater number of positioning injuries. Care must also be taken to ensure that movements of the large bulky robotic arms do not come in contact with the patient.

Kalmar AF, Foubert L, Hendrickx JF, et al. Influence of steep Trendelenburg position and CO_2 pneumoperitoneum on cardiovascular, cerebrovascular, and respiratory homeostasis during robotic prostatectomy. *Br J Anaesth*.

2010;104(4):433–439.

Klauschie J, Wechter ME, Jacob K, et al. Use of anti-skid material and patient-positioning to prevent patient shifting during robotic-assisted gynecologic procedures. *J Minim Invasive Gynecol*. 2010;17(4):504–507.

Phong SV, Koh LK. Anaesthesia for robotic-assisted radical prostatectomy: considerations for laparoscopy in the Trendelenburg position. *Anaesth Intensive Care*. 2007;35(2):281–285.

C.8. How will you ventilate the patient? What are the respiratory and circulatory effects of the Trendelenburg position during laparoscopy?

Respiratory

Vital capacity and FRC are reduced. The abdominal contents restrict movement of the diaphragm, especially in the obese and in older adults. Decreased compliance, increased ventilation-perfusion abnormalities, and cephalad displacement of the mediastinum commonly occur. Upper airway edema and displacement of the endotracheal tube may occur.

Circulatory

In healthy patients, the Trendelenburg position results in minimal circulatory changes. Venous return and cardiac output are increased, whereas CVP, PAOP, SVR, and heart rate are essentially unchanged. In patients with cardiovascular disease, the Trendelenburg position may result in increased CVP, PAOP, and decreased cardiac output. The increase in venous return and myocardial oxygen demand that occurs in severe cardiovascular disease can precipitate acute heart failure.

These respiratory and circulatory changes caused by the Trendelenburg position are further amplified by the CO_2 insufflation. Ventilation may become difficult, especially in obese patients. Use of positive end-expiratory pressure (PEEP) is advised to prevent atelectasis. To prevent peak inspiratory pressures from becoming excessive, switching from volume-

controlled to pressure-controlled ventilation may be warranted. In addition, a prolonged inspiratory duration, such as an inspiratory-to-expiratory (I:E) ratio of 1:1 or 2:1 rather than the conventional 1:2, may provide better gas exchange.

Choi EM, Na S, Choi SH, et al. Comparison of volume-controlled and pressure-controlled ventilation in steep Trendelenburg position for robot-assisted laparoscopic radical prostatectomy. *J Clin Anesth*. 2011;23(3):183–188.

Kim JY, Shin CS, Kim HS, et al. Positive end-expiratory pressure in pressure-controlled ventilation improves ventilatory and oxygenation parameters during laparoscopic cholecystectomy. *Surg Endosc*. 2010;24(5):1099–1103.

Kim MS, Kim NY, Lee KY, et al. The impact of two different inspiratory to expiratory ratios (1:1 and 1:2) on respiratory mechanics and oxygenation during volume-controlled ventilation in robot-assisted laparoscopic radical prostatectomy: a randomized controlled trial. *Can J Anaesth*. 2015;62(9):979–987.

Kim WH, Hahm TS, Kim JA, et al. Prolonged inspiratory time produces better gas exchange in patients undergoing laparoscopic surgery: a randomised trial. *Acta Anaesthesiol Scand*. 2013;57:613–622.

Lestar M, Gunnarsson L, Lagerstrand L, et al. Hemodynamic perturbations during robot-assisted laparoscopic radical prostatectomy in 45° Trendelenburg position. *Anesth Analg*. 2011;113:1069–1075.

Oğurlu M, Küçük M, Bilgin F, et al. Pressure-controlled vs volume-controlled ventilation during laparoscopic gynecologic surgery. *J Minim Invasive Gynecol*. 2010;17(3):295–300.

Russo A, Di Stasio E, Scagliusi A, et al. Positive end-expiratory pressure during laparoscopy: cardiac and respiratory effects. *J Clin Anesth*. 2013;25:314–320.

Tyagi A, Kumar R, Sethi AK, et al. A comparison of pressure-controlled and volume-controlled ventilation for laparoscopic cholecystectomy. *Anaesthesia*. 2011;66:503–508.

C.9. What techniques are available for initial access to the peritoneal cavity? What anesthetic problems can arise during insufflation?

Pneumoperitoneum can be achieved by a “blind” or closed technique of percutaneous insertion of the 2-mm diameter

hollow Veress needle, which after verification of correct positioning, is connected to the CO_2 insufflator.

Alternatively, if previous surgery or adhesions are to be avoided, an "open" approach or periumbilical mini-incision is created, and the blunt-tipped Hasson cannula is inserted without prior pneumoperitoneum. The laparoscope is then inserted through the trocar to verify the intra-abdominal position before insufflation begins.

Before either technique is attempted, the stomach must be decompressed with an orogastric tube and the bladder with a Foley catheter. During insufflation, abdominal distention should be evenly distributed in all four quadrants. CO_2 is insufflated slowly until a pressure of 10 to 15 cm is reached. Respiratory variations of intraperitoneal pressure should be visible, and peak inspiratory pressures will gradually increase as the abdomen distends. It is at this time that the anesthesiologist should be alert to the possibility of vagally mediated reflexes. Bronchospasm, bradycardia, and even sinus arrest have been reported, especially in young women. Visceral and vascular perforations are also well-reported complications, especially with the blind technique. Cardiovascular collapse and gas emboli have been reported when CO_2 has been inadvertently insufflated directly into a blood vessel.

Merlin TL, Hiller JE, Maddern GJ, et al. Systematic review of the safety and effectiveness of methods used to establish pneumoperitoneum in laparoscopic surgery. *Br J Surg*. 2003;90(6):688–679.

Teoh B, Sen R, Abbott J. An evaluation of four tests used to ascertain Veres needle placement at closed laparoscopy. *J Minim Invasive Gynecol*. 2005;12(2):153–158.

Vilos GA, Vilos AG. Safe laparoscopic entry guided by Veress needle CO_2 insufflation pressure. *J Am Assoc Gynecol Laparosc*. 2003;10(3):415–420.

C.10. What intravenous (IV) solution and how much fluid

volume do you plan to infuse?

Large-bore IV catheters should be placed because of the possibility of major hemorrhage. The amount of IV fluid infused is of vital importance, especially in older adults. Transient oliguria during laparoscopy is common. In calculating fluid requirements during laparoscopy, it is important to remember that much less "third spacing" occurs than in open surgery, no fluid loss is caused by evaporation, and the volume of retained (after suctioning) intraperitoneal saline used for irrigation by the surgeon should be added to the final total volume of infused IV fluids. In addition, the intra-abdominal humidification of the insufflated dry CO_2 gas results in only a negligible insensible water loss. Unlike open intraperitoneal cases, our starting fluid replacement is approximately 4 mL/kg/hr of Ringer's lactate solution; as needed, additional fluid is given based on the patient's preoperative hemodynamic status, intraoperative blood loss, and the volume of residual intraperitoneal irrigation fluid used by the surgeon.

After the pneumoperitoneum is released, diuresis occurs promptly and renal function quickly returns to normal (see section C.22).

For robotic laparoscopies, surgeons prefer that IV fluids are minimized until the anastomoses are completed. This keeps excessive fluids out of the surgical field and also helps prevent edema of the face, eyes, and larynx while in the steep Trendelenburg position. At our institution, after the anastomoses are complete, we infuse the majority of the IV hydration, the average blood loss is less than 250 mL, and the usual total fluid replacement is 3 to 3.5 L of lactated Ringer's solution.

Concha MR, Mertz VF, Cortínez LI, et al. The volume of lactated Ringer's solution required to maintain preload and cardiac index during open and laparoscopic surgery. *Anesth Analg*. 2009;108(2):616–622.

London ET, Ho HS, Neuhaus AM, et al. Effect of intravascular volume expansion on renal function during prolonged CO_2 pneumoperitoneum. *Ann Surg*. 2000;231:195–201.

Olsson J, Svensén CH, Hahn RG. The volume kinetics of acetated Ringer's solution during laparoscopic cholecystectomy. *Anesth Analg*. 2004;99(6):1854–1860.

C.11. Under what circumstances should laparoscopy be converted to laparotomy?

Laparotomy should be performed immediately in cases of major bleeding or organ damage. Other circumstances include persistent problems with inadequate exposure, a procedure beyond the surgeon's capability, a procedure taking too long, the inability to create or maintain pneumoperitoneum, patient deterioration, equipment failure, and discovery of other unsuspected disease.

Tabboush ZS. When hypotension during laparoscopic cholecystectomy indicates termination of the laparoscopy. *Anesth Analg*. 1994;79:195–196.

C.12. What is the arterial to end-tidal CO_2 gradient ($PaCO_2$–$EtCO_2$) in the normal awake patient? What is the cause of the gradient? Does the gradient change during laparoscopy? Why?

In the awake person at rest, the normal arterial to end-tidal co_2 gradient is small, ranging from 2 to 6 mmHg. The gradient and its variations are measures of the alveolar dead space. The gradient is the sum of the difference between the arterial CO_2 ($Paco_2$) and alveolar CO_2 ($PAco_2$) plus the difference between the alveolar CO_2 ($PAco_2$) and end-tidal CO2 ($Etco_2$). It is commonly increased in emphysema. The difference is increased when underperfused alveoli are ventilated, as often occurs during hyperventilation in laparoscopy.

The total physiologic dead space consists of the anatomic

dead space (passageways that do not participate in gas exchange, approximately 150 mL) and the alveolar dead space (i.e., underperfused alveoli). The alveolar dead space gas is expired at the same time as the alveolar ideal gas from well-perfused alveoli in equilibrium with pulmonary capillary blood. The dilution of the ideal alveolar gas by the alveolar dead space gas is represented by the end-tidal CO_2.

Some of the factors resulting in a relative increase in ventilation:perfusion ratio include mechanical ventilation, hyperventilation, rapid or shallow ventilation, and the Trendelenburg or lateral decubitus position.

Some of the factors resulting in a relative decrease in ventilation:perfusion ratio include hypotension, decreased cardiac output, myocardial depression from inhalational anesthetics, pulmonary emboli, high positive airway pressure, and ablation of the hypoxic pulmonary vasoconstriction reflex.

Christensen MA, Bloom J, Sutton KR. Comparing arterial and end-tidal carbon dioxide values in hyperventilated neurosurgical patients. *Am J Crit Care*. 1995;4:116–121.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:291–324.

C.13. Is an arterial line necessary? Why? Does end-tidal CO_2 tension accurately reflect arterial CO_2 tension? Under what circumstances may the $Et CO_2$ exceed the $Pa CO_2$? Why?

An arterial line is recommended whenever the laparoscopic procedure is unusually complex or long or when the patient has significant cardiopulmonary disease. In such cases, ventilation-perfusion abnormalities, intraoperative hypoxemia, marked hypercarbia, or high airway pressures may be expected. During these situations, and possibly in all laparoscopies, an unsteady state exists with respect to CO_2, and the assumption that $Et CO_2$

may accurately reflect a predictable relationship to $PaCO_2$ is not valid.

End-tidal CO_2 tension can either estimate $PaCO_2$, frequently underestimate $PaCO_2$, or infrequently overestimate $PaCO_2$. Furthermore, the values for these two measurements do not always change proportionally or do they always change in the same direction. The relationship between $EtCO_2$ and $PaCO_2$ varies during the course of the procedure. At the beginning of insufflation, $EtCO_2$ can be used as a rough estimate of $PaCO_2$. However, when redistribution of the excess CO_2 from the well-perfused tissues to the less well-perfused tissues begins, $EtCO_2$ begins to underestimate the $PaCO_2$. Characteristically, the arterial to end-tidal CO_2 difference progressively increases as hyperventilation (and dead space) increases.

Especially during strenuous exercise when metabolic CO_2 production is increased and during laparoscopy when excess exogenous CO_2 must be excreted, the $EtCO_2$ may be found to exceed the $PaCO_2$. This condition has also been reported in a hyperventilating patient during cesarean section. This occurs because the $PaCO_2$ fluctuates during each deep breath and may not represent the highest value at that instant, whereas the $EtCO_2$ shows the maximal value (i.e., because of tidal ventilation and pulsatile blood flow in exercise, $EtCO_2$ may exceed mean alveolar and arterial CO_2).

Bhavani-Shankar K, Steinbrook RA, Brooks DC, et al. Arterial to end-tidal carbon dioxide pressure difference during laparoscopic surgery in pregnancy. *Anesthesiology*. 2000;93(2):370–373.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:291–324.

Scheid P, Meyer M, Piiper J. Arterial-expired PCO_2 differences in the dog during acute hypercapnia. *J Appl Physiol Respir Environ Exerc Physiol*. 1979;47:1074–1078.

Strang CM, Hachenberg T, Fredén F, et al. Development of atelectasis and arterial to end-tidal PCO_2 difference in a porcine model of pneumoperitoneum. *Br J Anaesth*. 2009;103(2):298–303.

Wulkan ML, Vasudevan SA. Is end-tidal CO_2 an accurate measure of arterial CO_2 during laparoscopic procedures in children and neonates with cyanotic congenital heart disease? *J Pediatr Surg*. 2001;36(8):1234–1236.

C.14. What are the possible causes of hypercarbia?

- Hypoventilation
- CO_2 in the inspired gas—rebreathing endogenous CO_2 will increase $PaCO_2$ by 3 to 6 mmHg per minute.
- Increased endogenous CO_2 production or exogenous CO_2 supply—occurring in the hypermetabolic states of malignant hyperpyrexia, fever, and hyperthyroidism or occurring during laparoscopy and following the administration of bicarbonate or lactate (One ampule of 50 mEq of bicarbonate liberates more than 1 L of CO_2.)
- Increased dead space (rare) as in pulmonary embolism, ventilation of a lung cyst, or advanced COPD

Lumb AB. *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:319–326.

Wolf JS Jr, Clayman RV, Monk TG, et al. Carbon dioxide absorption during laparoscopic pelvic operation. *J Am Coll Surg*. 1995;180:555–560.

C.15. What factors play a role in the unusually rapid and marked elevation of CO_2 that is sometimes seen in laparoscopy?

- Patients with significant cardiopulmonary disease
- Intra-abdominal pressure greater than 15 mmHg
- Presence of subcutaneous emphysema
- Retroperitoneal rather than intraperitoneal approach
- Long duration of laparoscopy

Bozkurt P, Kaya G, Yeker Y, et al. Arterial carbon dioxide markedly increases during diagnostic laparoscopy in portal hypertensive children. *Anesth Analg*.

2002;95(5):1236–1240.

Liem MS, Kallewaard JW, de Smet AM, et al. Does hypercarbia develop faster during laparoscopic herniorrhaphy than during laparoscopic cholecystectomy? Assessment with continuous blood gas monitoring. *Anesth Analg*. 1995;81:1243–1249.

C.16. How rapidly does the $PaCO_2$ rise in the apneic patient (endogenous CO_2)? How rapidly does the $PaCO_2$ rise if 5% CO_2 gas is inhaled (exogenous)? How rapidly can the CO_2 rise during laparoscopy? What factors explain the differences?

In the apneic patient, $Paco_2$ rises at the rate of 3 to 6 mmHg per minute. Rebreathing, or inhalation of 5% CO_2 in oxygen, causes a much more rapid rise in $Paco_2$ up to 8 to 10 mmHg per minute. The difference in rate of rise between endogenous and exogenous CO_2 is explained by the presence of large body stores of CO_2. Approximately 120 L of CO_2 exist in the body (100 times the amount for oxygen) distributed among well-perfused tissue (e.g., blood, brain), moderately perfused tissue (e.g., muscle), and poorly perfused tissue (e.g., fat, bone). These storage places adjust slowly to acute CO_2 changes. In the steady state, the amount of CO_2 produced metabolically in the body is equal to the amount expired through the lungs, and there is no change in the body stores of CO_2. During laparoscopy, an unsteady state exists, with the rate of rise of Pco_2 being greatest during the first 20 to 30 minutes. After that time, new equilibrium levels are reached between the different compartments, and the Pco_2 rate of rise is slower.

Frumin et al. studied the hypercarbic state during their classic study of apneic oxygenation. In paralyzed apneic intubated denitrogenated oxygenated patients receiving only thiopental for amnesia, Frumin et al. demonstrated at least a 3 mmHg average

rise in $Paco_2$ per minute and an ultimate $Paco_2$ as high as 250 mmHg (pH 6.72) while maintaining 98% to 100% oxygen saturation after 53 minutes of apnea. They also found that the hypercarbia was accompanied by hypertension; mean arterial pressure rose 26% and then fell 14% after the return of respirations and normocarbia. Other features accompanying apneic hypercarbic hypertension included normal sinus rhythm with an essentially unchanged rate, rising arterial epinephrine and norepinephrine concentrations, and rising arterial potassium levels (which rose still further after ventilation and normocarbia resumed) with unchanged sodium levels.

Frumin MJ, Epstein RM, Cohen G. Apneic oxygenation in man. *Anesthesiology*. 1959;20:789–798.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:319–326.

C.17. What is the net effect of pneumoperitoneum, hypercarbia, and steep Trendelenburg on the cardiovascular system?

The effects of hypercarbia on the circulatory system are complex and often contradictory. At the cellular level, hypercarbia is a direct depressor of myocardial contractility and rate of contraction; it is also a direct stimulant of myocardial irritability and arrhythmicity. These effects may be enhanced by acidosis.

The direct effect of hypercarbia on isolated or denervated blood vessels is a diminished responsiveness to catecholamines and vasodilation especially on the venous side, leading to peripheral pooling, decreased venous return, and decreased cardiac output. The exception to the dilatory effect of hypercarbia and acidosis on blood vessels exists in the pulmonary vessels, which vasoconstrict. It appears, however, that the effects on the pulmonary vessels are actually due to

acidosis rather than hypercarbia because if the pH is kept constant while the P_{CO_2} rises, pulmonary vascular resistance (PVR) does not change.

In the patient, however, the direct or local effects of CO_2 can be overshadowed by a variety of systemic effects. Simultaneous with these local or direct effects, hypercarbia causes profound systemic changes secondary to stimulation of the central nervous system and sympathoadrenal system. The net effect usually includes an increase in cardiac output, heart rate, force of myocardial contraction, BP, and CVP, vasoconstriction in the pulmonary (capacitance) vessels, and a decrease peripheral resistance. The rise in cardiac output of up to 50% exceeds the rise in BP because of the drop in peripheral resistance and increase in blood flow primarily in the cerebral and coronary circulations. This net stimulatory effect accompanies the elevation of Pa_{CO_2} up to approximately 90 mmHg. Above this level, further increases in CO_2 cause a marked drop in response.

In a normal anesthetized human breathing 7% to 15% inspired CO_2, these stimulatory changes were shown to correspond primarily to rising plasma concentrations of epinephrine and norepinephrine. When the sympathoadrenal response was prevented by subarachnoid block, ganglioplegics, or α-adrenergic blockers, the cardiovascular response to inhaled CO_2 were hypotension and decreased cardiac output. The stimulatory response also is diminished by general anesthesia.

Hypercarbia can cause arrhythmias during epinephrine infiltrations or in the presence of halothane but not other anesthetics. Other than in these two circumstances, hypercarbia is not arrhythmogenic unless hypoxia also is present.

The full range of possible effects of hypercarbia on the cardiovascular system are subject to many influences. Healthy (ASA class I) patients are less likely than ASA class III patients

to undergo extreme changes. Similarly, a brief surgical duration, head-up positioning, low intra-abdominal pressures, and intraperitoneal (rather than extraperitoneal) surgery can limit the range of physiologic and metabolic responses to near normal.

In the patient with marginal cardiovascular function, however, peritoneal insufflation can result in a significant increase in cardiac workload. In this situation, transesophageal echocardiography can be a useful noninvasive method to assess left ventricular function.

Arrhythmias such as bradycardia, nodal rhythm, or even asystole can follow rapid peritoneal distention and vagal stimulation. In general, BP, pulse, cardiac output, and CVP will increase up to an intra-abdominal pressure of 15 mmHg. At insufflation pressures of 20 to 30 mmHg, a decrease in BP, cardiac output, and CVP will occur because pressure on the inferior vena cava decreases venous return. Pneumoperitoneum also may induce changes in the cardiac electrical axis, which may affect interpretation of the ECG seen on the monitor during the operation.

Ekici Y, Bozbas H, Karakayali F, et al. Effect of different intra-abdominal pressure levels on QT dispersion in patients undergoing laparoscopic cholecystectomy. *Surg Endosc*. 2009;23:2543–2549.

Falabella A, Moore-Jeffries E, Sullivan MJ, et al. Cardiac function during steep Trendelenburg position and CO_2 pneumoperitoneum for robotic-assisted prostatectomy: a trans-oesophageal Doppler probe study. *Int J Med Robot*. 2007;3(4):312–315.

Hofer CK, Zalunardo MP, Klaghofer R, et al. Changes in intrathoracic blood volume associated with pneumoperitoneum and positioning. *Acta Anaesthesiol Scand*. 2002;46:303–308.

Joshi GP, Hein HA, Mascarenhas WL, et al. Continuous transesophageal echo-Doppler assessment of hemodynamic function during laparoscopic cholecystectomy. *J Clin Anesth*. 2005;17(2):117–121.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:319–326.

Rist M, Hemmerling TM, Rauh R, et al. Influence of pneumoperitoneum and

patient positioning on preload and splanchnic blood volume in laparoscopic surgery of the lower abdomen. *J Clin Anesth*. 2001;13:244–249.

Russo A, Marana E, Viviani D, et al. Diastolic function: the influence of pneumoperitoneum and Trendelenburg positioning during laparoscopic hysterectomy. *Eur J Anaesthesiol*. 2009;26(11):923–927.

C.18. What is the net effect of pneumoperitoneum, hypercarbia, and steep Trendelenburg on the respiratory system?

Hypercarbia and acidosis stimulate the respiratory center both directly and indirectly through chemoreceptors, hormones, and autonomic nerves. In the conscious patient breathing oxygen, the maximal stimulating effect occurs at 100 to 150 mmHg, producing minute volumes of up to 75 L. Above these levels, CO_2 becomes a respiratory depressant. Current anesthetics blunt the stimulatory respiratory response to CO_2. Diethyl ether, however, the only volatile anesthetic known to stimulate respiration, reportedly allowed a patient to continue to breathe spontaneously with an inadvertent P_{CO_2} of 234 mmHg.

In the awake patient, each millimeter of mercury increase in $Paco_2$ increases ventilation by 2 to 3 L per minute (if Pa_{O_2}, is constant). This response is diminished by anesthesia. Hypercarbia also produces bronchodilatation; acidosis, rather than hypercarbia per se, causes pulmonary vascular constriction.

General anesthesia with intubation and mechanical ventilation results in a decrease in FRC, which is caused by loss of muscle tone, diaphragmatic displacement, and loss of thoracic volume. Lung compliance drops, airway pressures increase, and ventilation/perfusion mismatch occurs. However, most patients have no difficulty tolerating these changes. These changes are exaggerated in the Trendelenburg position, especially in older adults, the obese, and those with preexisting cardiopulmonary disease. Intrathoracic, peak inspiratory, and plateau pressures increase and then increase even further when

pneumoperitoneum creates an increase in pressure and volume by pushing abdominal contents cephalad. Endobronchial intubation can occur as a result of cephalad movement of the carina, and it should be ruled out if hypoxemia occurs.

Andersson LE, Bååth M, Thörne A, et al. Effect of carbon dioxide pneumoperitoneum on development of atelectasis during anesthesia, examined by spiral computed tomography. *Anesthesiology*. 2005;102(2):293–299.

Kendall AP, Bhatt S, Oh TE. Pulmonary consequences of carbon dioxide insufflation for laparoscopic cholecystectomies. *Anaesthesia*. 1995;50:286–289.

Lobato EB, Paige GB, Brown MM, et al. Pneumoperitoneum as a risk factor for endobronchial intubation during laparoscopic gynecologic surgery. *Anesth Analg*. 1998;86:301–303.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:291–324.

Rauh R, Hemmerling TM, Rist M, et al. Influence of pneumoperitoneum and patient positioning on respiratory system compliance. *J Clin Anesth*. 2001;13:361–365.

Sprung J, Whalley DG, Falcone T, et al. The effects of tidal volume and respiratory rate on oxygenation and respiratory mechanics during laparoscopy in morbidly obese patients. *Anesth Analg*. 2003;97:268–274.

Whalen FX, Gajic O, Thompson GB, et al. The effects of the alveolar recruitment maneuver and positive end-expiratory pressure on arterial oxygenation during laparoscopic bariatric surgery. *Anesth Analg*. 2006;102:298–305.

C.19. What is the net effect of pneumoperitoneum, hypercarbia, and steep Trendelenburg on the central nervous system?

The brain is particularly sensitive to changes in Pa_{CO_2}. Slight elevations of CO_2 cause direct cortical depression and increase the threshold for seizures. Higher levels of CO_2 (25% to 30%) stimulate subcortical hypothalamic centers, resulting in increased cortical excitability and seizures. This hyperexcitability level is enhanced by adrenal cortical and medullary hormones released secondary to hypercarbia-induced

stimulation of the hypothalamus. Further elevations of CO_2 cause an anesthetic-like state of cortical and subcortical depression.

CO_2 was first used as an anesthetic by Hickman in 1824 and reintroduced by Leake and Waters in 1928. CO_2 caused an N_2O-like narcosis at approximately 90 to 120 mmHg. However, hypercarbia also causes increased excitability of neurons so that seizures occurred shortly afterward.

CO_2, not H^+, crosses the blood–brain barrier and the brain cell membrane and affects the cell's metabolism. Therefore, a change in $Paco_2$ also causes a rapid change in cerebrospinal fluid (CSF) pH. CO_2 is the most important factor in regulating cerebral blood flow (CBF). The relation between CBF and $Paco_2$ is essentially linear from 20 to 100 mmHg, with maximal vasodilatation occurring at approximately 120 mmHg. Normal CBF is approximately 12% to 15% of cardiac output or 50 mL/100 g/min. For each 1 mmHg increase in $Paco_2$ between 20 and 80 mmHg, CBF increases by 2% to 4%. Hypercarbia decreases cerebral vascular resistance, causing CBF to increase.

Hypercarbia causes an increase in intracranial pressure, probably secondary to vasodilation. When the patient is placed in the Trendelenburg position, venous congestion of the head and neck occurs. Additional increases in intra-abdominal and intrathoracic pressures contribute to further increase intracranial and CSF pressures.

Therefore, an acute rise in intra-abdominal pressure (pneumoperitoneum) causes an immediate rise in intracranial pressure. This occurs through intermediary steps that include compression of the inferior vena cava (resulting in decreased drainage in the lumbar plexus), increased CVP, increased mean arterial pressure, increased intrathoracic pressure, increased venous stasis, increased pressure in the sagittal sinus, and

decreased resorption of CSF. Hypercarbia contributes to the increased intracranial pressure, but hyperventilation will not decrease the elevated intracranial pressure until the elevated intra-abdominal pressure is released.

Intraocular pressure is also increased during Trendelenburg position with pneumoperitoneum but apparently is well tolerated by most patients.

Awad H, Santilli S, Ohr M, et al. The effects of steep Trendelenburg positioning on intraocular pressure during robotic radical prostatectomy. *Anesth Analg*. 2009;109(2):473–478.

Hoshikawa Y, Tsutsumi N, Ohkoshi K, et al. The effect of steep Trendelenburg positioning on intraocular pressure and visual function during robotic-assisted radical prostatectomy. *Br J Ophthalmol*. 2014;98:305–308.

Irgau I, Koyfman Y, Tikellis JI. Elective intraoperative intracranial pressure monitoring during laparoscopic cholecystectomy. *Arch Surg*. 1995;130:1011–1013.

Kalmar AF, Dewaele F, Foubert L, et al. Cerebral haemodynamic physiology during steep Trendelenburg position and CO(2) pneumoperitoneum. *Br J Anaesth*. 2012;108:478–484.

Kim MS, Bai SJ, Lee JR, et al. Increase in intracranial pressure during carbon dioxide pneumoperitoneum with steep Trendelenburg positioning proven by ultrasonographic measurement of optic nerve sheath diameter. *J Endourol*. 2014;28:801–806.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:291–324.

Park EY, Koo BN, Min KT, et al. The effect of pneumoperitoneum in the steep Trendelenburg position on cerebral oxygenation. *Acta Anaesthesiol Scand*. 2009;53(7):895–899.

Schramm P, Treiber AH, Berres M, et al. Time course of cerebrovascular autoregulation during extreme Trendelenburg position for robotic-assisted prostatic surgery. *Anaesthesia*. 2014;69:58–63.

C.20. What are the neuroendocrine changes that occur during laparoscopy?

Excessive intra-abdominal pressure and hypercarbia may activate the sympathoadrenal axis, resulting in increased plasma levels of epinephrine and norepinephrine. Renin, cortisol,

aldosterone, antidiuretic hormone, and atrial natriuretic peptide levels are also increased. In awake patients in the Trendelenburg position, increased secretion of atrial natriuretic peptide occurs, probably in response to increased venous return and atrial stretching. During pneumoperitoneum, however, secretion of atrial natriuretic peptide diminishes, suggesting interference with venous return.

Mann C, Boccara G, Pouzeratte Y, et al. The relationship among carbon dioxide pneumoperitoneum, vasopressin release, and hemodynamic changes. *Anesth Analg*. 1999;89:278–283.

Marana E, Colicci S, Meo F, et al. Neuroendocrine stress response in gynecological laparoscopy: TIVA with propofol versus sevoflurane anesthesia. *J Clin Anesth*. 2010;22(4):250–255.

Mikami O, Fujise K, Matsumoto S, et al. High intra-abdominal pressure increases plasma catecholamine concentrations during pneumoperitoneum for laparoscopic procedures. *Arch Surg*. 1998;133:39–43.

C.21. What is the net effect of pneumoperitoneum, hypercarbia, and steep Trendelenburg on the renal system?

Oliguria has been observed frequently during laparoscopy despite adequate hydration. Although prerenal causes such as hypovolemia, positive pressure ventilation, and PEEP can contribute to oliguria, it is believed that neurohumoral changes (e.g., antidiuretic hormone secretion) secondary to hypercarbia and increased intra-abdominal pressure secondary to insufflation may be responsible for the oliguria that occurs during laparoscopy. Sympathetic stimulation causes a release of catecholamines, resulting in decreased renal cortical blood flow with shunting of blood to the adrenal medulla, constriction of glomerular afferent arterioles, and decreased glomerular filtration rate. It has been shown that when intraperitoneal insufflation reaches a pressure of 15 mmHg, renal cortical blood flow decreases approximately 60% and a reversible 50% drop in

urine volume occurs. In contrast, no decrease in urine output occurred when the abdominal wall was lifted with a force of 15 mmHg during "gasless laparoscopy." It has also been shown that pneumoretroperitoneum, which causes a more gradual increase in intra-abdominal pressure, also caused a more gradual decrease in renal perfusion. Finally, it has been shown that unilateral retroperitoneal insufflation causes decreased renal cortical perfusion of only the ipsilateral kidney if the intra-abdominal pressure is not elevated.

Cho JE, Shim JK, Chang JH, et al. Effect of nicardipine on renal function after robot-assisted laparoscopic radical prostatectomy. *Urology*. 2009;73:1056–1060.

Demyttenaere S, Feldman LS, Fried GM. Effect of pneumoperitoneum on renal perfusion and function: a systematic review. *Surg Endosc*. 2007;21:152–160.

Dunn MD, McDougall EM. Renal physiology. Laparoscopic considerations. *Urol Clin North Am*. 2000;27:609–614.

Hazebroek EJ, de Vos tot Nederveen Cappel R, Gommers D, et al. Antidiuretic hormone release during laparoscopic donor nephrectomy. *Arch Surg*. 2002;137:600–605.

Nguyen NT, Perez RV, Fleming N, et al. Effect of prolonged pneumoperitoneum on intraoperative urine output during laparoscopic gastric bypass. *J Am Coll Surg*. 2002;195:476–483.

Wiesenthal JD, Fazio LM, Perks AE, et al. Effect of pneumoperitoneum on renal tissue oxygenation and blood flow in a rat model. *Urology*. 2011;77:1508.e9–1508.e15.

C.22. What is the net effect of pneumoperitoneum, hypercarbia, and steep Trendelenburg on the bowel and gastrointestinal system?

Although CO_2 directly causes vasodilatation of the splanchnic capillary beds, the increased intra-abdominal pressure of laparoscopy decreases perfusion, increases SVR, impairs gastric submucosal perfusion and metabolism, and may cause bowel hypoxia at high pressures. On release of the intra-abdominal

pressure, residual CO_2 again causes vascular dilation, allowing additional CO_2 to enter the bloodstream. Myoelectric activity and recovery from ileus is faster after laparoscopic than after open surgery. The combined effect of the increase in abdominal pressure, stretching of the peritoneum by insufflation, and diffusion of CO_2 into bowel is probably responsible for any postoperative nausea.

Böhm B, Milsom JW, Fazio VW. Postoperative intestinal motility following conventional and laparoscopic intestinal surgery. *Arch Surg*. 1995;130:415–419.

Meierhenrich R, Gauss A, Vandenesch P, et al. The effects of intraabdominally insufflated carbon dioxide on hepatic blood flow during laparoscopic surgery assessed by transesophageal echocardiography. *Anesth Analg*. 2005;100:340–347.

Schwarte LA, Scheeren TW, Lorenz C, et al. Moderate increase in intraabdominal pressure attenuates gastric mucosal oxygen saturation in patients undergoing laparoscopy. *Anesthesiology*. 2004;100:1081–1087.

Takagi S. Hepatic and portal vein blood flow during carbon dioxide pneumoperitoneum for laparoscopic hepatectomy. *Surg Endosc*. 1998;12:427–431.

Trencheva K, Dhar P, Sonoda T, et al. Physiologic effects of simultaneous carbon dioxide insufflation by laparoscopy and colonoscopy: prospective evaluation. *Surg Endosc*. 2011;25:3279–3285.

C.23. How would you recognize a CO_2 embolism during laparoscopy? How does this differ from an air embolism? Why should N_2O be discontinued during suspected embolization? Will N_2O increase the size of CO_2 emboli?

The incidence of venous gas embolism is less in robotic-assisted laparoscopic radical prostatectomies than in radical retropubic prostatectomies. It is more likely to occur during the transection of the deep dorsal venous plexus than during the initial insufflation.

Gas embolism can occur whenever the internal pressure of an open vessel is less than the external pressure. Gas embolism may cause increased ventilatory dead space, increased PVR, increased pulmonary artery pressure, and decreased cardiac output. Early signs include a rapid drop in end-tidal CO_2 and Pa_{O_2} and an increased Pa_{CO_2}. During laparoscopy, insufflation of a large amount of CO_2 directly into a blood vessel can occur initially after blind Veress needle insertion, especially at high pressures. Hypotension, hypoxia, cyanosis, and/or cardiac arrest can occur. If the gas volume is large enough, a "mill-wheel" murmur may be heard through a precordial or esophageal stethoscope. If ventilation is kept constant, a sudden decrease in end-tidal CO_2 may be noted. The most sensitive means to detect gas emboli are the precordial and transesophageal Doppler and transesophageal echocardiography. Aspiration of foamy blood from a central venous catheter is diagnostic.

CO_2 embolism, however, must be distinguished from air embolism, which is a far more ominous event, as shown in **Table 26.2**. CO_2, being extremely soluble in the presence of red blood cells, is much less life-threatening than an identically sized intravascular bolus of air. It has been reported that the lethal volume of intravascular CO_2 gas in cats is 30 times greater than the lethal volume of intravascular air.

TABLE 26.2 Differences between Air and Carbon Dioxide Emboli

Embolism	Air	CO_2
Composition	79% N_2, 21% O_2	100% CO_2
Origin	Vein open to air	No contact with air
Pressure source	Hydrostatic	Insufflator
Solubility	Negligible	Large
Effect of N_2O	Enlarged	Not enlarged

CO_2, carbon dioxide; N_2, dinitrogen; N_2O; nitrous oxide; O_2, oxygen.

Air emboli can be entrained into open veins above the level of the heart (e.g., head and neck surgery, neurosurgery, cesarean section). Other gases that are present, N_2O, for example, will diffuse into that air space according to their diffusion capacities and pressure gradients. Therefore, N_2O will diffuse in, oxygen will be consumed and/or diffuse out, and the size or pressure of the bubble will increase in proportion to the concentration and duration of N_2O being administered until equilibrium is reached. It has been demonstrated that inhalation of 70% N_2O increased the volume of intestinal gas pockets in dogs by twofold in 2 hours and up to threefold in 4 hours. They calculated that at equilibrium, bowel volume could increase up to a maximum of 400%. When N_2O is limited to 50%, however, the size of the gas pocket will not be more than doubled at equilibrium. It has also been demonstrated that inhalation of 68% to 78% N_2O would cause 300 mL of air in the pleural space to double in volume in 10 minutes and to triple in 45 minutes.

A gas bubble composed of 100% CO_2, however, will not enlarge in a patient inhaling 50% or even 75% N_2O because more CO_2 will diffuse out, be absorbed, or be buffered (also more quickly) than N_2O will move in. CO_2 gas has caused fatal embolisms, and N_2O should be discontinued if embolism is suspected. A study using transesophageal echocardiography in 16 patients undergoing laparoscopic cholecystectomy reported that 11 of the 16 patients (5 during peritoneal insufflation and 6 during gallbladder dissection) had a gas embolism, but all were subclinical with no signs of cardiorespiratory instability. In addition, conditions for creating a CO_2 embolism differ from the conditions required for an air embolism. Other than during direct insufflation of CO_2 into a vein, as during Veress needle insufflation, the capillaries and veins within the abdomen are

collapsed by the positive pressure within the abdomen, thereby minimizing the chance for CO_2 to enter open vessels.

Fong J, Gadalla F, Pierri MK, et al. Are Doppler-detected venous emboli during cesarean section air emboli? *Anesth Analg*. 1990;71:254–257.

Hong JY, Kim WO, Kil HK. Detection of subclinical CO2 embolism by transesophageal echocardiography during laparoscopic radical prostatectomy. *Urology*. 2010;75(3):581–584.

Ishiyama T, Hanagata K, Kashimoto S, et al. Pulmonary carbon dioxide embolism during laparoscopic cholecystectomy. *Can J Anaesth*. 2001;48:319–320.

Jayaraman S, Khakhar A, Yang H, et al. The association between central venous pressure, pneumoperitoneum, and venous carbon dioxide embolism in laparoscopic hepatectomy. *Surg Endosc*. 2009;23(10):2369–2373.

Kim CS, Kim JY, Kwon JY, et al. Venous air embolism during total laparoscopic hysterectomy: comparison to total abdominal hysterectomy. *Anesthesiology*. 2009;111(1):50–54.

C.24. What is the mechanism of increase in shunting resulting from embolization?

Emboli in the pulmonary capillaries cause an increase in PVR (i.e., vasoconstriction), which leads to increased pulmonary artery, right ventricle, and right atrium pressures and an opening of pulmonary precapillary arteriovenous anastomoses, resulting in shunt and hypoxemia.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:109–136.

C.25. How is a gas embolism (CO_2 or air) treated?

- N_2O should be discontinued, and the F_{IO_2} should be increased to 100%.
- Identify and occlude the air entrainment site. Insufflation (in the case of CO_2) should be halted, and the pneumoperitoneum should be released immediately.
- An increase in the rate and volume of controlled ventilation with PEEP has been suggested as a method of minimizing air

entrainment. However, this may decrease the cardiac output and excessively increase the airway pressure and PVR and can lead to paradoxical air embolization.

- If possible, the patient should be placed in steep left lateral decubitus Trendelenburg position to prevent obstruction of the pulmonary outflow tract and right ventricular failure. However, during robotic surgery, movement of the patient is prevented until the robot is undocked.
- A CVP catheter can be useful for diagnosis and for therapeutic aspiration of air. Radial artery cannulation can be useful to track improvement or deterioration.
- Therapy is essentially supportive and may include fluids, vasopressors, and pulmonary arterial catheterization. A large bolus of gas may form a gas lock in the right atrium, decreasing the cardiac output. Smaller bubbles can lodge in the lungs, causing pulmonary hypertension, right ventricular failure, and pulmonary edema. Venous gas emboli may also enter the arterial circulation through an atrial septal defect or patent foramen ovale, a condition that may exist in 20% of patients.

Hong JY, Kim JY, Choi YD, et al. Incidence of venous gas embolism during robotic-assisted laparoscopic radical prostatectomy is lower than during radical retropubic prostatectomy. *Br J Anaesth*. 2010;105:777–781.

Lobato EB, Gravenstein N, Kirby RR, eds. *Complications in Anesthesiology*. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:198–200.

C.26. What are the causes of pneumothorax or pneumomediastinum during laparoscopy? How would you diagnose it? How would you treat it?

A pneumothorax can result from the migration of the laparoscopic gas under pressure or from direct pulmonary barotrauma. CO_2 gas insufflated retroperitoneally gains rapid direct access to a vast space and may result in widespread

subcutaneous emphysema and a pneumomediastinum.

During laparoscopy, CO_2 under pressure can pass from the abdominal cavity into the pleural and pericardial spaces through anatomic or congenital paths (e.g., the hiatus around the esophagus) or through acquired defects in the diaphragm. (Embryologically, before the formation of the diaphragm, the peritoneal and pleural cavities are derived from one sac.)

A pneumothorax can be diagnosed by a sudden decrease in pulmonary compliance, an increase in airway pressure, an increase in Et_{CO_2} and Pa_{CO_2}, an unchanged or decreased Pa_{O_2}, an unchanged or decreased BP, abnormal motion of the involved side hemidiaphragm, and the absence of breath sounds without wheezing on the affected side. The shape of the capnogram usually is unchanged. Fiberoptic bronchoscopy will rule out endobronchial intubation, and an intraoperative chest fluoroscopy or x-ray film will confirm the diagnosis.

A pneumothorax caused by laparoscopic gas is easily treated, or it can resolve spontaneously. One study reports an incidence of pneumothorax in 7 of 46 patients undergoing laparoscopic fundoplication for repair of hiatus hernia. In these cases, intraoperative treatment consisted of PEEP and increased minute ventilation to reinflate the lung and increased pressure to decrease the gradient from abdomen to pleural cavity and possibly to seal the tear.

Alternatively, a pneumothorax may be undetected until the patient wakes up and exhibits respiratory distress and restlessness, which can be misinterpreted as pain or inadequate reversal of the muscle relaxant. Treatment consists of 100% oxygen by mask. CO_2 will quickly diffuse out, as can be easily seen by serial blood gases and x-ray films; invasive treatment is unnecessary.

Subcutaneous emphysema is usually identified by finding

crepitus on physical examination; it can also be seen on a radiograph. A pneumomediastinum is diagnosed with a portable chest radiograph. The treatment usually only consists of oxygen and supportive measures. However, tension pneumomediastinum and a compartment syndrome due to severe subcutaneous emphysema will require surgical intervention.

Because of the increased volumes and pressures in the lung during laparoscopy, pneumothorax, pneumomediastinum, and subcutaneous emphysema can also result from barotrauma. This cause of pneumothorax is far more serious and may require tube thoracostomy. Attempts at hyperventilating to decrease the Et_{CO_2} can result in overdistention and rupture of alveoli, with subsequent dissection of the anesthetic gases into the perivascular sheaths, mediastinum, pleura, and fascial planes of the head and neck. Large tidal volumes and rapid ventilator rates can be especially dangerous in patients with COPD or bullae because insufficient emptying time may increase air trapping.

Bartelmaos T, Blanc R, De Claviere G, et al. Delayed pneumomediastinum and pneumothorax complicating laparoscopic extraperitoneal inguinal hernia repair. *J Clin Anesth*. 2005;17:209–212.

Joris JL, Chiche JD, Lamy ML. Pneumothorax during laparoscopic fundoplication: diagnosis and treatment with positive end-expiratory pressure. *Anesth Analg*. 1995;81:993–1000.

C.27. How would you decide when to extubate?

In addition to the usual criteria for extubation, prolonged laparoscopy in the Trendelenburg position requires that the following problems are resolved before the patient is extubated.

If significant subcutaneous emphysema has occurred (diagnosed by crepitus and persistent hypercarbia), continue mechanical ventilation with oxygen. A significant amount of CO_2 may be held in the vast retroperitoneal space.

Delay extubation if the patient has edema, venous congestion, and duskiness of the head and neck. Check the tongue for edema and the eyes for periorbital, conjunctival, or lid edema. The cuff of the endotracheal tube should be deflated to make sure that a gas leak exists. If it does not, the patient should remain intubated. Keep the patient in head-up position until the conjunctivae no longer seem raised or watery. Potential laryngeal edema will also be diminished by the head-up position.

Causes of edema include dependent stasis from the Trendelenburg position, resistance from elevated abdominal and thoracic pressures, and temporary fluid overload after intraoperative oliguria or anuria. In some cases, it is best to leave the patient intubated with a Foley catheter in place until diuresis has begun.

D. Postoperative Management

D.1. What are some of the unique complications of laparoscopy?

Injuries from Instruments

Improper placement of Veress needle or trocars can cause abdominal wall bleeding, blood vessel or visceral puncture, subcutaneous emphysema, peritonitis, wound infections, hernia at the trocar site, and hemorrhage. Thermal injuries may occur from cautery or laser use. Staples and clips can cause nerve entrapment.

Complications of Pneumoperitoneum

Increased intra-abdominal pressure can result in bowel ischemia, omental or bowel herniation, gastric regurgitation, excessive compression of vena cava, decreased venous return, venous

stasis in legs, hypotension, increased intrathoracic pressure, mediastinal and subcutaneous emphysema, pneumothorax, barotrauma, CO_2 gas embolism, atelectasis, bradyarrhythmias from vagal stimulation of trocar insertion and peritoneal distention, dysfunction of ventriculoperitoneal shunts, referred shoulder pain from CO_2 gas retained under the diaphragm, and nausea and vomiting.

Systemic Effects of CO_2 Absorption

Among the systemic effects of CO_2 absorptions are hypercarbia, acidosis, increased sympathoadrenal stimulation, hypertension, tachycardia, increased intracranial pressure, subcutaneous emphysema, embolization, and sickle cell crisis. Arrhythmias can occur from hypercarbia, hypoxia, and catecholamines.

Trendelenburg Position

Venous congestion of head and neck; increased venous pressure; increased intracranial pressure; retinal hemorrhage; retinal detachment; increased intraocular pressure and glaucoma attack; corneal and conjunctival edema; endobronchial intubation and hypoxemia; ventilation/perfusion mismatch and hypoxia; edema of airway including larynx; airway obstruction and closure; brachial plexus injury from shoulder braces, femoral nerve, peroneal, and other neuropathies; and an assortment of respiratory complications have been reported with use of the Trendelenburg position.

Late Complications

Among the late complications are bowel obstruction from injury, cautery burn, intestine or omentum herniation through the trocar site, adhesions, deep vein thrombosis, and nerve injury resulting from improper padding. Fever may indicate infection from bowel necrosis. Cutaneous metastasis can occur at the port site.

Awad H, Santilli S, Ohr M, et al. The effects of steep Trendelenburg positioning on intraocular pressure during robotic radical prostatectomy. *Anesth Analg*. 2009;109(2):473–478.

Fahlenkamp D, Rassweiler J, Fornara P, et al. Complications of laparoscopic procedures in urology: experience with 2,407 procedures at 4 German centers. *J Urol*. 1999;162:765–771.

Fuller J, Ashar BS, Carey-Corrado J. Trocar-associated injuries and fatalities: an analysis of 1399 reports to the FDA. *J Minim Invasive Gynecol*. 2005;12:302–307.

Gkegkes ID, Karydis A, Tyritzis SI, et al. Ocular complications in robotic surgery. *Int J Med Robot*. 2015;11(3):269–274.

Joshi GP. Complications of laparoscopy. *Anesthesiol Clin North Am*. 2001;19:89–105.

Koç G, Tazeh NN, Joudi FN, et al. Lower extremity neuropathies after robot-assisted laparoscopic prostatectomy on a split-leg table. *J Endourol*. 2012;26:1026–1029.

Miele VJ, Bendok B, Bloomfield SM, et al. Ventriculoperitoneal shunt dysfunction in adults secondary to conditions causing a transient increase in intra-abdominal pressure: report of three cases. *Neurosurgery*. 2004;55:434.

Mills JT, Burris MB, Warburton DJ, et al. Positioning injuries associated with robotic assisted urological surgery. *J Urol*. 2013;190:580–584.

Nishikawa K, Nagashima C, Shimodate Y, et al. Migration of the endotracheal tube during laparoscopy-assisted abdominal surgery in young and elderly patients. *Can J Anaesth*. 2004;51:1053–1054.

Pridgeon S, Bishop CV, Adshead J. Lower limb compartment syndrome as a complication of robot-assisted radical prostatectomy: the UK experience. *BJU Int*. 2013;112(4):485–488.

Sharma A, Berkeley A. Intraoperative drug-eluting stent thrombosis in a patient undergoing robotic prostatectomy. *J Clin Anesth*. 2009;21(7):517–520.

D.2. In the postanesthesia care unit (PACU), our patient complains of numbness and weakness of the lower extremities after 6 hours of anesthesia for robotic prostatectomy. What tests will you order? When would you remove the Foley catheter and arterial line? Under what circumstances would you order a chest x-ray film?

Rhabdomyolysis and compartment syndrome must be ruled out because both occur more frequently in obese patients undergoing long immobilizing procedures. Serial monitoring should be begun for creatine phosphokinase (CPK), lactate dehydrogenase (LDH), creatinine, electrolytes including potassium and calcium, and urinalysis for presence of myoglobin and presence of casts. Treatment should include diuretics and alkalinization of the urine with the aim of high urine output.

Immediate chest x-ray film is ordered if respiratory distress, subcutaneous emphysema, and actual or suspected pneumothorax occurred.

Do not remove the arterial line until the patient is stable and blood gas values are normal. For those patients who have an uneventful recovery, expect an immediate diuresis. Do not remove the Foley catheter until the patient is stable with fluid intake and volume output stable. Order IV fluids. Check voiding after the catheter is removed. Appropriate medications for nausea and pain control must be written. Ketorolac may be given if the surgeon agrees and there is no contraindication. Prophylactic antimuscarinic belladonna and opium (B&O) suppositories may be given to reduce the pain from bladder spasms. Patient-controlled analgesia usually is not necessary. For ambulatory patients, an adult escort must be available to take them home. Most patients, however, stay overnight.

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Keene R, Froelich JM, Milbrandt JC, et al. Bilateral gluteal compartment syndrome following robotic-assisted prostatectomy. *Orthopedics*. 2010;33(11):852.

Scavonetto F, Lamborn DR, McCaffrey JM, et al. Prophylactic belladonna suppositories on anesthetic recovery after robotic assisted laparoscopic prostatectomy. *Can J Urol*. 2013;20:6799–6804.

D.3. What is the incidence of postoperative nausea and vomiting?

The incidence of nausea and vomiting after laparoscopy has been reported to be as high as 42%. It is the most important factor in causing an overnight admission after ambulatory surgery. IV antiemetics such as ondansetron, often with dexamethasone, may be given, preferably during surgery. The cause of nausea and vomiting is believed to be rapid peritoneal distention. Neurogenic pathways are activated by traction reflexes and by splanchnic pressure and manipulation.

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Wilson EB, Bass CS, Abrameit W, et al. Metoclopramide versus ondansetron in prophylaxis of nausea and vomiting for laparoscopic cholecystectomy. *Am J Surg*. 2001;181:138–141.

SECTION 7 The Reproductive System

27 Placenta Previa/Placenta Accreta Spectrum

Jill Fong

A 40-year-old woman, gravida 6 para 5, is electively scheduled for her fourth cesarean section at 36 weeks of gestation. She has placenta previa that was diagnosed by sonography after a single episode of painless vaginal bleeding at 27 weeks of gestation, which resolved spontaneously. Her vital signs are as follows: blood pressure, 110/56 mmHg; heart rate, 85 beats per minute; respiratory rate, 18 breaths per minute; and oxygen saturation (SpO_2), 98% on room air. Her hematocrit (Hct) is 35%.

A. Medical Disease and Differential Diagnosis

1. What are the leading causes of maternal mortality, and what role does anesthesia play in this mortality?
2. What is the differential diagnosis for an antepartum

hemorrhage?

3. How would you diagnose the etiology of antepartum bleeding after midpregnancy?
4. What is the incidence of placenta previa, and what are the associated conditions?
5. What are the different types of placenta previa?
6. What is the usual obstetric management for placenta previa?
7. What is vasa previa? How is it diagnosed and managed?
8. What are the risk factors for the development of a placental abruption?
9. How is placental abruption diagnosed and managed?
10. What complications are associated with placental abruption?
11. Who is at risk for uterine rupture, and how is uterine rupture diagnosed?
12. What is the treatment for uterine rupture?
13. Is this patient at risk for postpartum bleeding?
14. What is the placenta accreta spectrum (PAS)?
15. How is the PAS diagnosed?
16. How is the PAS managed obstetrically?
17. What tests and/or interventions can improve neonatal outcome of a preterm birth?

B. Preoperative Evaluation and Preparation

1. How does pregnancy change respiratory function, and what impact does this have on anesthetic care?
2. What are the maternal cardiovascular changes of pregnancy?
3. What are the maternal gastrointestinal changes of pregnancy?
4. What hematologic changes occur during pregnancy?
5. What laboratory data do you need before taking this patient to the operating room?
6. What preoperative medications would you administer to this patient?

C. Intraoperative Management

1. What monitors would you use for this patient?
2. What anesthetic could be used in this patient?
3. What are the absolute and relative contraindications for neuraxial anesthesia?
4. How is postpartum hemorrhage (PPH) defined, and what are the etiologies of this bleeding?
5. After delivery of the fetus, the placenta is removed with some difficulty in one small area and generalized oozing from the placental implantation site is noted. What is the most likely cause of this patient's bleeding?
6. After delivery of the placenta in a cesarean section, what maneuvers and drugs can enhance myometrial contractility and therefore decrease blood loss?
7. When should this patient receive tranexamic acid (TXA)?
8. If this patient had ongoing bleeding intraoperatively, what guidelines help determine when red blood cell (RBC) transfusions should be given?
9. What laboratory tests should be ordered during the resuscitation of this patient?
10. If this patient had a massive blood loss, what blood replacement therapy would be indicated?
11. What is the role of recombinant activated factor VII (rFVIIa) in the hemorrhaging obstetric patient?
12. What is the role of type O Rh-negative (universal donor) uncrossmatched blood in emergency transfusions, and how does this change your future management?
13. What complications can occur from the transfusion of blood products?
14. What is the role of autologous transfusion in obstetric patients?
15. Significant intraoperative blood loss required the transfusion of 8 units of type-specific, crossmatched packed RBCs (pRBCs). This patient had generalized oozing in the surgical field and hematuria. What is your differential diagnosis?

16. What is disseminated intravascular coagulation (DIC)?
17. Define amniotic fluid embolism (AFE) syndrome and discuss treatment.

D. Postoperative Management

1. If the patient received epidural anesthesia and subsequently developed DIC, when should the epidural catheter be removed?
2. You have successfully treated the patient's massive hemorrhage. Her laboratory values have returned to normal. The patient, however, is still hypotensive despite appropriate intravascular volume replacement and support with vasopressors. What is your concern in this case?

A. Medical Disease and Differential Diagnosis

A.1. What are the leading causes of maternal mortality, and what role does anesthesia play in this mortality?

According to 2018 World Health Organization (WHO) reporting, 99% of maternal deaths occur in developing countries. The WHO defines the maternal mortality ratio (MMR) as the number of direct and indirect maternal deaths per 100,000 live births; it does not include late maternal deaths occurring more than 42 days but less than 1 year after pregnancy termination. The 2015 MMR in developing versus developed countries was approximately 239 versus 12 maternal deaths per 100,000 live births, respectively. Between 1990 and 2015, the worldwide maternal mortality rate dropped by about 44%. Nearly 75% of all maternal deaths are due to severe bleeding, infections, hypertensive disorders of pregnancy, delivery complications, and unsafe abortions. The remainder of deaths are caused by or associated with diseases such as malaria and AIDS during pregnancy. The highest risk of maternal mortality is for

adolescent girls younger than 15 years old, and complications in pregnancy and childbirth are a leading cause of death for adolescent girls in developing countries.

In the United States, based on data from the Pregnancy Mortality Surveillance System of the Centers for Disease Control and Prevention, the pregnancy-related mortality ratio (PRMR) fell significantly during the 20th century. The PRMR tallies the pregnancy-related deaths per 100,000 live births; it includes maternal deaths while pregnant and within 1 year of the termination of pregnancy that occur from any cause related to or aggravated by the pregnancy regardless of the duration or site of that pregnancy but excludes accidental or incidental causes. Because this Pregnancy Mortality Surveillance System was implemented, the number of pregnancy-related deaths has steadily increased from 7.2 deaths per 100,000 live births in 1987 to 18.0 deaths per 100,000 live births in 2014. The reason for this increase is unclear. It may be that more actual deaths are occurring, that reporting has improved, that there is an artificial increase due to code changes with the new International Statistical Classification of Diseases, 10th Revision (ICD-10), that the number of pregnant women with severe chronic health conditions is greater, or that there is an increased proportion of births to women older than 40 years of age. From 2011 to 2014, hemorrhage accounted for 11.5% of these pregnancy-related maternal deaths, cardiovascular disease for 15.2%, other noncardiovascular medical disorders for 14.7%, sepsis 12.8%, cardiomyopathy for 10.3%, thrombotic pulmonary embolism 9.1%, cerebrovascular accidents for 7.4%, hypertensive disorders of pregnancy for 6.8%, AFE for 5.5%, and anesthesia complications for 0.3% of the pregnancy-related deaths. The risk of maternal death is increased in non-Hispanic Black women compared to non-Hispanic White women and in women of advanced maternal age.

In the United Kingdom, the Confidential Enquiry into Maternal Deaths found that from 2014 to 2016, 9.8 women per 100,000 died during pregnancy or up to 6 weeks after childbirth. Most of the women had multiple health problems or other vulnerabilities. The Enquiry includes surveillance data on women who died during or up to a year after pregnancy in the United Kingdom, on women who have died in the United Kingdom and Ireland from mental health conditions, thrombosis/thromboembolism, malignancy and homicide, and on the morbidity associated with the care of women having a major obstetrical hemorrhage. The rate of maternal deaths from direct causes did not change significantly from 2011 to 2013 to 2014 to 2016. Thrombosis/thromboembolism were the leading cause of direct maternal death during or up to 6 weeks after pregnancy. Suicide was the third largest cause of direct maternal deaths occurring during or within 42 days of the end of pregnancy, but it was the leading cause within a year after the end of pregnancy with a mortality rate of 2.8 per 100,000 maternities. The maternal mortality from hemorrhage in the United Kingdom was 0.78 per 100,000 maternities. Of the women who died with obstetrical hemorrhage, they found that 28% of the women had good care, whereas improvements in care may have made a difference for 38% of the women.

In developed regions, the estimated anesthesia-related MMR ranges between 1 and 3 deaths per 1,000,000 live births. If a maternal death can be attributed to an anesthetic complication and if an ideal anesthetic would have likely avoided this death, the death is considered anesthetic related. Based on data from the United States, historically, cesarean sections under general anesthesia were more hazardous than those under neuraxial anesthesia, but case fatality rates for general anesthesia have decreased considerably, whereas those for neuraxial anesthesia have risen slightly leading to no significant difference between

the two in the 1997 to 2002 time period. Looking at 257,000 parturients receiving neuraxial or general anesthesia between 2004 and 2009, the Serious Complication Repository Project of the Society for Obstetric Anesthesiology and Perinatology found that approximately 1 of 3,000 patients had serious anesthesia-related complications with high neuraxial block; respiratory arrest in the labor suite and unrecognized spinal catheters were the most common of these complications. In low- and middle-income countries, however, about 1 in 7 maternal deaths during or after cesarean section were due to anesthesia, which is a very high mortality rate compared with that in developed countries.

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Creanga AA, Syverson C, Seed K, et al. Pregnancy-related mortality in the United States, 2011–2013. *Obstet Gynecol*. 2017;130(2):366–373.

Hawkins JL, Chang J, Palmer SK, et al. Anesthesia-related maternal mortality in the United States: 1979–2002. *Obstet Gynecol*. 2011;117:69–74.

Knight M, Bunch K, Tuffnell D, Jayakody H, et al, eds; for MBRRACE-UK. *Saving Lives, Improving Mothers' Care—Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2014-16*. Oxford: National Perinatal Epidemiology Unit, University of Oxford; 2018:i–iii, 8, 23.

MacDorman MF, Declercq E, Thoma ME. Trends in maternal mortality by sociodemographic characteristics and cause of death in 27 states and the District of Columbia. *Obstet Gynecol*. 2017;129(5):811–818.

Sobhy S, Zamora J, Dharmarajah K, et al. Anesthesia-related maternal mortality in low-income and middle-income countries: a systemic review and meta-analysis. *Lancet Global Health*. 2016;4(5):e320–e327.

A.2. What is the differential diagnosis for an antepartum hemorrhage?

Up to one-fourth of pregnant women may have antepartum vaginal bleeding, but only a small fraction experience an antepartum hemorrhage. Most of this bleeding occurs in the first

trimester, and bleeding in the first 20 weeks is presumed to be a threatened abortion or an ectopic pregnancy. Even if pregnancy loss does not occur, the risk for adverse outcomes later in pregnancy is increased. The rest of this discussion will be confined to pregnancies with a viable living fetus.

Antepartum bleeding generally poses a greater threat to the fetus than the mother. The most common causes of antepartum hemorrhage are placenta previa and placental abruption. From the Canadian Perinatal Network, Sabourin et al. looked at 806 women with an antepartum hemorrhage between 22 and 28 weeks of gestation. The most common causes were placental abruption (31.7%), placenta previa (21.2%), and cervical bleeding (6.6%), whereas no cause for hemorrhage was found in a third of the cases. Placenta previa is the abnormal implantation of the placenta over or adjacent to the cervical os and in front of the fetal presenting part. Placental abruption, or abruptio placentae, refers to the premature separation of a normally implanted placenta from the uterus' decidua basalis before delivery of the fetus.

Rare causes of antepartum bleeding include velamentous insertion of the umbilical cord with the involved placental vessels overlying the cervix, which is known as vasa previa, uterine rupture, cervicitis, and local genital tract lesions.

In the remaining cases, it is not always possible to identify the source of antepartum bleeding. Usually, this type of bleeding begins with minimal symptoms, if any, and stops; no anatomic cause is identified at delivery, and it is likely attributable to marginal placenta separation. However, these pregnancies have a higher risk of poor neonatal outcome and preterm delivery.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 25th ed. New York: McGraw-Hill Education; 2018:757–758.

McCormack RA, Doherty DA, Magann EF, et al. Antepartum bleeding of unknown origin in the second half of pregnancy and pregnancy outcomes.

BJOG. 2008;115(1):1451–1457.

Sabourin JN, Lee T, Magee LA, et al. Indications for, timing of, and modes of delivery in a national cohort of women admitted with antepartum hemorrhage at 22+0 to 28+6 weeks' gestation. *J Obstet Gynaecol Can*. 2012;34(11):1043–1052.

A.3. How would you diagnose the etiology of antepartum bleeding after midpregnancy?

With antepartum uterine bleeding after midpregnancy, placenta previa and placenta abruption should always be considered in the differential diagnosis. Digital examination of the cervix *should be avoided* until the diagnosis of placenta previa has been excluded because it can cause immediate, severe hemorrhaging. Classically, it has been taught clinically that painless uterine bleeding is indicative of placenta previa, whereas painful uterine bleeding signifies placental abruption. The differential diagnosis, however, is not actually that straightforward; for instance, labor or placental separation accompanying a previa may cause pain, whereas pain from an abruption may mimic normal labor. Transabdominal sonography is a simple and safe method of locating the placenta in a suspected placenta previa. Transvaginal sonography has been shown to be superior to transabdominal sonography and is currently the imaging modality of choice. Recently, transperineal sonography has been shown to have a 98% positive-predictive value and 100% negative-predictive value of placenta previa. On the other hand, sonography infrequently aids in the diagnosis of an acute placental abruption because fresh clot and placenta appear sonographically similar. Negative findings on sonographic examination do not rule out a placental abruption. Magnetic resonance imaging (MRI) has been used by numerous investigators to visualize placental abnormalities, including placenta previa and placental abruption, and should be considered if the diagnostic information would change patient

management.

Masselli G, Brunelli R, Di Tola M, et al. MR imaging in the evaluation of placental abruption: correlation with sonographic findings. *Radiology*. 2011;259(1):222–230.

Quant HS, Friedman AM, Wang E, et al. Transabdominal ultrasonography as a screening test for second-trimester placenta previa. *Obstet Gynecol*. 2014;123(3):628–633.

Rani PR, Haritha PH, Gowri R. Comparative study of transperineal and transabdominal sonography in the diagnosis of placenta previa. *J Obstet Gynaecol Res*. 2007;33(2):134–137.

A.4. What is the incidence of placenta previa, and what are the associated conditions?

The incidence of placenta previa in the United States is about 1 in 300 to 400 deliveries. The risk of having placenta previa increases with advancing maternal age, multiparity, multifetal gestations, previous cesarean delivery, prior uterine surgery, cigarette smoking, cocaine use, infertility treatments, and unexplained increases in maternal serum α-fetoprotein levels. In approximately 90% of the patients with sonographic evidence of placenta previa at 20 weeks, the placenta moved away from the cervix and out of the lower uterine segment by term.

Placenta previa is associated with an increased risk of antepartum bleeding, intrapartum and PPH, abnormalities of placental adherence, peripartum hysterectomy, blood transfusions, preterm birth with perinatal morbidity and mortality, congenital malformations, and septicemia. In the presence of a prior cesarean section, the patient with placenta previa is at greater risk for having a PAS; this risk increased, as the number of cesarean sections increased. Silver et al. found that in women with placenta previa, the risk of placenta accreta was 3%, 11%, 40%, 61%, and 67% for the first, second, third, fourth, and fifth or greater repeat cesarean deliveries, respectively.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 25th ed. New York: McGraw-Hill Education; 2018:773–777.

Gibbins KJ, Einerson BD, Varner MW, et al. Placenta previa and maternal hemorrhagic morbidity. *J Matern Fetal Neonatal Med*. 2018;31(4):494–499.

Oyelese Y, Smulian JC. Placenta previa, placenta accreta, and vasa previa. *Obstet Gynecol*. 2006;107:927–941.

Silver RM, Landon MB, Rouse DJ, et al. Maternal morbidity associated with multiple repeat cesarean deliveries. *Obstet Gynecol*. 2006;107(6):1226–1232.

A.5. What are the different types of placenta previa?

Classifications and terminology for placenta previa based on the degree to which the internal cervical os is covered have been confusing; they have been simplified to two terms. Normally, the placenta implants in the upper uterine segment. Currently, *placenta previa* is a term used to describe a placenta that partially or totally covers the internal cervical os, whereas the term *low-lying placenta* refers to a placenta implanted in the lower uterine segment but does not cover and is less than 2 cm away from the os. Clearly, the classification in some cases of placenta previa depends on the degree of cervical dilation at the time of cervical assessment. In vasa previa, the fetal vessels course through the membranes and cover the internal cervical os.

Bronsteen R, Whitten A, Balasubramanian M, et al. Vasa previa: clinical presentations, outcomes, and implications for management. *Obstet Gynecol*. 2013;122(2, pt 1):352–357.

Reddy UM, Abuhamad AZ, Levine D, et al. Fetal imaging: executive summary of a joint Eunice Kennedy Shriver National Institute of Child Health and Human Development, Society for Maternal-Fetal Medicine, American Institute of Ultrasound in Medicine, American College of Obstetricians and Gynecologists, American College of Radiology, Society for Pediatric Radiology, and Society of Radiologists in Ultrasound Fetal Imaging workshop. *Obstet Gynecol*. 2014;123(5):1070–1082.

A.6. What is the usual obstetric management for placenta previa?

Obstetric management of placenta previa patients depends on three things: fetal age and therefore maturity, presence or absence of labor, and severity of bleeding. The goal of management is to maximize fetal growth and minimize the possibility of antepartum hemorrhage. With many previa patients, the first episode of bleeding usually begins without warning or pain, stops spontaneously, and rarely causes maternal or fetal compromise, but bleeding often recurs. A mature fetus with or without labor should be delivered; if bleeding occur at or beyond 36 weeks, immediate delivery is indicated. If hemorrhaging is severe or there is concern about the fetal condition, delivery should take place regardless of gestational age. Otherwise, conservative management may safely prolong the pregnancy by an average of 4 weeks after the initial bleed. Between 24 and 34 weeks of gestation, betamethasone, a corticosteroid, often is given to the patient with placenta previa to accelerate fetal lung maturity (FLM), and the Society for Maternal-Fetal Medicine (SMFM) recommends that antenatal steroids be given to women being managed expectantly if delivery is likely within 7 days, the gestational age is between 34 0/7 and 36 6/7 weeks of gestation, and antenatal corticosteroids have not been given previously.

With a preterm fetus and no persistent active uterine bleeding, management consists of close observation for bleeding and activity restriction in an inpatient setting or, in certain selected patients, an outpatient setting. For stable patients with no bleeding in the previous 48 hours who have ready access to hospital care, maternal and fetal outcome did not differ between outpatient and inpatient management. Maternal vital signs and hemoglobin (Hgb) are checked at regular intervals depending on when the bleeding, if it exists, subsides. The American Association of Blood Banks recommends that a blood type and screen be done every 3 days in actively bleeding pregnant

women because of the risk for developing new alloantibodies. Fetal well-being also is assessed regularly. The use of tocolytic therapy in placenta previa patients with preterm labor and bleeding is controversial; it has been used to prolong gestation if both the mother and fetus are stable.

The SMFM recommends that delivery for stable women with placenta previa without bleeding should take place at 36 to 37 6/7 weeks, and if a placenta accreta is suspected, it has been recommended that delivery take place between 34 to 37 weeks. As gestational age increases, there is an increased risk of significant bleeding that would necessitate delivery: 4.7% at 35 weeks, 15% at 36 weeks, 30% at 37 weeks, and 59% at 38 weeks. If an indication for delivery is present, FLM testing does not aid in guiding management in the late preterm period when an indication for delivery is present.

Patients with placenta previa almost always are delivered by cesarean section, and some contend that all women whose placentas lie within 2 cm of the cervical os should be delivered by cesarean section. When the placenta is greater than 1 cm away from the cervical os, however, Vergani et al. and Bronsteen et al. suggest that vaginal delivery may be safe.

Normally, with placenta removal, the myometrium of the uterus contracts and reestablishes vascular integrity by constricting the open vessels in the placental bed. In patients with placenta previa, bleeding after placenta removal can be brisk because the lower uterine segment contracts poorly and therefore does not constrict the avulsed vessels. There is a known association between placenta previa and placenta accreta syndrome that may further exacerbate uterine bleeding and require additional surgical and/or radiologic interventions to staunch the bleeding.

As needed, adequate intravenous access and laboratory studies, including a complete blood count, coagulation profile,

and a type and screen/crossmatch, should be obtained as circumstances dictate. In United States, Rh (anti-D) immunoglobulin (IG) is offered to unsensitized Rh-negative women at 28 weeks of gestation when the fetal blood type is unknown or known to be Rh-positive and again after delivery if the neonate is Rh-positive. Anti-D IG should be administered to Rh-negative women who have an antenatal hemorrhage after 20 weeks. Management of the patient who has intermittent antenatal bleeding is complex. With an acute bleeding episode in an Rh-negative parturient, the most conservative approach is to do a quantitative Kleihauer-Betke test to determine if a fetal–maternal transfusion has occurred and if additional IG is required. It has been proposed that cell-free DNA testing to determine the fetal Rh D status be done to avoid repeated administration of anti-D IG if the fetus is Rh-D negative.

American College of Obstetricians and Gynecologists Committee on Practice Bulletins—Obstetrics. Practice Bulletin No. 181: prevention of Rh D alloimmunization. *Obstet Gynecol*. 2017;130:e57–e70.

Bronsteen R, Valice R, Lee W, et al. Effect of a low-lying placenta on delivery outcome. *Ultrasound Obstet Gynecol*. 2009;33:204–208.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 25th ed. New York: McGraw-Hill Education; 2018:773–777.

Fan D, Wu S, Liu L, et al. Prevalence of antepartum hemorrhage in women with placenta previa: a systematic review and meta-analysis. *Sci Rep*. 2017;7:40320.

Gyamfi-Bannerman C; for Society for Maternal-Fetal Medicine. Society for Maternal-Fetal Medicine (SMFM) Consult Series #44: management of bleeding in the late preterm period. *Am J Obstet Gynecol*. 2018;218(1):B2–B8.

Spong CY, Mercer BM, D'alton M, et al. Timing of indicated late-preterm and early-term birth. *Obstet Gynecol*. 2011;118(2, pt 1):323–333.

Vergani P, Ornaghi S, Pozzi I, et al. Placenta previa: distance to internal os and mode of delivery. *Am J Obstet Gynecol*. 2009;201(3):266.e1–266.e5.

A.7. What is vasa previa? How is it diagnosed and managed?

Vasa previa refers to intramembranous fetal vessels, unprotected by placenta or umbilical cord, coursing through the membranes over the cervical os and under the fetal presenting part. The incidence is approximately 1 in 2,500 deliveries and associated risk factors include a second trimester low-lying placenta/placenta previa, a placenta with accessory lobes, velamentous umbilical cord insertions, multiple pregnancies, and pregnancies from in vitro fertilization. An undiagnosed vasa previa is associated with a high fetal mortality (about 60%). Because fetal blood volume is small, any bleeding puts the fetus in jeopardy. When membranes rupture, either spontaneously or artificially, the fetal vessels running through these membranes often rupture. Vaginal bleeding with fetal distress or death when the membranes rupture is seen in an undiagnosed vasa previa and necessitate an emergency cesarean section based on fetal distress. If vaginal blood is present, the presence of fetal (RBCs) can be determined using a Kleihauer-Betke test or flow cytometry, although there is rarely time for this. Fortunately, the majority of cases of vasa previa can be diagnosed prenatally by routinely evaluating placental cord insertion by ultrasound examination and transvaginal sonographic color Doppler if the insertion site cannot be delineated clearly. Good outcomes in patients with vasa previa require a prenatal diagnosis and delivery by cesarean section before the membranes rupture. If stable, the SMFM recommends that women with vasa previa be delivered between 34 and 37 weeks of gestation.

Bronsteen R, Whitten A, Balasubramanian M, et al. Vasa previa: clinical presentations, outcomes, and implications for management. *Obstet Gynecol*. 2013;122(2, pt 1):352–357.

Gyamfi-Bannerman C; for Society for Maternal-Fetal Medicine. Society for Maternal-Fetal Medicine (SMFM) Consult Series #44: management of bleeding in the late preterm period. *Am J Obstet Gynecol*. 2018;218(1):B2–B8.

Kulkarni A, Powel J, Aziz M, et al. Vasa previa: prenatal diagnosis and outcomes: thirty-five cases from a single maternal-fetal medicine practice. *J*

Ultrasound Med. 2018;37:1017–1024.

Oyelese Y, Smulian JC. Placenta previa, placenta accreta, and vasa previa. *Obstet Gynecol*. 2006;107:927–941.

A.8. What are the risk factors for the development of a placental abruption?

The frequency of placental abruption is about 1 in 200 deliveries. The premature separation of the normally implanted placenta can be total or partial and can lead to external or concealed bleeding. Concealed hemorrhage is associated with greater maternal and fetal risks. The most common condition associated with placental abruption is some type of hypertension, either gestational hypertension, preeclampsia, chronic hypertension, or some combination thereof. The incidence of placental abruption is increased with increased maternal age, body mass index, use of assisted fertility methods, African-American or Caucasian race, prematurely ruptured membranes, a history of previous abruption, cigarette smoking, cocaine use, leiomyomas, an isolated uterine artery, and external trauma. The bleeding in the nontraumatic placental abruption almost always is maternal because the placental separation is within the maternal decidua.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 25th ed. New York: McGraw-Hill Education; 2018:767–773.

Downes KL, Grantz KL, Shenassa ED. Maternal, labor, delivery, and perinatal outcomes associated with placental abruption: a systematic review. *Am J Perinatol*. 2017;34(10):935–957.

A.9. How is placental abruption diagnosed and managed?

The signs and symptoms of placental abruption vary considerably. Ultrasonography often does not confirm the diagnosis as the placenta and fresh clots have similar appearances. In severe placental abruptions, the diagnosis often is obvious with fetal distress and demise common. With a live

fetus and vaginal bleeding, milder abruptions may be difficult to diagnose. If knowing would change the patient's management, MRI is a highly sensitive test for detecting placental abruption and should be considered.

Treatment depends on fetal gestational age and fetal and maternal condition. If the diagnosis is uncertain and the fetus is uncompromised, inpatient expectant management with close observation can be practiced. However, further placental separation can occur at any time and lead to serious fetal compromise or death. The use of tocolytics to prolong pregnancy is controversial. Rapid delivery of the compromised, but alive, fetus is by cesarean delivery. Kayani et al. looked at 33 pregnancies with a clinically overt placental abruption and fetal bradycardia. Of the 22 neurologically intact neonates, 15 were delivered within a 20-minute decision to delivery time, whereas 8 of the 11 neonates who died or had cerebral palsy on 1 year follow-up had a >20-minute interval.

If placental separation has led to fetal death, a vaginal delivery usually is preferred; there are two exceptions: a massive hemorrhage that cannot be managed with vigorous blood replacement and obstetric complications that prevent vaginal delivery will necessitate an operative delivery.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 25th ed. New York: McGraw-Hill Education; 2018:767–773.

Kayani SI, Walkinshaw SA, Preston C. Pregnancy outcome in severe placental abruption. *BJOG*. 2003;110(7):679–683.

Masselli G, Brunelli R, Di Tola M, et al. MR imaging in the evaluation of placental abruption: correlation with sonographic findings. *Radiology*. 2011;259(1):222–230.

A.10. What complications are associated with placental abruption?

Maternal complications with severe abruption can include PPH, hemorrhagic shock, a consumptive coagulopathy, acute renal

injury, and Sheehan syndrome (pituitary failure). Placental abruption can lead to fetal compromise or fetal demise.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 25th ed. New York: McGraw-Hill Education; 2018:772.

A.11. Who is at risk for uterine rupture, and how is uterine rupture diagnosed?

Women who have had a uterine rupture in a prior pregnancy have a higher risk of having another one. Women with a previous cesarean delivery have an increased risk of uterine rupture with a classical, T-shaped, or low vertical uterine incision increasing the incidence when compared to a low transverse incision. Other risk factors associated with uterine rupture include previous uterine surgery involving the myometrium; a tumultuous labor; difficult forceps delivery; uterine trauma; breech extraction; external and internal version; labor stimulation with oxytocin or prostaglandins; inappropriate uterotonic medication use; uterine anomalies; placenta increta/percreta; connective tissue defects such as Marfan or Ehlers-Danlos syndrome; and uterine overdistention by fetal macrosomia, hydramnios, or multifetal pregnancy. Primary uterine rupture is defined as a rupture occurring in a previously intact unscarred uterus, whereas a secondary rupture is associated with a preexisting myometrial incision, injury, or anomaly. Uterine rupture is typically classified as either complete, with all of the uterine wall layers separated, or incomplete (uterine dehiscence), with the uterine muscle separated but the visceral peritoneum intact. Uterine dehiscence is more common; it is less likely to cause adverse maternal and fetal derangements or necessitate cesarean delivery. The morbidity and mortality rates are higher when the rupture is complete. Fortunately, uterine ruptures are rare. In developed countries, Getahun et al. report the uterine rupture incidence to

be 1 in 4,800, whereas in developing countries, the incidence is higher. Al-Zirqi et al. found that the incidence of uterine rupture in Norway over a 40-year period increased significantly to about 1 in 1,560 deliveries with obstetric interventions contributing to this increase but not entirely explaining it. The frequency of primary rupture is about 1 in 10,000 to 15,000 births, whereas the incidence in women attempting a trail of labor after previous cesarean delivery varies between about 0.5% and 4%.

Uterine rupture can be difficult to diagnose because of the varied symptoms and physical findings that can occur. The most consistent sign of uterine rupture is a nonreassuring fetal heart rate pattern. In some patients, the symptoms of uterine rupture will be indistinguishable from those of placental abruption. Other signs that may be present include maternal hypotension, tachycardia, vaginal bleeding, abdominal pain, change in the uterine contour, changes in the uterine contraction pattern, and cessation of labor. There may be little pain, and because most of these ruptures occur during labor, any pain may be masked by the analgesics given to treat the discomfort of labor.

Al-Zirqi L, Stray-Pedersen B, Forsén L, et al. Uterine rupture: trends over 40 years. *BJOG*. 2016;123(5):780–787.

American College of Obstetricians and Gynecologists Committee on Practice Bulletins—Obstetrics. Practice Bulletin No. 184: vaginal birth after cesarean delivery. *Obstet Gynecol*. 2017;130:e217–e233.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 25th ed. New York: McGraw-Hill Education; 2018:596–599, 761–763.

Getahun BS, Yeshi MM, Roberts DJ. Case records of the Massachusetts General Hospital: Case 34-2012: a 27-year-old woman in Ethiopia with severe pain, bleeding, and shock during labor. *N Engl J Med*. 2012;367(19):1839–1845.

Gibbins KJ, Weber T, Holmgren CM, et al. Maternal and fetal morbidity associated with uterine rupture of the unscarred uterus. *Am J Obstet Gynecol*. 2015;213(3):382.e1–382.e6.

Porreco RP, Clark SL, Belfort MA, et al. The changing specter of uterine rupture. *Am J Obstet Gynecol*. 2009;200(3):269.e1–269.e4.

A.12. What is the treatment for uterine rupture?

With a complete uterine rupture, fetal distress and maternal bleeding occur; an emergent cesarean delivery is imperative to deliver the fetus and stabilize the mother. After delivery of the fetus, the uterus can be repaired, the uterine arteries can be ligated, or a hysterectomy can be performed, depending on the size of the rupture and the patient's condition. Fetal distress and/or death are common, whereas maternal death in the developed world is not.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 25th ed. New York: McGraw-Hill Education; 2018:598–600, 767.

A.13. Is this patient at risk for postpartum bleeding?

Yes, this patient has a higher chance of postpartum bleeding because of her known placenta previa and the increased risk of having an associated PAS. There is a strong association between placenta previa, prior uterine surgery, and the PAS. In the absence of placenta previa, the frequency of PAS in women having cesarean sections was much lower. The rate of PAS increased from 0.3% in women with one prior cesarean section to 6.74% for women with five or more cesarean deliveries.

Silver RM. Abnormal placentation: placenta previa, vasa previa, and placenta accreta. *Obstet Gynecol*. 2015;126(3):654–668.

A.14. What is the placenta accreta spectrum (PAS)?

PAS, which includes placenta accreta, increta, and percreta, refers to a placenta that adheres abnormally to the myometrium of the uterus due to a partial or total absence of the decidual basalis and an incomplete development of the fibrinoid layer. It was formerly referred to as morbidly adherent placenta. The normal placenta has three general layers: the decidua, which is maternal in origin and adherent to the uterus; the chorion, including the chorionic villi; and the amnion. Both the chorion

and amnion are of fetal origin. Normally, in the first few minutes after delivery of the neonate, the placenta separates from its implantation site at a physiologic cleavage line through the spongy layer of the decidua basalis. In PAS, evidence suggests that not only is the decidua basalis scanty or absent but also that the cytotrophoblasts may exert some control of over decidua invasion via angiogenesis and growth expression allowing chorionic villi to attach to and invade uterine myometrium. Placenta accreta occurs when the placental chorionic villi are attached directly to the uterine myometrium without a decidual layer. With placenta increta, the villi invade into the myometrium, and with placenta percreta, the villi penetrate through the myometrium and serosa of the uterus and, sometimes, into adjacent organs. The abnormal adherence may involve the entire placenta (total placenta accreta), several placental lobules (partial accreta), or part or all of a single lobule (focal placenta accreta).

The incidence of PAS is increasing due mainly to rising cesarean section rates. The incidence was approximately 1 in 2,510 deliveries in the 1980s versus 1 in 533 deliveries for the period from 1982 to 2002. Other more recent reports cite a rate as high as 1 in 300 pregnancies. Increasing cesarean section rates and placenta previa are by far the two most important risk factors. Decidual formation is commonly defective over a previous cesarean section scar, in the lower uterine segment, and/or after uterine surgery. Maternal age greater than 35 years, multiparity, Asherman syndrome, and otherwise unexplained elevations in maternal serum α-fetoprotein concentration and β-human chorionic gonadotropin (β-hCG) are other risk factors associated with placenta accreta.

American College of Obstetricians and Gynecologists Committee on Obstetric Practice. Committee Opinion No. 529: placenta accreta. *Obstet Gynecol*. 2012;120(1):207–211.

Cahill AG, Beigi R, Heine RP, et al; for Society of Gynecologic Oncology, American College of Obstetricians and Gynecologists, Society for Maternal–Fetal Medicine. Placenta accreta spectrum. *Am J Obstet Gynecol*. 2018;219(6):B2–B16.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 25th ed. New York: McGraw-Hill Education; 2018:777–782.

Silver RM. Abnormal placentation: placenta previa, vasa previa, and placenta accreta. *Obstet Gynecol*. 2015;126(3):654–668.

A.15. How is the PAS diagnosed?

In patients with conditions such as placenta previa and previous uterine surgery that are highly associated with the PAS, it is important to have a high index of suspicion and to look carefully for signs of PAS. Prenatal diagnosis of PAS allows for effective planning that helps minimize maternal morbidity.

Transabdominal and transvaginal ultrasonography are useful modalities for evaluating placental position and implantation; perhaps the most important ultrasonographic association in the second and third trimesters is the presence of placenta previa, which is present in more than 80% of accreta in most large series. Intraplacental vascular lacunae, the loss of the hypoechoic (i.e., clear space) boundary between the placenta and myometrium and/or bladder, decreased retroplacental myometrial thickness, and increased vascularity of the uterine serosa-bladder interface are strongly suggestive of PAS. The sensitivity and specificity of grayscale ultrasonography in detecting PAS are approximately 77% to 87% and 96% to 98%, respectively. Although ultrasound evaluation is important, the lack of ultrasound findings does not rule out a diagnosis of PAS. Clinical factors remain equally important predictors of PAS; there is no single diagnostic modality that determines the diagnosis of PAS with absolute accuracy. Color flow Doppler and MRI can be used as adjunctive diagnostic tools. Placental biomarkers, such as α-fetoprotein, are too nonspecific for clinical use.

American College of Obstetricians and Gynecologists Committee on Obstetric Practice. Committee Opinion No. 529: placenta accreta. *Obstet Gynecol*. 2012;120(1):207–211.

Cahill AG, Beigi R, Heine RP, et al; for Society of Gynecologic Oncology, American College of Obstetricians and Gynecologists, Society for Maternal–Fetal Medicine. Placenta accreta spectrum. *Am J Obstet Gynecol*. 2018;219(6):B2–B16.

Jauniaux E, Collins S, Burton GJ. Placenta accreta spectrum: pathophysiology and evidence-based anatomy for prenatal ultrasound imaging. *Am J Obstet Gynecol*. 2018;218(1):75–87.

A.16. How is the PAS managed obstetrically?

Optimal management of PAS has yet to be defined. Care should be individualized for each patient, and a multidisciplinary approach to delivery planning should be taken. Prenatal diagnosis and management is important because it provides the opportunity to optimize outcome. The problems associated with PAS depend on the site of implantation, depth of myometrial penetration, and the number of placental lobules involved. Only a focal placenta accreta may not require aggressive surgical intervention. Otherwise, surgical management can be difficult and requires a multidisciplinary approach in order to minimize maternal complications. If PAS is known to exist antenatally, it is generally accepted that it is treated with an elective cesarean section and hysterectomy; the placenta should be left in place during surgery. The optimal timing for the delivery of the patient with PAS remains controversial and should be individualized. In a retrospective series, Warshak et al. found that patients with a predelivery diagnosis of accreta, who had a planned en bloc hysterectomy without the removal of the placenta at 34 to 35 weeks of gestation after betamethasone administration, had decreased maternal hemorrhagic morbidity and no significant increase in neonatal morbidity. Optimal maternal and neonatal outcome in a stable patient seems to occur with a planned delivery at 34 weeks, with a window of 34 0/7 to

35 6/7 weeks, of gestation without amniocentesis. For women with suspected PAS, some suggest preoperative placement of balloon catheters into the internal iliac arteries. After delivery of the fetus, the catheters may be inflated intermittently during hysterectomy, which may potentially decrease blood loss and provide optimum exposure of the operative field. They also may be used for intraoperative or postoperative embolization of persistent bleeders. The placement of these catheters is not risk-free; thrombosis and thromboemboli have been reported. The American College of Obstetricians and Gynecologists (ACOG) found that data on the efficacy of this intervention is unclear. Some investigators suggest that the placement of preoperative ureteral stents reduced morbidity in cesarean hysterectomies; others use stents intraoperatively as needed.

Because a hysterectomy renders the patient infertile, there has been some interest in attempting to leave the uterus intact in those patients with a strong desire to maintain their fertility. The success of "conservative" expectant management, which is defined as leaving part or all of the placenta in situ without removing the uterus seems to correlate to the degree of the placental attachment abnormality. Timmermans et al. reviewed publications using "conservative" management. They found that in some reports, the placenta was partially removed, whereas in others, it was left intact; some reported the use of methotrexate and/or uterine artery embolization. Overall, 15% of this whole patient population required hysterectomy for hemorrhaging and 3% for infection; approximately 13% of the patients had subsequent pregnancies. They concluded that only in highly select cases when blood loss is minimal and maintenance of fertility is desired should "conservative" management be considered. In one of the largest retrospective reviews, Sentilhes et al. reported that 22% of the patients required a hysterectomy after an attempt at expectant management with the failure rate of

44% in percreta patients compared with 7% in those with less extensive defects. In addition to leaving the placenta in situ in conservative management, adjunct techniques to diminish blood loss and/or speed placental resorption have been tried. Uterine devascularization using uterine artery balloon placement, embolization, or ligation has been used with varying results, and ACOG states that "there is no convincing data for the use of methotrexate for postpartum management of placenta accreta." This method of management is rarely indicated, but if the placenta is left in situ, these women should have serial ultrasounds or MRIs because serum β-hCG test are not helpful.

Although antepartum diagnosis of PAS would be ideal, currently, there is no single diagnostic modality that determines the diagnosis of PAS with absolute accuracy. Unfortunately, the diagnosis is occasionally made postpartum during the third stage of labor when separation of the placenta does not occur with the first clinical manifestation of PAS being profuse, potentially life-threatening bleeding at the time of attempted manual placental separation. During vaginal delivery, uterine inversion can occur. Studies have shown that these PAS patients have a higher blood loss and transfusion requirement when compared to patients with a known antenatal diagnosis of PAS.

American College of Obstetricians and Gynecologists Committee on Obstetric Practice. Committee Opinion No. 529: placenta accreta. *Obstet Gynecol*. 2012;120(1):207–211.

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Timmermans S, van Hof AC, Duvekot JJ. Conservative management of abnormally invasive placentation. *Obstet Gynecol Surv*. 2007;62(8):529–539.

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A.17. What tests and/or interventions can improve neonatal outcome of a preterm birth?

Because significant neonatal morbidity has been reported with elective delivery before 39 weeks of gestation, elective planned repeat cesarean deliveries are to be done after 39 weeks of gestation. Neonatal survival increases as birth weight and/or gestational age increases. The pivotal complication of preterm delivery is respiratory distress syndrome (RDS). ACOG considers first-trimester ultrasonography the most accurate method for establishing or confirming gestational age. Pregnancies without an ultrasound confirming or revising the estimated due date before 22 0/7 weeks of gestation should be considered suboptimally dated. Amniocentesis for FLM is not recommended as a routine component when considering delivery in this patient population; ACOG recommends a late-term delivery at "41 weeks' gestation" using the best clinical estimate of gestational age instead. If an indication for delivery is present, the use of amniocentesis to assess FLM does not aid in guiding management. In our case of preterm vaginal bleeding from a sonographically documented placenta previa, the patient should be electively delivered before 39 weeks because the risk of bleeding increases, as gestation progresses. If there is maternal hemorrhaging, fetal maturity would not impact the decision to perform an immediate cesarean delivery.

RDS is the leading cause of morbidity and mortality in preterm infants. Sixty percent of infants born below 28 weeks of gestation will develop RDS, whereas the incidence of RDS is 30% and <5% in infants born between 28 and 34 weeks and after 34 weeks, respectively. The use of maternal antenatal

corticosteroids, neonatal nasal continuous positive airway pressure (nCPAP) and neonatal exogenous surfactant, if needed, have helped decrease neonatal morbidity and mortality.

According to ACOG, antenatal corticosteroids should be administered when a woman is at risk of preterm delivery within 7 days to decrease the rate of neonatal respiratory complications. Between 24 and 34 weeks of gestation, a single-dose course of corticosteroid, such as betamethasone (two doses of 12 mg intramuscularly, 24 hours apart) or dexamethasone (four doses of 6 mg intramuscularly, 12 hours apart), should be given to accelerate FLM in a parturient who is at risk for imminent preterm delivery. A single repeat course of antenatal steroids should be considered if the first course was greater than 14 days, the fetus is <34 0/7 weeks of gestation, and the delivery is likely within the next 7 days. At 23 0/7 weeks of gestation, corticosteroids may be considered based on a family's decision about resuscitation, irrespective of membrane rupture status and fetal number. A single course of betamethasone is recommended for pregnant women at risk for late-preterm delivery, 34 0/7 to 36 6/7 weeks of gestation, who have not had a previous course of antenatal corticosteroids.

Early CPAP with subsequent selective surfactant administration in extremely preterm infants, defined as <32 weeks of gestation or weighing <1,500 g, results in lower rates of mechanical ventilation, surfactant administration, and bronchopulmonary dysplasia (BPD)/death when compared to treatment with prophylactic or early surfactant treatment. In neonates who receive the combination of maternal antenatal steroids and early nCPAP in the delivery room, prophylactic surfactant therapy is no longer recommended. Infants with RDS on CPAP who fail to maintain an SpO_2 above 90% on a fraction of inspired oxygen (FIO_2) of 0.40 or higher, have a respiratory acidosis (arterial pH <7.2 and partial pressure of arterial carbon

dioxide ($PaCO_2$) >60 to 65 mmHg), or are apneic, require intubation and surfactant administration. Surfactant is most effective when given within the first 30 to 60 minutes of life.

Caffeine is used to treat apnea of prematurity, lower BPD rates, and improve neurodevelopment during early childhood; it is widely used for newborns weighing ≤1,250 g. Vitamin A administration has been shown to decrease BPD rates in neonates weighing <1500 g.

The use of magnesium sulfate for fetal neuroprotection in threatened preterm delivery is recommended; recommendations about dose, duration, upper gestational age, and repeating treatment vary and differ. Of those physicians using magnesium sulfate, patients at risk for preterm delivery have received a range of 4 to 6 g loading bolus over 20 to 30 minutes followed by a 1 to 2 g per hour infusion until birth or for up to 12 to 24 hours. Some use it in patients at risk for a preterm delivery from 24 0/7 to 27 6/7 weeks of gestation, whereas others use 31 6/7, not 27 6/7, weeks as the cut-off time. ACOG recommends that women at risk for imminent delivery before 32 0/7 weeks of gestation be considered candidates for fetal neuroprotection treatment with magnesium sulfate.

The use of amniocentesis for FLM tests is rarely done in the United States. ACOG does not recommend it for assessment to guide the timing of delivery. Some may still use it in patients with poorly dated gestations when FLM may influence plans for delivery (e.g., repeat cesarean delivery in a woman with a prior classical cesarean delivery and unconfirmed gestational age). FLM is not generally assessed before 32 weeks of gestation because pulmonary maturity is unlikely before this time and is not assessed after 39 weeks. There are two types of tests used to determine pulmonary maturity. One type measures the concentration of particular components of pulmonary surfactant and includes lamellar body counts, phosphatidylglycerol

analysis, lecithin-sphingomyelin (L/S) ratio, and surfactant-to-albumin ratio (TDx-FLM II). The other, the foam stability test, evaluates the surfactant function of these phospholipids. Other tests exist, and the choice of test should be based on availability, presence or absence of contaminants, and physician preference.

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Jayaram PM, Mohan MK, Farid I, et al. Antenatal magnesium sulfate for fetal neuroprotection: a critical appraisal and systematic review of clinical practice guidelines. *J Perinat Med*. 2019;47(3):262–269. doi:10.1515/jpm-2018-0174.

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for respiratory distress syndrome: past, present, and future. *Pediatr Res*. 2017;81(1–2):240–248.

Schmidt B, Roberts RS, Anderson PJ, et al. Academic performance, motor function, and behavior 11 years after neonatal caffeine citrate therapy for apnea of prematurity: an 11-year follow-up of the CAP randomized clinical trial. *JAMA Pediatr*. 2017;171(6):564–572.

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B. Preoperative Evaluation and Preparation

B.1. How does pregnancy change respiratory function, and what impact does this have on anesthetic care?

A number of maternal respiratory changes are seen:

- Capillary engorgement of the mucosa is found throughout the respiratory tract, causing swelling of the nasal and oral pharynx, larynx, and trachea; this begins in the first trimester and increases progressively throughout pregnancy.
- By term, there are increases in minute ventilation (45%), tidal volume (45%), and oxygen consumption (30% to 40%); respiratory rate does not change. These changes do not return to their prepregnancy state for at least 6 to 8 weeks after delivery.
- Arterial $Paco_2$ decreases to about 30 mmHg by 12 weeks of gestation and remains there until it slowly increases after delivery over about 6 to 8 weeks postpartum.
- Arterial pH increases to about 7.44, and there is a partial metabolic compensation for the respiratory alkalosis (20 mEq per L).
- Functional residual capacity (FRC) begins to decrease by the fifth month and by term is 20% below prepregnancy values. After delivery, FRC increases and by 1 to 2 weeks postpartum returns to its prepregnant level. Additionally, the

supine position will further decrease the FRC to approximately 70% of prepregnant volume.

Capillary engorgement of the airway mucosa necessitates the use of a smaller, internal diameter (I.D.) 6.0, 6.5, or 7.0 mm, cuffed endotracheal tube in pregnant women. This vascular engorgement results in airway edema and increased airway friability, which may potentially make tracheal intubation more difficult. Because epistaxis is more likely to occur, nasal intubation is relatively contraindicated. Pilkington et al. showed that the number of pregnant women with a Mallampati class IV airway increased 34% between 12 and 38 weeks of gestation. Boutonnet et al. found that the incidence of Mallampati classes III and IV increased during labor when compared to the prelabor period; these changes are not fully reversed by 48 hours after delivery. No predictive factors for the increase in airway class were found; these changes occurred irrespective of any increase in body weight, the duration of first and second stages of labor, or the volume of intravenous fluid received. Regardless of the cause, difficult and failed intubations are more common in the pregnant than in the nonpregnant population.

The combination of a decreased FRC and increased oxygen consumption make the pregnant patient more susceptible to the rapid onset of hypoxemia in the apneic state. Therefore, before the induction of general anesthesia, the parturient should be “preoxygenated” with 100% oxygen for 3 to 5 minutes while taking normal tidal breaths or, if time is limited, for four vital capacity breaths. This effectively washes nitrogen out of FRC and provides maximal maternal oxygen reserves to allow longer apneic time during tracheal intubation. The reduced FRC combined with the increased minute ventilation increase the rapidity of changes in the depth of anesthesia while employing an inhaled anesthetic technique. In addition, the minimum alveolar concentration (MAC) of inhaled anesthetic agents has

been found to be decreased by about 40% in pregnancy. In a small prospective electroencephalographic study, Ueyama et al. found that pregnancy did not enhance the hypnotic effect of sevoflurane, and they suggest that the decreased MAC during pregnancy is not indicative of an enhanced volatile anesthetic effect on the brain but reflects the anesthetic effect on the spinal cord.

Bobrowski RA. Pulmonary physiology in pregnancy. *Clin Obstet Gynecol*. 2010;53(2):285–300.

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Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:17–22.

Pilkington S, Carli F, Dakin MJ, et al. Increase in Mallampati score during pregnancy. *Br J Anaesth*. 1995;74:638–642.

Ueyama H, Hagihira S, Takashina M, et al. Pregnancy does not enhance volatile anesthetic sensitivity on the brain: an electroencephalographic analysis study. *Anesthesiology*. 2010;113(3):577–584.

B.2. What are the maternal cardiovascular changes of pregnancy?

Most cardiovascular changes of pregnancy begin early in the first trimester and peak by 30 to 34 weeks of gestation. At term, the cardiovascular changes include the following:

- Cardiac output increases 40% to 50%. During the first trimester of pregnancy, the cardiac output increases to 40% or 50% above normal and plateaus at approximately 28 weeks of gestation. It remains fairly stable until the stresses imposed by labor increase it further. During labor, cardiac output increases approximately 15% with uterine contractions during the latent phase, 30% in the active phase, and 45% in the expulsive phase when compared to prelabor values. The greatest increase in cardiac output occurs immediately

postpartum when it increases an average of 80% above prelabor values. Cardiac output and heart rate decline to prelabor values within 1 hour of delivery. Postpartum, over the next 2 to 4 weeks, cardiac hemodynamic parameters return toward pregravid levels. It can take a year, however, for the residual effects of cardiovascular remodeling to subside.

- Stroke volume increases approximately 30%.
- Heart rate increases to about 15%.
- Systolic blood pressure is minimally affected by pregnancy.
- Diastolic blood pressure decreases up to 20% by midpregnancy but returns to its prepregnant level at term.
- Systemic vascular resistance decreases 20%.
- Central venous pressure (CVP) remains unchanged.
- *Aortocaval compression* refers to the gravid uterus compressing the inferior vena cava (IVC) and/or the abdominal aorta. The extent of the compression depends on the patient's position and weeks of gestation. In the supine position, compression of the IVC begins by 20 weeks of gestation. At term in the supine position, the IVC is occluded almost completely with venous return from the lower extremities occurring through the dilated azygos system of veins as the dominant pathway of collateral circulation. On MRI, this IVC occlusion was significantly reduced with a 30-degree, but not the standard 15-degree, left uterine tilt position. At term, compression of the aorta did not occur on MRI in the supine position at the level of the renal veins but was reduced at the level of the aortic bifurcation. Despite this impaired blood flow and concomitant decrease in cardiac output, the majority of supine women are not hypotensive or symptomatic because of the compensatory rise in systemic vascular resistance and venous return via collateral circulation. However, up to 11% of supine women at term

develop supine hypotension syndrome with hypotension, bradycardia, and symptoms of dizziness, light-headedness, nausea, and even syncope. Studies of the impact of aortocaval compression on uteroplacental perfusion provide inconsistent results; aortocaval compression, however, can decrease uteroplacental perfusion and have a negative impact on the fetus. For these reasons, it has been customary for all patients after 20 weeks of gestation to be positioned with left lateral uterine displacement. Recently, this practice has been questioned, Lee and Landau have suggested that maternal tilt during elective cesarean delivery of healthy women with uncomplicated pregnancies may not be necessary because they found that after spinal anesthesia, the maternal supine position when compared to 15 degrees left tilt was not detrimental to neonates if the maternal blood pressure was supported with a phenylephrine infusion and a fluid coload.

Armstrong S, Fernando R, Columb M, et al. Cardiac index in term pregnant women in the sitting, lateral, and supine positions: an observational, crossover study. *Anesth Analg*. 2011;113(2):318–322.

Chestnut DH. The aortocaval compression conundrum. *Anesth Analg*. 2017;125(6):1838–1839.

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Higuchi H, Takagi S, Zhang K, et al. Effect of lateral tilt angle on the volume of the abdominal aorta and inferior vena cava in pregnant and nonpregnant women determined by magnetic resonance imaging. *Anesthesiology*. 2015;122:286–293.

Humphries A, Mirjalili SA, Tarr GP, et al. The effect of supine positioning on maternal hemodynamics during late pregnancy. *J Matern Fetal Neonatal Med*. 2019;32(23):3923–3930. doi:10.1080/14767058.2018.1478958.

Lee AJ, Landau R. Aortocaval compression syndrome: time to revisit certain dogmas. *Anesth Analg*. 2017;125(6):1975–1985.

Lee AJ, Landau R, Mattingly JL, et al. Left lateral table tilt for elective cesarean delivery under spinal anesthesia has no effect on neonatal acid-base status: a randomized controlled trial. *Anesthesiology*. 2017;127:241–249.

Practice guidelines for obstetric anesthesia: an updated report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia and the Society for Obstetric Anesthesia and Perinatology. *Anesthesiology*. 2016;124(2):270–300.

B.3. What are the maternal gastrointestinal changes of pregnancy?

Parturients are considered to be at an increased risk for aspiration of gastric contents. Pregnancy itself does not alter gastric emptying of liquid or solid materials, but during labor, gastric motility does decrease. Gastric acid secretion appears to be unchanged. Because of the upward displacement of the stomach by the gravid uterus, tone in lower esophageal high-pressure zone, however, is decreased. This zone normally prevents the reflux of gastric contents. In the first trimester, the tone in this zone may be unchanged, but in the second and third trimesters, lower esophageal high-pressure zone tone falls gradually to about 50% of its preconceptual level. By 36 weeks of gestation, it reaches its lowest point and does not return to prepregnancy levels until 1 to 4 weeks postpartum. As a result, 30% to 50% of women experience heartburn during pregnancy. The increased aspiration risk is thought to be due to the parturient's decrease lower esophageal high-pressure zone tone and the increased risk of having difficulty with intubation.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:20–21.

Ramu B, Mohan P, Rajasekaran MS, et al. Prevalence and risk factors for gastroesophageal reflux in pregnancy. *Indian J Gastroenterol*. 2011;30:144–147.

B.4. What hematologic changes occur during pregnancy?

The hematologic changes seen by term are as follows:

- Intravascular fluid volume increases 45%.
- Plasma volume increases 55%.
- RBC volume increases 30%.

The disproportionate increase in plasma volume compared to RBC volume results in the relative, or physiologic, anemia of pregnancy. By midgestation, Hct has typically fallen approximately 15% below prepregnant levels; the Hgb and Hct are approximately 11.2 g per dL and 34%, respectively. In late gestation, RBC volume increases, and at term, maternal Hgb and Hct are approximately 11.6 g per dL and 35.5%, respectively. This decreased viscosity may aid in maintaining the patency of the uteroplacental vascular bed.

In addition, the following coagulation factors are increased at term: factors I (fibrinogen), VII, VIII, IX, X, and XII. Plasminogen, fibrin degradation products, and fibrinopeptide A are also increased. Factors II and V are unchanged. Factors XI and XIII are decreased as is antithrombin III. Overall, pregnancy is associated with an accelerated, but compensated, rate of intravascular coagulation. Both, the prothrombin time (PT) and activated partial thromboplastin time (aPTT) are shortened 20%, and thromboelastography (TEG) suggests a hypercoagulable state. The platelet count is typically unchanged at term. However, 0.9% of otherwise normal women will have a platelet count less than 100,000 per μL; gestational thrombocytopenia refers to maternal platelet counts of less than 150,000 μL in otherwise normal women.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:22–25.

B.5. What laboratory data do you need before taking this patient to the operating room?

The laboratory values needed in this healthy parturient having an elective scheduled cesarean section are minimal. A complete blood count with platelets and a type and crossmatch should be sent because this patient is at an increased risk for bleeding due not only to her placenta previa but also to the increased

likelihood of an associated placenta accreta because it is her third cesarean delivery. There is no consensus on the type or amount of blood products that should be available. However, many obstetricians and anesthesiologists suggest that at least 4 units of pRBCs be immediately available with other blood products readily available. Unless the patient has a coagulation disorder or is actively bleeding, a PT, an aPTT, and a fibrinogen level are not needed because the values should be within normal limits.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:571–572, 917–918.

B.6. What preoperative medications would you administer to this patient?

Patients at increased risk for aspiration should receive a nonparticulate oral antacid such as sodium citrate 30 minutes prior to the induction of anesthesia. Intravenous H_2-receptor antagonists, such as ranitidine, and/or metoclopramide may also be given preoperatively for aspiration prophylaxis. This patient is having an elective cesarean delivery and should have a 6- to 8-hour fasting period for solids depending on the fatty content of the consumed food; if the fatty content is high, wait 8 hours.

This patient should receive antimicrobial prophylaxis within the 60-minute period before skin incision for the cesarean delivery. As per the 2018 ACOG guidelines, a single dose of the first-generation cephalosporin, cefazolin, is the first-line antibiotic of choice unless a patient is allergic to this medication. Weight-based dosing can be done with patients weighing ≤80 kg receiving 1 g intravenously and those over 80 kg receiving 2 g; for ease of administration, some institutions, including ours, uniformly give 2 g of cefazolin to all adult patients undergoing cesarean delivery. If an allergy exists, then a single intravenous

dose of clindamycin (900 mg) and an aminoglycoside (e.g., gentamicin 5 mg per kg infused over 30 to 120 minutes. The dose is based on the patient's actual body weight unless the patient's actual weight is 20% above ideal body weight [IBW] and then the dose can be determined by the formula: dose = IBW + 0.4[actual weight − IBW]). In addition, azithromycin 500 mg infused over 1 hour may be added to the standard antibiotic regimen if a patient is undergoing a nonelective cesarean delivery.

American College of Obstetricians and Gynecologists Committee on Practice Bulletins—Obstetrics. ACOG Practice Bulletin No. 199: use of prophylactic antibiotics in labor and delivery. *Obstet Gynecol*. 2018;132(3):e103–e119.

Practice guidelines for obstetric anesthesia: an updated report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia and the Society for Obstetric Anesthesia and Perinatology. *Anesthesiology*. 2016;124(2):270–300.

C. Intraoperative Management

C.1. What monitors would you use for this patient?

Standard monitors should be used and include the following: electrocardiogram (ECG), blood pressure cuff, pulse oximeter, end-tidal carbon dioxide monitor, and Foley catheter. In addition, two large-bore intravenous lines, a forced air body warming blanket, intravenous fluid warmers, and intermittent pneumatic compression stockings should be used. A radial arterial line should also be considered if multiple blood samples will be needed and/or hemodynamic instability occurs. Central venous access, placed above the diaphragm, should be considered if vasoactive drugs and additional volume are required for hemodynamic resuscitation. Equipment for the rapid infusion of intravenous fluids and blood products should be readily available.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:572–574.

Kolettis D, Craigo S. Thromboprophylaxis in pregnancy. *Obstet Gynecol Clin North Am*. 2018;45(2):389–402.

Lier H, von Heymann C, Korte W, et al. Peripartum haemorrhage: haemostatic aspects of the new German PPH guideline. *Transfus Med Hemother*. 2018;45(2):127–135.

C.2. What anesthetic could be used in this patient?

In the patient with placenta previa, a regional or general anesthetic technique could be used. Many anesthesiologists would choose to perform a continuous neuraxial anesthetic in this patient. The choice of anesthetic depends on the cesarean section indication and urgency and the maternal volume status. All patients with placenta previa are at risk for increased intraoperative blood loss due to the poor contractility of the lower uterine segment, the increased risk of an associated placenta accreta, and the possibility of an anterior placenta being cut during uterine incision. Markley et al. retrospectively reviewed the anesthetics of 129 patients having nonemergent cesarean deliveries for placenta previa with suspected PAS and found that 95% of these parturients had neuraxial anesthesia as their primary anesthetic; the type of neuraxial anesthesia was not reported. Twenty-one percent of the 72 neuraxial anesthesia patients who needed a hysterectomy had their anesthetic converted to a general anesthesia intraoperatively. Options for neuraxial anesthesia include continuous spinal, combined spinal epidural, and continuous epidural anesthesia. Single-injection spinal anesthesia can be used, but the unpredictable length of the surgery may make this a poor choice. All patients having neuraxial anesthesia should be informed that if the need arises, general anesthesia may be induced. If the patient has a suspected placenta percreta, a general anesthetic is the usual choice for the operative cesarean section and hysterectomy because of the

extensive surgery that may be required.

If postpartum hemorrhaging occurs, a coordinated multidisciplinary team approach aimed at early recognition and treatment is essential.

American College of Obstetricians and Gynecologists Committee on Practice Bulletins—Obstetrics. Practice Bulletin No. 183: postpartum hemorrhage. *Obstet Gynecol*. 2017;130(4):e168–e186.

Markley JC, Farber MK, Perlman NC, et al. Neuraxial anesthesia during cesarean delivery for placenta previa with suspected morbidly adherent placenta: a retrospective analysis. *Anesth Analg*. 2018;127(4):930–938.

C.3. What are the absolute and relative contraindications for neuraxial anesthesia?

Absolute contraindications

- Patient inability to cooperate or patient refusal
- Uncorrected maternal hypovolemia or hypovolemic shock
- Infection at the site of needle insertion
- Frank coagulopathies
- Recent pharmacologic anticoagulation
- Mass lesions causing increased intracranial pressure
- Providers' lack of experience in techniques
- Lack of appropriate monitoring and/or resuscitative equipment

Relative contraindications have included maternal systemic infection, neurologic disease, severe stenotic heart lesions, and some isolated blood coagulation test abnormalities. Most cases of properly treated systemic infection or neurologic disease, however, do not currently contraindicate the use of neuraxial anesthesia. Each patient should be treated individually with careful consideration of the benefits and risks of neuraxial anesthesia.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 5th ed. Philadelphia, PA: Elsevier/Saunders; 2014:459.

C.4. How is postpartum hemorrhage (PPH) defined, and what are the etiologies of this bleeding?

The ACOG reVITALize program currently defines PPH as a cumulative blood loss equal to or greater than 1,000 mL or blood loss accompanied by signs and symptoms of hypovolemia within 24 hours of delivery regardless of the delivery route. This differs from the more traditionally accepted definition that an estimated blood loss greater than 500 mL for vaginal deliveries and 1,000 mL in cesarean sections constitutes PPH. Despite this new definition, ACOG suggests that a blood loss greater than 500 mL after a vaginal delivery should be considered abnormal and be investigated.

Depending on a woman's nonpregnant blood volume and the corresponding magnitude of pregnancy-induced hypervolemia, a dangerous feature of postpartum bleeding is the failure of the pulse and blood pressure to undergo more than moderate alterations until large amounts of blood, usually about 25% of the woman's blood volume, which is approximately ≥1,500 mL, have been lost. Recognition of PPH before vital sign deterioration should be the goal to improve outcomes. Risk assessment tools are available to help. Sixty percent to 85% of patients who will experience a significant obstetrical bleed may be identified, but diligent surveillance of all patients including those initially thought to be low risk is prudent.

Recognizing the severity of an obstetrical hemorrhage is crucial to management. Visual estimations of blood loss are inaccurate and usually underestimate the true blood loss. Quantification of blood loss by measuring the amount of blood in the suction canister and drapes and weighing surgical lap pads is significantly more accurate than estimated blood loss.

The etiologies of PPH generally can be categorized as those occurring early within 24 hours of delivery and those occurring late, 24 hours after delivery. Because the obstetrician typically is

faced with early PPH, the remainder of this discussion focuses on its causes. The two broad etiologies of early PH are based on bleeding from the placental implantation site and genital tract trauma. Within the category of placental site bleeding, bleeding is usually due to either myometrial hypotonia, such as that seen with uterine atony and placenta previa, or retained placental tissue as can be seen with invasive placentation, such as that seen with placenta accreta syndrome and uterine inversion. Genital tract traumas that lead to postpartum bleeding include genital tract lacerations and uterine rupture. Coagulation defects intensify the bleeding that occurs with any of the earlier abnormalities.

American College of Obstetricians and Gynecologists Committee on Practice Bulletins—Obstetrics. Practice Bulletin No. 183: postpartum hemorrhage. *Obstet Gynecol*. 2017;130(4):e168–e186.

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Sentilhes L, Vayssière C, Deneux-Tharaux C, et al. Postpartum hemorrhage: guidelines for clinical practice from the French College of Gynaecologists and Obstetricians (CNGOF): in collaboration with the French Society of Anesthesiology and Intensive Care (SFAR). *Eur J Obstet Gynecol Reprod Biol*. 2016;198:12–21.

C.5. After delivery of the fetus, the placenta is removed with some difficulty in one small area and generalized oozing from the placental implantation site is noted. What is the most likely cause of this

patient's bleeding?

The most likely causes of bleeding in this patient are myometrial hypotonia due to the poor contraction of the lower uterine segment and a focal placenta accreta syndrome. Near term, at least 600 mL per minute of blood flows through the intervillous space carried by about 120 spiral arteries and their accompanying veins. Due to endotrophoblastic remodeling to create a low-pressure system, these arteries have no muscular layer. With placental separation, these vessels are avulsed; hemostasis at the placental implantation site is first achieved by contraction of the myometrium that compresses these relatively large vessels and reestablishes vascular integrity. Subsequently, clotting occurs and the vessel lumens are obliterated. Ineffective myometrial contractions, such as occur with retained placenta or massive blood clots, can impair hemostasis at the implantation site. In this patient, the lower uterine segment, which contains less myometrial tissue, contracts poorly, and hemorrhaging can result despite normal coagulation. Bleeding that occurs after placenta delivery is usually a steady, not a sudden massive, hemorrhage. The constant seepage, however, can lead to an enormous blood loss. Severe PPH, therefore, can result from uterine atony despite normal coagulation. Conversely, even if coagulation is impaired, vigorous myometrial contraction within and adjacent to the denuded placental implantation site makes severe hemorrhage from this implantation site unlikely. During rapid bleeding, the Hct may not accurately reflect the amount of blood lost due to the lack of equilibration with other fluid compartments.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 25th ed. New York: McGraw-Hill Education; 2018:90–95, 787–794.

C.6. After delivery of the placenta in a cesarean section, what maneuvers and drugs can enhance myometrial

contractility and therefore decrease blood loss?

Regarding guidelines for PPH management, national and professional guidelines are based on the same literature, but differences in definition and treatment exist between different guidelines on this subject.

Uterotonic medications, such as oxytocin, cause myometrial contractions and decrease postpartum bleeding. They should be the first-line treatment for PPH caused by uterine atony, which accounts for 70% to 80% of the PPH cases. Synthetic oxytocin (Pitocin, Syntocinon) is usually recommended as the drug of choice and is given once the fetus is born and the placenta is delivered. Given prophylactically, the uterotonics prevent most cases of uterine atony. Oxytocin increases the frequency and duration of uterine contractions; these contractions are most likely mediated through an increase in intracellular calcium levels. The number of oxytocin receptors in the uterus increases from about 20 weeks of gestation to 34 weeks of gestation, and receptor sensitivity increases during labor. Although oxytocin is routinely given, there is no standard prophylactic dose for either vaginal or cesarean delivery. Intravenous therapy is often the preferred route of administration, but intramuscular (IM) dosing is possible. Intravenous oxytocin has a rapid onset of about 1 minute and a fast mean elimination half-life of 3 to 5 minutes. ACOG recommends 10 to 40 units per 500 to 1,000 mL as a continuous infusion or 10 units intramuscularly. At our institution, 30 units of Pitocin per 500 mL of normal saline (NS) is run intravenously over 2 hours after vaginal or cesarean delivery; the infusion rate may be adjusted to sustain uterine contraction and control uterine atony. Different countries do have different guidelines on oxytocin dosing. Lavoie et al. found that women having cesarean deliveries after exposure to exogenous oxytocin during labor required higher infusion rates of oxytocin to prevent uterine atony than women without prior

exposure. The posterior pituitary produces the polypeptide hormones, oxytocin and antidiuretic hormone. Because they differ from one another by only two amino acids, oxytocin exhibits a small antidiuretic effect that is clinically insignificant unless very large doses are given; in this situation, water intoxication might occur. A bolus of oxytocin can decrease peripheral vascular resistance due to a direct relaxing effect on vascular smooth muscle leading to hypotension that on occasion requires treatment with appropriate vasopressors (ephedrine or phenylephrine). Patients may also exhibit tachycardia and arrhythmias. In some countries other than the United States, carbetocin (Duratocin), a long-acting oxytocin analogue, is available.

When oxytocin fails to produce adequate uterine tone and uterine atony is present, other uterotonic medications are often used in prompt succession. The second-line agent chosen depends on its side effect profile and contraindications. Ergot alkaloids, methylergonovine (Methergine) and ergonovine (ergometrine), are effective uterotonic agents; they are usually given intramuscularly and produce tetanic contractions of the uterus that may be mediated through α-adrenergic receptors. Their usefulness is limited because the induced hypertension, due to vasoconstriction, can be prominent. These agents should be avoided in patients with preexisting hypertensive disease. Other cardiovascular affects include coronary artery spasm leading to myocardial infarction, arrhythmias, or cerebrovascular accidents. Pulmonary complications have been reported including pulmonary artery vasoconstriction and pulmonary hypertension. Associated side effects include headache, dizziness, nausea, and vomiting.

Prostaglandins are uterotonic agents. The prostaglandins cause an increase in myometrial intracellular calcium levels leading to an increase in myosin light-chain kinase activity and

uterine contraction. IM and intrauterine administration of 15-methyl prostaglandin $F_{2\alpha}$ (carboprost tromethamine [Hemabate]) can be used to control uterine atony. Due to its bronchoconstrictive properties, its use is strongly contraindicated in asthma patients. Rectally administered prostaglandin E_2 (Prostin E_2) is a naturally occurring uterotonic agent that has not been tested in clinical trials for postpartum bleeding, and its unfavorable side effects include fever/chills, nausea/vomiting, diarrhea, and headaches. In Europe, there is an intravenous prostaglandin E_2 available (Sulprostone), which can be used as a second-line drug in PPH. Finally, Mousa et al. reported that rectally administered misoprostol (Cytotec), a synthetic prostaglandin E_1 analogue, provided no added benefit when compared to standard therapy with oxytocin and ergometrine (ergonovine) in primary PPH patients.

Manual uterine massage is often done and is thought to stimulate the myometrium to contract. The evidence for this common practice, however, is not strong.

If pharmacologic methods fail to control atony-related hemorrhage, prompt alternative measures, including uterine tamponade, selective arterial embolization, and surgical intervention must be undertaken.

American College of Obstetricians and Gynecologists Committee on Practice Bulletins—Obstetrics. Practice Bulletin No. 183: postpartum hemorrhage. *Obstet Gynecol*. 2017;130(4):e168–e186.

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C.7. When should this patient receive tranexamic acid (TXA)?

Once this patient has an estimated blood loss of more than 1,000 mL after cesarean delivery or any blood loss sufficient to compromise her hemodynamic stability, she should receive intravenous TXA. The WHO now considers TXA a standard part of the treatment regimen for PPH following vaginal or cesarean delivery. The WHO recommends that it be given in all cases of PPH, regardless of whether the bleeding is due to genital tract trauma or other causes, unless there is a clear contraindication to antifibrinolytic therapy. It should be given as soon as possible after the onset of bleeding and within 3 hours of birth. TXA is a competitive inhibitor of plasminogen activation and can reduce bleeding by inhibiting fibrinolysis. TXA should be administered intravenously over 10 minutes in a fixed dose of 1 g in 10 mL; if bleeding continues after 30 minutes or restarts

within 24 hours of completing the first dose, a second dose of 1 g should be given. The WHO recommends against giving a first dose of TXA more than 3 hours after birth. The WOMAN Trial found that TXA reduced death due to bleeding in women with PPH with no adverse effects. It should be noted that ACOG is less definitive about TXA administration and recommends that it be considered in the setting of obstetric hemorrhage when initial medical therapy fails.

American College of Obstetricians and Gynecologists Committee on Practice Bulletins—Obstetrics. Practice Bulletin No. 183: postpartum hemorrhage. *Obstet Gynecol*. 2017;130(4):e168–e186.

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C.8. If this patient had ongoing bleeding intraoperatively, what guidelines help determine when red blood cell (RBC) transfusions should be given?

Treatment of serious bleeding demands prompt and adequate refilling of the intravascular compartment. Normovolemia should be maintained, and usually non–dextrose-containing crystalloid solutions are used for the initial volume resuscitation. These solutions rapidly equilibrate into the extravascular space, and therefore, the volume of crystalloid given should be 3 times as much as the blood loss. Colloid solutions can also be used to

maintain normovolemia but confer no greater benefit than crystalloid solutions. Depending on colloid solution (e.g., 5% albumin), the volume that should be administered is the same as that of the blood loss; this may be helpful in facilitating a more rapid repletion of a preexisting volume deficit.

After the hypervolemia of pregnancy is lost at delivery, blood loss can be estimated by every 3 vol% drop in Hct representing a 500-mL loss of blood. With acute blood loss, the real-time Hct measured in the delivery or operating room is often at a maximum. In the PPH patient, the reason for their hypoperfusion is blood loss. If she is not receiving diuretics, urine output reflects renal perfusion, which in turn reflects perfusion of other vital organs, and should be maintained at ≥ 0.3 mL/kg/hr or at least 30 mL per hour but preferably >50 mL per hour. Although physiologic parameters, such as blood pressure, heart rate, urine output, and perhaps CVP, are monitored during surgery, use of these static parameters to guide fluid therapy may result in either hypovolemia or hypervolemia, and may not recognize significant intraoperative reductions in tissue perfusion. Dynamic hemodynamic parameters, such as pulse pressure variation, however, are often not practical in the hemorrhaging obstetrical patient if they are awake and breathing spontaneously with a neuraxial anesthetic.

Defining a universal Hct or Hgb value below or above, which transfusion is either mandatory or contraindicated is difficult. RBCs carry oxygen to the tissues, and the goal of RBC transfusions is to maintain adequate tissue oxygenation. The 2015 American Society of Anesthesiologists Practice Guidelines state that determining whether patients with an Hgb concentrations between 6 and 10 g per dL require RBC transfusion should be based on potential or actual ongoing bleeding, intravascular volume status, signs of organ ischemia, and adequacy of cardiorespiratory reserve. RBC transfusions

should be considered in all patients with clinical evidence of inadequate oxygen carrying capacity. In most bleeding obstetric patients, maintaining an Hgb level above 7 g per dL is suggested unless evidence of impaired pulmonary or cardiac function indicates a need for a higher Hgb level.

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C.9. What laboratory tests should be ordered during the resuscitation of this patient?

Once the patient loses 1,000 mL of blood with ongoing bleeding occurring, blood specimens for Hct, Hgb level, platelet count, coagulation tests (aPTT, PT, and fibrinogen levels) should be sent. An arterial blood gas and lactate level can be done to establish an early baseline. *Blood products should be administered without waiting for results if needed based on clinical assessment.* During the resuscitation, the aforementioned blood tests should be sent periodically to help guide treatment including blood component therapy. If the volume of blood lost requires treatment with a massive transfusion, then electrolyte levels, including potassium and calcium, also will need to be followed. Patients can develop hyperkalemia due to the elevated potassium levels in transfused blood and the cellular shifts caused by acidosis. Patients can develop hypocalcemia from citrate toxicity; citrate is the anticoagulant found in transfused pRBCs. Arterial blood gases

and serum lactate levels also should be monitored to evaluate the acidosis that may develop due to poor tissue perfusion and the development of shock. Changes in lactate levels have been used to follow the response to treatment. If DIC is a concern, the level of fibrin degradation products also should be checked.

Time is important in postpartum hemorrhaging patients. Results from the central laboratory take more time to receive than results from point-of-care devices. Devices for point-of-care measurements of blood gases, electrolytes, lactate, Hct, Hgb, and viscoelastic assays of coagulation, such as TEG or rotational thromboelastometry (ROTEM), should be used if available (also see Chapter 12, sections B.8, B.9, and B.10; Chapter 31, section A.1; and Chapter 57, section C.25).

American College of Obstetricians and Gynecologists Committee on Practice Bulletins—Obstetrics. Practice Bulletin No. 183: postpartum hemorrhage. *Obstet Gynecol*. 2017;130(4):e168–e186.

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C.10. If this patient had a massive blood loss, what blood replacement therapy would be indicated?

When blood replacement therapy is indicated, compatible whole blood is ideal for maintaining intravascular volume in the treatment of hypovolemia from catastrophic acute hemorrhage. One unit of whole blood raises the Hct by 3 to 4 vol% and replaces many coagulation factors, especially fibrinogen. Importantly, using whole blood versus pRBCs and components decreases the exposure of women with severe hemorrhage to blood donors. When whole blood transfusions were compared

with pRBCs transfusions or blood product combinations, Alexander et al. reported that the incidence of renal failure, adult RDS, pulmonary edema, hypofibrinogenemia, admission to an intensive care unit, and maternal death decreased significantly in women delivered at Parkland Hospital. However, availability of whole blood is limited. Few units of whole blood are kept in the modern blood bank because over 85% of globally collected donor blood is fractionated into blood components; in high-income countries compared to low-income countries, 97% versus 50% of whole blood is fractionated into components. For women who do not have massive blood loss, pRBC transfusions are suitable, and component therapy provides better treatment because only the specific component needed is given.

Blood component therapy provides the patient with only the components that they require. The products available are pRBCs, fresh frozen plasma (FFP), cryoprecipitate, and platelets. A unit of pRBC is prepared from 1 unit of whole blood; its plasma is removed and replaced with additives such as citrate, phosphate, dextrose, and adenine. Its volume is about 250 to 325 mL with an Hct of 55 to 80 vol% depending on the method used for preparation and storage. A unit of pRBCs increases the patient's Hct approximately 3 vol% and Hgb by about 1 g per dL. Crystalloid infusion and pRBC transfusion are the mainstays of therapy in the bleeding obstetric patient.

FFP contains all the necessary coagulation factors including 660 to 700 mg of fibrinogen per unit; each unit has a volume of approximately 250 mL and takes about 30 minutes to thaw. Fibrinogen falls earlier than other coagulation factors during postpartum hemorrhaging and can be low despite a normal PT and aPTT. Charbit et al. found that a fibrinogen level less than 200 mg per dL was associated with a high risk of severe bleeding as defined by either a ≥4 g per dL decrease in Hgb, ≥4 RBC unit transfusion, invasive hemostatic intervention, or death.

When replacement of coagulation factors is needed for hemostasis during massive transfusion, FFP transfusion is indicated. In a parturient with surgical bleeding, a fibrinogen level of less than 150 mg per dL, a prolonged PT, and/or a prolonged aPTT are indications for FFP administration in initial doses of 10 to 15 mL per kg. FFP administration is not indicated for hypovolemia. During active hemorrhaging, attempts should be made to maintain the fibrinogen level higher than 150 to 200 mg per dL. Cryoprecipitate is prepared from FFP and 15 mL contains 200 mg fibrinogen, factor VIII:C, factor VIII:von Willebrand, factor XIII, and fibronectin. Ten pooled bags (10 to 15 mL per bag) of cryoprecipitate will increase the fibrinogen level by 65 to 70 mg per dL. A critically low fibrinogen level should be anticipated in PPH due to placental abruption or AFE, and early use of cryoprecipitate is commonly used as part of the resuscitation.

With obstetric hemorrhage, the platelet count should be maintained above 50,000 per μL with the infusion of platelet concentrates. One unit of platelets increases the platelet count from 5,000 to 10,000 per μL in an adult woman. A single-donor platelet apheresis unit provides the equivalent amount of platelets as six random-donor platelet units and should be used if available. Platelets are difficult to store and have a short shelf life (5 days). Typically, the blood bank provides platelets from ABO- and Rh-compatible donors. Platelet unit donor plasma must be compatible with, not identical to, recipient erythrocytes, but only units from D-negative donors should go to D-negative recipients.

Massive transfusion protocols (MTP) function to speed blood product delivery to the operating room and permit product infusion early in the resuscitation process to prevent the adverse effects of aggressive resuscitation with only crystalloid and pRBC transfusions. Massive transfusion is often defined as

transfusing 10 or more pRBC units in a 24 hour period, 4 units of pRBCs within 1 hour with an anticipated ongoing need for more blood, or replacement of a complete blood volume. At our institution, once a hemorrhaging obstetrical patient has lost >1,500 mL of blood, has abnormal vital signs, and/or has received >2 units of pRBC with rapid ongoing losses expected, we notify the blood bank to activate the MTP. At other institutions, their MTP is not activated until >4 to 5 units of pRBCs have been given in a 2-hour period. When an MTP is needed, fixed ratios of pRBCs, FFP, and platelets should be used. Some protocols include TXA and rFVIIa.

Recommendations for the rapid transfusion protocols have been adapted from trauma literature and a few clinical reports. Although replacement therapy with plasma, platelets, and RBCs generally should not be based on any set formula, the results from these studies suggest that patients with severe trauma, massive blood replacement, and coagulopathy have improved survival when the ratio of transfused pRBCs (units) to FFP (units) to platelet (units) approaches 1:1:1. Most of these studies found that patients receiving between 5 and 10 units of pRBCs rarely needed component replacement. Pasquier et al. retrospectively found that PPH patients transfused a higher ratio of FFP:pRBC (1:1.2 vs. 1:1.6) had more successful bleeding control with the uterotonic therapy, sulprostone alone, and less need for advanced interventional procedures. In a recent survey, more than 80% of academic institutions in the United States reported using the 1:1 pRBC:FFP ratio. Previous MTP protocols have suggested different ratios, such as 4:4:1 or 6:4:1, and are related to how a unit of platelets is defined. Because there are only a limited number of studies in parturients requiring massive transfusion, what is more important than the actual ratio of blood products is that each institution has a specific protocol for multicomponent transfusions in place.

Data concerning the use of prothrombin concentrates (PCCs) and virus-inactivated fibrinogen concentrate in the PPH patient are limited. The ACOG recommends that their use should only be considered after multiple rounds of standard massive transfusion agents and in consultation with an expert in massive transfusion. Different preparations of PCCs, the human plasma–derived concentrates of vitamin K–dependent clotting factors, are available containing either three factors (factors II, IX, and X) or four factors (factors II, VII, IX, and X). Each gram of fibrinogen concentrate increases the fibrinogen level approximately 40 mg per dL.

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C.11. What is the role of recombinant activated factor VII (rFVIIa) in the hemorrhaging obstetric patient?

rFVIIa (NovoSeven), a synthetic vitamin K–dependent glycoprotein, has been used to facilitate hemostasis in patients bleeding from coagulopathies, surgery, trauma, and severe obstetric hemorrhage. Use of rFVIIa in obstetrics has been reported in case series and international registries; no randomized controlled trials have been published. The ACOG recommends that its use be reserved for extenuating circumstances after multiple rounds of standard transfusion agents and in consultation with an expert in massive hemorrhage.

At pharmacologic doses, rFVIIa promotes hemostasis by activating the extrinsic pathway of the coagulation cascade; it replaces deficient activated factor VII. It complexes with tissue factor and may activate the conversion of factor X to Xa and factor IX to IXa; when complexed with other factors, factor Xa converts prothrombin to thrombin, which is a key step in the formation of a fibrin-platelet plug that may control bleeding. Franchini et al. reviewed the literature and found that a median dose of 81.5 μg per kg of rFVIIa has been effective in stopping or decreasing bleeding in 85% of obstetric cases where it has been utilized. They outlined a treatment scheme for the off-label use of rFVIIa in the treatment of PPH. They suggest that rFVIIa be considered only after the failure of medical treatment, blood component therapy, and conservative surgical/invasive treatment. Before administering rFVIIa, acidosis, thrombocytopenia, hypofibrinogenemia, hypocalcemia, and hypothermia should be corrected. Although the optimal dose of rFVIIa for PPH has not been determined, 90 μg per kg can be given intravenously over 3 to 5 minutes. If no response has

occurred 20 minutes later, a second dose of 90 μg per kg may be given. If there is no response after two doses, hysterectomy should be considered. Because to date all of the information about rFVIIa in obstetrics is anecdotal, the use of rFVIIa should be determined on an individual case basis. There are unanswered concerns about the increased likelihood of thrombotic events, and the role of rFVIIa remains undefined.

American College of Obstetricians and Gynecologists Committee on Practice Bulletins—Obstetrics. Practice Bulletin No. 183: postpartum hemorrhage. *Obstet Gynecol*. 2017;130(4):e168–e186.

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C.12. What is the role of type O Rh-negative (universal donor) uncrossmatched blood in emergency transfusions, and how does this change your future management?

When typed and screened/crossed blood is unavailable and the hemodynamically unstable, hemorrhaging obstetric patient requires an RBC transfusion in addition to crystalloid and/or colloid solutions, uncrossmatched type O Rh-negative blood can be given. People with type O blood are considered universal donors because they lack A and B antigens, and therefore, their erythrocytes are not hemolyzed by a recipient's anti-A or anti-B antibodies if present. Some type O donors, however, produce high titers of hemolytic anti-A and anti-B antibodies. pRBCs, therefore, are preferable to whole blood because packed erythrocytes have a smaller volume of plasma and therefore a

minimal amount of anti-A and anti-B antibodies if present. If whole blood is to be used, the blood bank should supply type O blood that is free of anti-A and anti-B antibodies. Some confusion exists as to when it is safe to switch back to the patient's native blood type. After a patient has received 2 units of type O Rh-negative uncrossmatched whole blood, the patient should not be switched to their type-specific (A, B, AB) blood; additional transfusions should be continued with type O blood. The patient must not receive a transfusion of her correct blood type until the blood bank determines that switching back to the patient's native blood type is safe. Patients who have received uncrossmatched type O Rh-negative pRBCs can receive many more units without concern for antibody reactions. Individual centers have different policies governing the maximum number of uncrossmatched type O Rh-negative blood units that can be given before switching back to the patient's specific blood type. Most centers do recommend switching to the patient's native blood type as soon as safely possible in order to conserve the emergency supply of type O Rh-negative blood. Recommendations should be received from your local blood bank representative.

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C.13. What complications can occur from the transfusion of blood products?

Allogenic blood transfusion safety has improved over the past several decades. Deaths from allogenic transfusions are rare. When they occur, they are primarily due to transfusion-related acute lung injury (TRALI), ABO- and non-ABO hemolytic transfusion reactions (HTRs), and transfusion-related sepsis. Other transfusion-related adverse reactions include transfusion-associated circulatory overload, delayed HTRs, febrile and

allergic non-HTRs, infection due to bacterial and/or viral contamination of blood products, transfusion-associated graft-versus-host disease, transfusion-related immunomodulation, and posttransfusion purpura.

TRALI is the most common cause of transfusion-related mortality. TRALI is a noncardiogenic pulmonary edema that occurs within 6 hours after transfusion; this life-threatening complication is characterized by severe dyspnea and hypoxia. A delayed form of TRALI has been reported to occur 6 to 72 hours after transfusion. All blood products can cause TRALI, but plasma-containing products account for 50% to 63% of the fatalities. Its pathogenesis is incompletely understood, but the lung injury appears to involve the activation of recipient white blood cells by human leukocyte antigen antibodies and/or human neutrophil antigen antibodies in the donor plasma. Because the risk of multiparous female donors having these offending antibodies is increased, male-only plasma donation policies have decreased the TRALI rate. Currently, the American Red Cross plasma distribution from male donors exceed 99% for blood groups A, B, and O but is only 60% for group AB. The risk of TRALI after plasma transfusion has been markedly reduced for groups A, B, and O (1.8 per million distributed products) but not for AB (26.3 per million distributed products) due to the continuing use of AB plasma from female donors to meet demand.

HTRs can be acute or delayed. Fatalities from HTRs are rare but do continue to occur in about 1 in 1.5 million to 1.8 million transfusions. The severity of an HTR depends on the incompatible recipient antibody, which is most severe in an ABO mismatch, and the volume of blood transfused, with more than 200 mL transfused usually needed to cause a fatality. The accidental transfusion of ABO-incompatible blood can result in acute intravascular hemolysis. This is typically characterized by

the symptoms of fever, chills, nausea, flushing, chest and flank pain, tachycardia, hypotension, DIC, hemoglobinuria, acute renal failure, and potentially death. Immediate supportive care includes the discontinuation of the transfusion, treatment of the hypotension and hyperkalemia, administration of a diuretic, and urine alkalinization. The unused blood product should be sent back to the blood bank along with a new patient specimen for a second crossmatch. Assays for urine and plasma Hgb concentration and a direct antiglobulin antibody screen confirm the diagnosis. Reported fatalities due to acute HTRs secondary to non-ABO antibody incompatibilities have increased in the United States and were implicated in 69.2% of all fatal HTRs. Although acute HTRs occur within 24 hours of the transfusion, delayed reactions occur approximately 7 to 10 days after the transfusion of seemingly compatible blood. Death from delayed HTRs occurs much more infrequently than those from an acute reaction.

Because they are stored at room temperature, platelets present the greatest risk of bacterial contamination that can lead to transfusion-related sepsis. The introduction of culture-negative platelets has decreased the risk of receiving an infected platelet transfusion.

The risk of viral infection transmission is low. The risk of contracting human immunodeficiency virus (HIV) or hepatitis C is approximately 1 in 2 million units transfused. The risk of *hepatitis B* transmission is estimated to be less than 1 per 200,000 to 500,000 units transfused. The risk of transfusion-transmitted cytomegalovirus (CMV) can lead to serious morbidity in the immunocompromised patient and/or the fetus or neonate; therefore, pregnant women should receive blood that is seronegative and leukocyte-depleted to decrease the risk of CMV infection. There have been rare reports of West Nile virus infection, variant Creutzfeldt-Jakob disease, human T-

lymphocyte virus type 1, toxoplasmosis, and parvovirus B19 acquired via transfusion. In the United States, blood products are screened for the following infectious agents: HIV-1, HIV-2, human T-lymphocyte virus type I and II, Hepatitis B and C, West Nile virus, Zika virus, Treponema pallidum (syphilis), Trypanosoma cruzi, CMV (only on enough units to have a sufficient inventory for at-risk recipients), and Babesia microti (in high-risk regions only).

The biochemical changes that occur with the storage of blood can lead to problems in the recipient especially when large amounts are rapidly infused. Hypocalcemia, hyperkalemia, and hypothermia can occur and should be promptly corrected.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 25th ed. New York: McGraw-Hill Education; 2018:787–794.

Eder AF, Dy BA, Perez JM, et al. The residual risk of transfusion-related acute lung injury at the American Red Cross (2008-2011): limitations of a predominantly male-donor plasma mitigation strategy. *Transfusion*. 2013;53(7):1442–1449.

Müller MC, van Stein D, Binnekade JM, et al. Low-risk transfusion-related acute lung injury donor strategies and the impact on the onset of transfusion-related acute lung injury: a meta-analysis. *Transfusion*. 2015;55(1):164–175.

Osterman JL, Arora S. Blood product transfusions and reactions. *Hematol Oncol Clin North Am*. 2017;31(6):1159–1170.

Vamvakas EC, Blajchman MA. Transfusion-related mortality: the ongoing risks of allogeneic blood transfusion and the available strategies for their prevention. *Blood*. 2009;113:3406–3417.

C.14. What is the role of autologous transfusion in obstetric patients?

Autologous blood transfusion may avoid the risks of alloimmunization, hemolytic reactions, and viral infections; may potentially decrease the demands on the allogenic blood supply; and may provide a psychological benefit to the patient. There are three methods of autologous transfusion: preoperative (antepartum) donation, normovolemic hemodilution, and

intraoperative blood salvage.

Due to the inability to correctly anticipate which patients will require transfusions and the limited amount of transfusable blood obtained, preoperative donation and normovolemic hemodilution are ineffective strategies for avoiding allogenic transfusions in the obstetric patient. Women with rare blood types or unusual antibodies, however, may benefit from preoperative donation.

Intraoperative blood salvage has been used in obstetric patients and is considered to be safe. The limitations are primarily due to the availability of equipment and the appropriate staff, and it only provides RBCs. During cesarean section after placenta delivery, blood is suctioned from the surgical site, collected, and processed through a cell salvage machine that yields a washed, pRBC product for transfusion. Earlier concerns about the safety of blood salvage during cesarean section related to contamination with amniotic fluid have been dispelled with higher quality filtering. Leukocyte depletion filters may improve the margin of safety of the salvaged pRBC product. Because washed pRBCs may contain fetal RBCs, isoimmunization of the mother is possible; anti-D IG should be given when appropriate.

Jehovah's Witness patients have an increased risk of maternal death due to maternal hemorrhage because their religious beliefs prevent them from receiving blood transfusions. The use of intraoperative blood salvage during surgery sometimes is accepted because continuity of the salvaged blood with the patient's circulatory system can be maintained. The exact possibilities for acceptable treatment options should be discussed with each individual patient early in pregnancy.

American College of Obstetricians and Gynecologists Committee on Practice Bulletins—Obstetrics. Practice Bulletin No. 183: postpartum hemorrhage. *Obstet Gynecol*. 2017;130(4):e168–e186.

Goucher H, Wong C, Patel SK, et al. Cell salvage in obstetrics. *Anesth Analg*. 2015;121(2):465–468.

Lier H, von Heymann C, Korte W, et al. Peripartum haemorrhage: haemostatic aspects of the new German PPH guideline. *Transfus Med Hemother*. 2018;45(2):127–135.

Van Wolfswinkel ME, Zwart JJ, Schutte JM, et al. Maternal mortality and serious maternal morbidity in Jehovah's Witnesses in the Netherlands. *BJOG*. 2009;116(8):1103–1110.

C.15. Significant intraoperative blood loss required the transfusion of 8 units of type-specific, crossmatched packed RBCs (pRBCs). This patient had generalized oozing in the surgical field and hematuria. What is your differential diagnosis?

The obstetric patient can rapidly develop a coagulopathy. It may be a dilutional coagulopathy or DIC. A dilutional coagulopathy can occur when massive blood loss is replaced with crystalloid solutions and pRBCs leading to a relative depletion of platelets and soluble clotting factors. Thrombocytopenia, hypofibrinogenemia, and factor depletion occur. Pregnancy-related causes of DIC include hemorrhagic shock, AFE, placental abruption, intrauterine fetal demise, preeclampsia/hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome, sepsis, and acute fatty liver of pregnancy. Additionally, HTRs with acute intravascular hemolysis can cause DIC. Acidosis and hypothermia both interfere with the normal functioning of the coagulation system and worsen any coagulopathy.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 25th ed. New York: McGraw-Hill Education; 2018:782–794.

Erez O. Disseminated intravascular coagulation in pregnancy—clinical phenotypes and diagnostic scores. *Thromb Res*. 2017;151(suppl 1):S56–S60.

C.16. What is disseminated intravascular coagulation (DIC)?

DIC, a consumptive coagulopathy, is a pathologic activation of the coagulation system that occurs in response to a variety of diseases. The process of coagulation is dysregulated and widespread intravascular clotting and resultant bleeding due to the inappropriate consumption of factors and platelets occurs. Thrombi are deposited in the microcirculation and can diminish blood flow to the organs and lead to multisystem organ failure. Simultaneously, increased fibrinolysis occurs with the formation of fibrin degradation products (also called fibrin split products). Once DIC begins, the pathophysiology is the same regardless of the inciting cause. Resolution of DIC requires treatment of the underlying cause. Supportive treatment is aimed at replacing the consumed blood products-"feeding the fire." Laboratory values are indicative of this consumption of clotting products and the increased fibrinolysis that this excess clotting activates and can help guide management. Thrombocytopenia, decreased levels of fibrinogen and coagulation factors, increased levels of fibrin degradation products (D-dimers), increased PT, and increased aPTT are seen.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 25th ed. New York: McGraw-Hill Education; 2018:782–784, 789.

Erez O. Disseminated intravascular coagulation in pregnancy—clinical phenotypes and diagnostic scores. *Thromb Res*. 2017;151(suppl 1):S56–S60.

C.17. Define amniotic fluid embolism (AFE) syndrome and discuss treatment.

The typical presentation of AFE includes a triad of sudden cardiac and respiratory compromise with DIC occurring in relation to labor and delivery. Classically, it is characterized by the abrupt onset of maternal hypotension, dyspnea, hypoxemia, cyanosis, loss of consciousness, seizures, cardiopulmonary arrest, and hemorrhaging due to DIC. AFE is a complex disorder that is poorly understood.

The cause of AFE syndrome is unknown. The diagnosis of AFE is a clinical one of exclusion; no diagnostic tests exist. The pathophysiology seems to involve an abnormal activation of maternal proinflammatory mediators in response to fetal tissue exposure during breaks in the maternal–fetal barrier during parturition. Multiple possible mechanisms have been proposed, but none adequately explains this complex syndrome. The abnormal endogenous mediator release has clinical similarities to the systemic inflammatory response syndrome seen with severe sepsis and anaphylaxis. Laboratory findings are nonspecific. The detection of squamous cells, trophoblasts, and other debris of fetal origin is neither sensitive nor specific for AFE.

The estimated AFE incidence is approximately 1 in 40,000 deliveries. Cesarean or instrumented vaginal delivery, precipitous labor, advanced maternal age, placenta abruption, placenta previa, PAS, grand multiparity, cervical lacerations, uterine rupture, uterine or pelvic vein tears, eclampsia, pharmacologic labor induction, and polyhydramnios are risk factors.

The overall maternal mortality was reported to be between 11% and 90% but is currently reported to range from 20% to 60%. The reported incidence and outcome vary in part because AFE is a diagnosis of exclusion, and perhaps the changing mortality rates reflect improved intensive care. In survivors, the neurologic outcome is often poor with as many as 85% suffering significant neurologic dysfunction. The neonatal mortality rate is estimated to be between 20% and 60%, and up to 50% of the survivors are neurologically intact. Overall, neonatal outcomes have improved with prompt delivery.

Maternal treatment is primarily prompt supportive resuscitation. The need for delivery is made on a case-by-case basis, but prompt delivery of the fetus in the mother who has

sustained a cardiopulmonary arrest is critical. There is no data that any type of intervention improves maternal prognosis with AFE, although case reports using hemofiltration, exchange transfusion, cardiopulmonary bypass, or extracorporeal membrane oxygenation exist.

Clark SL. Amniotic fluid embolism. *Obstet Gynecol*. 2014;123(2, pt 1):337–348.

Clark SL, Romero R, Dildy GA, et al. Proposed diagnostic criteria for the case definition of amniotic fluid embolism in research studies. *Am J Obstet Gynecol*. 2016;215(4):408–412.

Fitzpatrick KE, Tuffnell D, Kurinczuk JJ, et al. Incidence, risk factors, management and outcomes of amniotic-fluid embolism: a population-based cohort and nested case-control study. *BJOG*. 2016;123(1):100–109.

Pacheco LD, Saade G, Hankins GD, et al; for Society for Maternal-Fetal Medicine. Amniotic fluid embolism: diagnosis and management. *Am J Obstet Gynecol*. 2016;215(2):B16–B24.

D. Postoperative Management

D.1. If the patient received epidural anesthesia and subsequently developed DIC, when should the epidural catheter be removed?

There is little information available concerning this topic. Sprung et al. made recommendations about the removal of an epidural catheter after DIC. First, they suggest that the patient's neurologic status be evaluated frequently and that the coagulopathy be treated; if there is no indication of intraspinal bleeding, they recommend removing the catheter as early as possible. If, however, bleeding is occurring around the catheter insertion site, the catheter may be left in place to tamponade this bleeding. Any neurologic deficits should be evaluated immediately; prompt surgical decompression may be needed. However, if a patient's neurologic status cannot be evaluated (e.g., postoperative intubation and sedation), an argument can be

made for the removal of an indwelling catheter as soon as possible after the replacement of coagulation factors has created a state of normal coagulation even if it is temporary. The recommendations for the best hemostatic conditions for epidural catheter removal should reflect those used for placement of a neuraxial block.

Horlocker TT, Vandermeuelen E, Kopp SL, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine evidence-based guidelines (fourth edition). *Reg Anesth Pain Med*. 2018;43(3):263–309.

Sprung J, Cheng EY, Patel S. When to remove an epidural catheter in a parturient with disseminated intravascular coagulation? *Reg Anesth*. 1992;17(6):351–354.

D.2. You have successfully treated the patient's massive hemorrhage. Her laboratory values have returned to normal. The patient, however, is still hypotensive despite appropriate intravascular volume replacement and support with vasopressors. What is your concern in this case?

She may have developed Sheehan syndrome. Sheehan syndrome refers to the development of a postpartum pituitary infarction with necrosis that is typically precipitated by an obstetric hemorrhage with severe hypotension. Sheehan syndrome is a rare complication. The damage to the pituitary may affect the secretion of one, several, or all of its hormones. Any of the manifestations of hypopituitarism (e.g., failure to lactate, amenorrhea/oligomenorrhea, hypotension, hyponatremia, hypothyroidism) can occur at any time from the immediate postpartum period to years after delivery. If the patient remains hypotensive after control of hemorrhage and adequate volume replacement, she should be evaluated and treated for adrenal insufficiency immediately; treatment of possible adrenal crisis

should not be delayed while diagnostic tests are performed. Glucocorticoids have a role in maintaining peripheral vascular adrenergic tone, and the sudden loss of corticotropin (adrenocorticotropic hormone) secretion, particularly in conjunction with other serious physical stress, can lead to hypotension and shock. Prompt treatment with stress doses of glucocorticoids (e.g., 4-mg dexamethasone by intravenous bolus) is necessary for survival. The workup includes measuring adrenocorticotropic hormone, cortisol, thyroxine, prolactin, and growth hormone levels. The evaluation of other hormonal deficiencies is not urgent and can be deferred until 4 to 6 weeks postpartum.

Diri H, Karaca Z, Tanriverdi F, et al. Sheehan's syndrome: new insights into an old disease. *Endocrine*. 2016;51(1):22–31.

Matsuzaki S, Endo M, Ueda Y, et al. A case of acute Sheehan's syndrome and literature review: a rare but life-threatening complication of postpartum hemorrhage. *BMC Pregnancy Childbirth*. 2017;17(1):188.

28 Hypertensive Disorders of Pregnancy

Sharon Abramovitz and
Jennifer Wagner

A 39-year-old woman gravida 1 para 0 at 29 weeks' gestation was admitted to the hospital because of an elevated blood pressure (BP) (182/111 mmHg), headache, and proteinuria.

A. Medical Disease and Differential Diagnosis

1. What is the classification of hypertension disorders in pregnancy as defined by the American College of Obstetricians and Gynecologists?
2. What is preeclampsia?
3. What is preeclampsia with severe features?
4. What is eclampsia?
5. What is HELLP syndrome?
6. What are the risk factors for developing preeclampsia?
7. What is the mortality associated with preeclampsia?
8. Discuss the pathogenesis of preeclampsia.
9. Discuss the pathologic alterations of preeclampsia.
10. What are some of the complications associated with preeclampsia?

B. Preoperative Evaluation and Preparation

1. What initial laboratory studies are recommended for patients with preeclampsia?
2. Discuss bleeding time and platelet count evaluation during preoperative assessment of a patient with preeclampsia requesting epidural analgesia/anesthesia for labor and delivery.
3. What types of monitoring are important for patients with preeclampsia? When is a central venous pressure (CVP) monitor indicated?
4. Discuss the obstetric management of preeclampsia with severe features.
5. What are the antihypertensive agents of choice for preeclampsia?
6. What drug therapy is the treatment of choice for seizure prophylaxis?
7. Discuss the mechanism of action of magnesium sulfate.
8. What are the fetal effects of magnesium sulfate therapy?
9. Discuss the treatment of magnesium sulfate toxicity.
10. What conditions mandate immediate delivery, regardless of the gestational age?
11. Discuss the management of eclampsia.

C. Intraoperative Management

1. What is your choice of labor analgesia for patients with preeclampsia?
2. What is the advantage of prehydration prior to initiation of neuraxial analgesia?
3. What sensory level of analgesia is required for labor and delivery?
4. Discuss the commonly used local anesthetics for labor analgesia.
5. Is the addition of epinephrine to local anesthetics advisable in preeclamptic patients?

6. What is the treatment for the abnormal fetal heart rate pattern seen with maternal hypotension after neuraxial analgesia is instituted?
7. What would you do after an accidental dural puncture? How do you treat postdural puncture headache?
8. How would you manage total spinal anesthesia?
9. Should methylergonovine be given to preeclamptic patients?
10. When and how would you give spinal anesthesia?
11. Discuss a general anesthesia technique for the patient with preeclampsia presenting for cesarean delivery.
12. What agents can you use to prevent hypertension during the induction of general anesthesia for cesarean delivery?

D. Postoperative Management

1. Discuss the postpartum management of preeclamptic patients.
2. Can nonsteroidal anti-inflammatory drugs (NSAIDs) be used to treat postpartum pain in preeclamptic patients?

A. Medical Disease and Differential Diagnosis

A.1. What is the classification of hypertension disorders in pregnancy as defined by the American College of Obstetricians and Gynecologists?

Hypertensive disorders of pregnancy are classified as follows:

- Gestational hypertension
- Preeclampsia
- Preeclampsia without severe features
- Preeclampsia with severe features
- Chronic hypertension preceding pregnancy
- Chronic hypertension with superimposed preeclampsia

American College of Obstetricians and Gynecologists Task Force on Hypertension in Pregnancy. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on

Hypertension in Pregnancy. *Obstet Gynecol*. 2013;122:1122–1131.

A.2. What is preeclampsia?

Preeclampsia is a multiorgan disease characterized by the development of hypertension, along with proteinuria or end-organ dysfunction, after the 20th week of gestation. It is a disorder affecting approximately 2% to 8% of all pregnancies worldwide, with most cases occurring during the first pregnancy, and is unique to humans. Preeclampsia is a leading cause of maternal and perinatal morbidity and mortality worldwide, particularly in developing countries. Hypertension is defined as a systolic BP of at least 140 mmHg or a diastolic BP of at least 90 mmHg on two occasions at least 4 hours apart in a previously normotensive patient. A single reading of a systolic BP of 160 mmHg or more or diastolic BP of 110 mg Hg or more also defines hypertension. Proteinuria is defined as 300 mg or more of protein in a 24-hour urine collection, a protein–creatinine ratio of 0.3 or greater, or 1+ protein on a urine dipstick. (Dipstick results may be variable and should only be used if other tests are not readily available.) Signs of end-organ dysfunction may include thrombocytopenia (platelet count less than 100,000 per μL), elevated liver transaminases (twice the normal concentration), elevated serum creatinine (greater than 1.1 mg per dL or a doubling of the serum creatinine in the absence of other renal disease), pulmonary edema, or new-onset cerebral or visual disturbances. Peripheral edema is no longer part of the diagnostic criteria because it lacks specificity and is found in many healthy pregnant women.

American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 202: gestational hypertension and preeclampsia. *Obstet Gynecol*. 2019;133(1):e1–e25.

American College of Obstetricians and Gynecologists Task Force on Hypertension in Pregnancy. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on

Hypertension in Pregnancy. *Obstet Gynecol*. 2013;122:1122–1131.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:840–842.

Sibai BM, Stella CL. Diagnosis and management of atypical preeclampsia-eclampsia. *Am J Obstet Gynecol*. 2009;200(5):481.e1–481.e7.

A.3. What is preeclampsia with severe features?

Preeclampsia with severe features includes at least one of the following features:

- BP: systolic BP ≥160 mmHg or diastolic BP ≥110 mmHg on two occasions at least 4 hours apart while the patient is on bedrest
- Thrombocytopenia (platelet count less than 100,000 per μL)
- Serum creatinine concentration greater than 1.1 mg per dL or greater than two times the baseline serum creatinine concentration
- Pulmonary edema
- New-onset cerebral or visual disturbances
- Impaired liver function, indicated by elevated blood concentrations of liver enzymes (twice baseline values) or severe, persistent right upper quadrant or epigastric pain
- Fetal growth restriction and severe proteinuria (<5 g in 24 hours) are *no* longer considered features of severe preeclampsia.

American College of Obstetricians and Gynecologists Task Force on Hypertension in Pregnancy. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. *Obstet Gynecol*. 2013;122:1122–1131.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:840–842.

A.4. What is eclampsia?

Eclampsia is defined as convulsions and/or coma not caused by coincidental neurologic disease (e.g., epilepsy), which occurs during pregnancy or the puerperium in a woman whose

condition also meets the criteria for preeclampsia.

Broughton Pipkin F. The hypertensive disorders of pregnancy. *BMJ*. 1995;311:609–613.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:866–868.

Sibai BM. Diagnosis, prevention, and management of eclampsia. *Obstet Gynecol*. 2005;105(2):402–410.

A.5. What is HELLP syndrome?

HELLP syndrome is a severe form of preeclampsia characterized by hemolysis (*H*), elevated liver enzymes (*EL*), and low platelets (*LP*). It can occur antepartum or postpartum. Delivery represents the only definitive treatment of HELLP syndrome. HELLP syndrome is associated with maternal and neonatal morbidity and mortality. Hemolysis is defined by an abnormal peripheral blood smear and an increased bilirubin level (1.2 mg per dL or greater). Elevated liver enzymes are defined as an increased serum glutamic-oxaloacetic transaminase (aspartate aminotransferase) of at least 70 U per L and a lactate dehydrogenase level of more than 600 U per L. A low platelet count is generally defined as a count of less than 100,000 per μL. Patients with HELLP syndrome have a high incidence of serious maternal complications including disseminated intravascular coagulation, placental abruption, need for blood transfusion, pleural effusion, acute renal failure, and wound infection.

Audibert F, Friedman SA, Frangieh AY, et al. Clinical utility of strict diagnostic criteria for the HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome. *Am J Obstet Gynecol*. 1996;175:460–464.

Pauli JM, Repke JT. Preeclampsia: short-term and long-term implications. *Obstet Gynecol Clin North Am*. 2015;42(2):299–313.

A.6. What are the risk factors for developing preeclampsia?

The risk factors for developing preeclampsia are as follows:

Hypertensive disease

- Preeclampsia in prior pregnancy
- History of chronic hypertension
- Family history of hypertension during pregnancy
- Systolic hypertension during early pregnancy

Coexisting vascular and endothelial disease

- Diabetes mellitus (pregestational or gestational)
- Chronic renal disease
- Systemic lupus erythematosus
- Protein S deficiency
- Activated protein C resistance
- Antiphospholipid antibody syndrome
- Angiotensinogen gene *T235*
- Thrombophilia

Obstetric factors

- Nulliparity
- Increased trophoblastic mass (e.g., multiple gestation, molar pregnancy)
- Large-for-gestational-age fetus
- Polyhydramnios, particularly in young primigravidas
- Use of assisted reproductive technology
- Erythroblastosis fetalis

Other

- African-American race
- Obesity
- Obstructive sleep apnea
- Advanced maternal age (greater than 35 years)

American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 202: gestational hypertension and preeclampsia. *Obstet Gynecol*. 2019;133(1):e1–e25.

Bartsch E, Medcalf KE, Park AL, et al. Clinical risk factors for pre-eclampsia determined in early pregnancy: systematic review and meta-analysis of large

cohort studies. *BMJ*. 2016;353:i1753.

Boxer LM, Malinow AM. Pre-eclampsia and eclampsia. *Curr Opin Anesth*. 1997;10:188–198.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:843–844.

A.7. What is the mortality associated with preeclampsia?

From 2011 to 2016, hypertensive disorders of pregnancy accounted for 6.9% of pregnancy-related deaths in the United States.

Centers for Disease Control and Prevention. Pregnancy Mortality Surveillance System. https://www.cdc.gov/reproductivehealth/maternalinfanthealth/pmss.html. Accessed November 8, 2019.

Khan KS, Wojdyla D, Say L, et al. WHO analysis of causes of maternal death: a systematic review. *Lancet*. 2006;367:1066–1074.

Knight M, Bunch K, Tuffnell D, et al, eds. *Saving Lives, Improving Mothers' Care: Lessons Learned to Inform Maternity Care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2014–16*. Oxford: National Perinatal Epidemiology Unit, University of Oxford; 2018:i–iii, 8, 23.

Sobhy S, Zamora J, Dharmarajah K, et al. Anaesthesia-related maternal mortality in low-income and middle-income countries: a systematic review and meta-analysis. *Lancet Glob Health*. 2016:4(5):e320–e327.

A.8. Discuss the pathogenesis of preeclampsia.

Preeclampsia is most likely a disease of heterogeneous causes of both maternal and placental origin.

Immunologic Factors

Immunologic disorders may arise from an abnormal maternal–fetal antigen–antibody response or from the contents of seminal fluids; spermatozoa may cause antibody formation or prostaglandins may initiate uterine vasoconstriction. The fetus acquires 50% of its genes from the father, which represents in part a paternal allograft that interacts with maternal tissue as the fetal trophoblast migrates into the maternal decidua after implantation. Migration normally occurs in two phases.

Trophoblasts displace the muscular structure of the maternal spiral arteries before 20 weeks of gestation, causing their adrenergic denervation and converting them from high-resistance to low-resistance vessels. At the same time, biochemical adaptations occur in the maternal vasculature, with an increased dominance of endothelium-dependent vasodilators, prostacyclin (prostaglandin I [PGI]), and nitric oxide (NO). In preeclampsia, the second wave of trophoblastic migration fails. This failure can result in a high-resistance, low-flow uteroplacental circulation and consequent placental ischemia and hypoxia. These changes may represent an aberrant immunologic mechanism.

Genetic Factors

A familial tendency toward preeclampsia exists in some populations, and it may result from a recessive genetic inheritance.

Endothelial Factors

Vascular endothelial damage or dysfunction is the common pathologic feature of preeclampsia and occurs in the placental decidual vessels and renal microvasculature. Endothelial cell dysfunction in response to unknown factors may cause a hormonal imbalance in women with preeclampsia (**Fig. 28.1**).

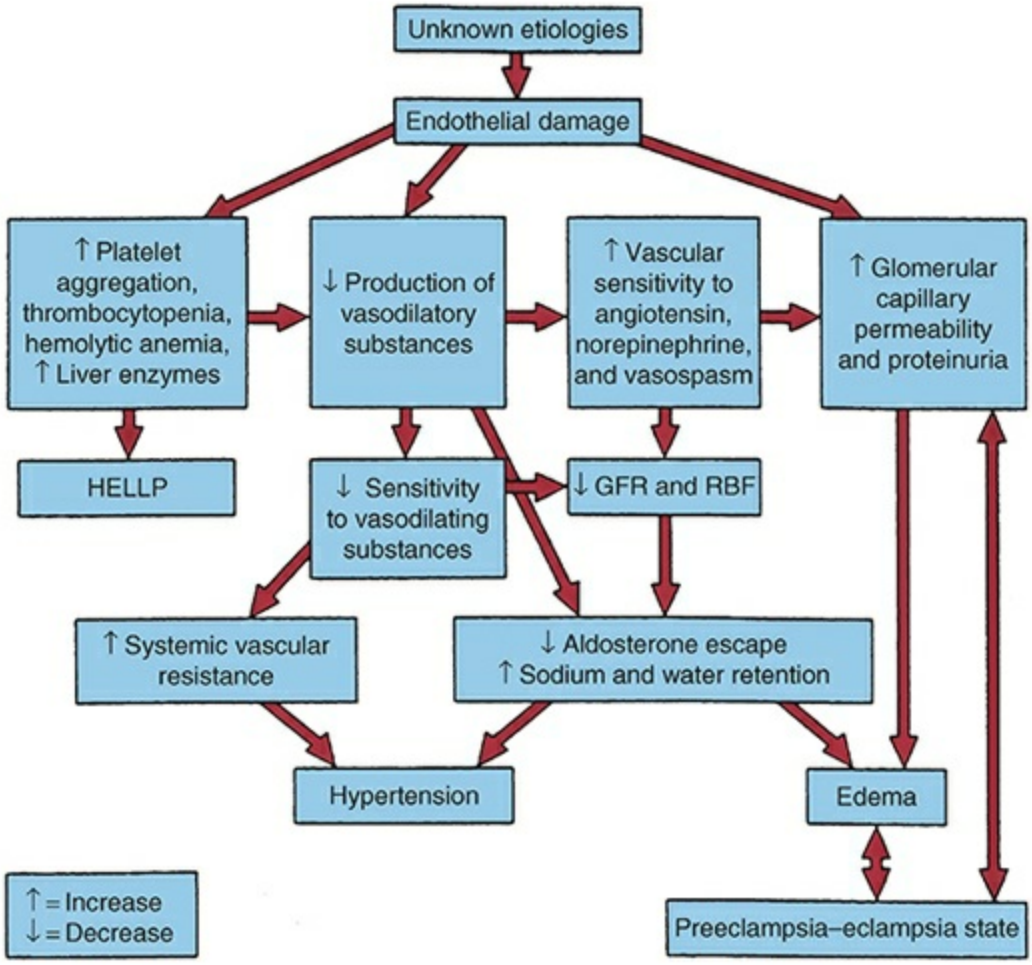


FIGURE 28.1. Endothelial cell dysfunction in response to unknown factors may cause a hormonal imbalance in women with pregnancy-induced hypertension. GFR, glomerular filtration rate; HELLP, hemolysis, elevated liver enzymes, and low platelets; RBF, renal blood flow. (*Reprinted from Chestnut DH, Wong CA, Tsen LC, et al, eds*. Chestnut's Obstetric Anesthesia: Principles and Practice. *6th ed. Philadelphia, PA: Elsevier; 2019. Copyright © 2019 Elsevier. With permission.*)

The metabolic end products of normal vascular endothelium include PGI_2 and endothelium-derived relaxing factor (EDRF), which is either NO or a related nitrosyl substance. Both PGI_2 and EDRF are potent vasodilators. In patients with preeclampsia, the failure of the trophoblast to invade the uteroplacental vascular bed may encourage an increased production of free radicals and lipid peroxides by the decidual lymphoid tissue. As a result, an imbalance occurs between the production of the vasoconstrictor thromboxane A_2 (TXA_2),

which is derived from platelets, and the production of endothelium-derived PGI_2. This imbalance results in a reduced perfusion of the intervillous space. Some investigators have concluded that hypoxia-induced impairment of NO production by the syncytiotrophoblast results in uteroplacental insufficiency and production of a toxin responsible for the clinical manifestations of preeclampsia.

It has been shown that production of endothelin-1 (ET-1), which is the most potent endogenous vasoconstrictor and produced mainly by vascular smooth muscle cells as well as by the vascular endothelium, is markedly increased in preeclampsia and correlates inversely with NO production. Therefore, the imbalance between NO and ET-1 may play a significant role in the pathophysiology of preeclampsia.

Fetoplacental blood vessels or, more specifically, the human placental chorionic plate arteries constrict in response to ET-1. There is now some evidence that amniotic concentration of ET-1 is elevated in pregnancies associated with preeclampsia. Margarit et al. found a statistically significant increase in ET-1 concentration in the amniotic fluid of women at 17 weeks' gestation who developed preeclampsia, as compared to those who did not develop preeclampsia. By the second trimester, higher levels of ET-1 have also been shown in the amniotic fluid of women with preterm premature rupture of the membranes.

Platelet Factors

In mild preeclampsia, serotonin (5-HT) released from aggregating platelets interacts with endothelial $5\text{-}HT_1$ receptors, resulting in the release of prostacyclin and NO (EDRF). The released prostacyclin induces angiotensin II release, improving uteroplacental perfusion. In early-onset severe preeclampsia, damaged uteroplacental vessels cannot respond to $5\text{-}HT_1$ effects. Instead, serotonin interacts with $5\text{-}HT_2$ receptors on vascular

smooth muscle cells, inducing vasoconstriction. Platelet-derived serotonin also activates 5-HT_2 platelet receptors, establishing a positive feedback loop and intensifying platelet aggregation. The loss of 5-HT_1 receptors prevents stimulation of angiotensin II release (**Fig. 28.2**).

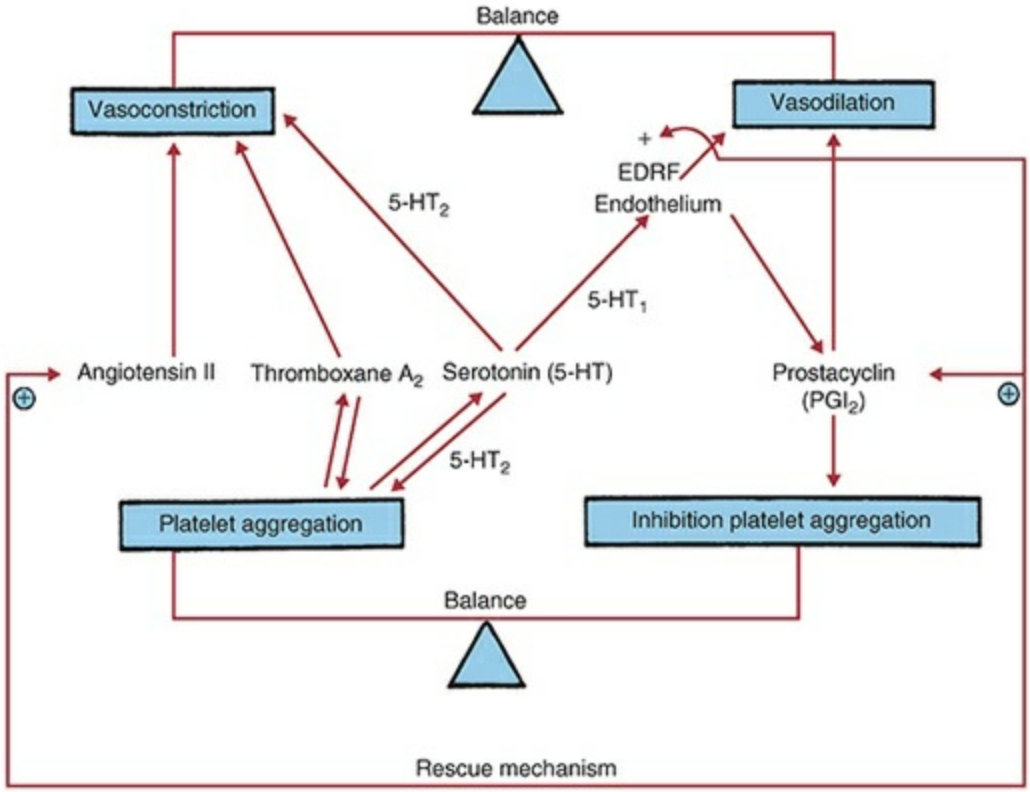


FIGURE 28.2. The loss of 5-HT_1 receptors prevents stimulation of angiotensin II release. EDRF, endothelium-derived relaxing factor. (*Reprinted from Chestnut DH, Wong CA, Tsen LC, et al, eds.* Chestnut's Obstetric Anesthesia: Principles and Practice. *6th ed. Philadelphia, PA: Elsevier; 2019. Copyright © 2019 Elsevier. With permission.*)

Calcium

In normal pregnancy, the intracellular free calcium concentration increases slowly, but this increase is significantly greater in the third trimester in women with preeclampsia. The increase in cytoplasmic calcium levels is enhanced by angiotensin II, and the enhancement is greater in women with preeclampsia compared with normotensive women. This

response to angiotensin II occurs long before signs of preeclampsia become evident and is a sensitive indicator of its subsequent development.

Coagulation Factors

Platelet activation in preeclampsia is surface mediated. Women with preeclampsia have an increased tendency toward thromboembolism, which may result in part from an alteration in the plasma ratio between von Willebrand factor and factor VIII coagulant activity.

Fatty Acid Metabolism

Altered handling of fatty acids by the liver is a key factor in the pathogenesis of preeclampsia. Both increased hepatic uptake of free fatty acids and hypertriglyceridemia are seen more frequently in women who develop preeclampsia.

Markers of Angiogenesis

Preeclamptic patients have elevated plasma levels of endoglin and soluble FLT-1, the receptor for vascular endothelial growth factor, throughout gestation. Recent research suggests that these molecules are not just disease markers but are involved in the pathogenesis of preeclampsia.

Baksu B, Davas I, Baksu A, et al. Plasma nitric oxide, endothelin-1 and urinary nitric oxide and cyclic guanosine monophosphate levels in hypertensive pregnant women. *Int J Gynaecol Obstet*. 2005;90(2):112–117.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:844–848.

Margarit L, Griffiths A, Tsapanos V, et al. Second trimester amniotic fluid endothelin concentration. A possible predictor for pre-eclampsia. *J Obstet Gynaecol*. 2005;25(1):18–20.

Venkatesha S, Toporsian M, Lam C, et al. Soluble endoglin contributes to the pathogenesis of preeclampsia. *Nat Med*. 2006;12:642–649.

A.9. Discuss the pathologic alterations of preeclampsia.

Cardiovascular Changes

- *Blood pressure*. The increase in BP results from an increase in peripheral vascular resistance secondary to a state of sympathetic overactivity.
- *Blood volume*. Reduction in intravascular volume leads to hemoconcentration.

Hemodynamic Changes

- Three hemodynamic subsets exist:
  - Hyperdynamic with increased cardiac output, normal or slightly increased systemic vascular resistance (SVR), and normal or slightly decreased blood volume and filling pressures
  - High SVR with normal cardiac output and lower filling pressures
  - Markedly increased SVR with decreased blood volume and depressed left ventricular function
- Poor correlation between CVP and pulmonary artery (PA) occlusion pressure exist.
  - Decreased colloid oncotic pressure occurs in pregnancy with further reduction in preeclampsia. The low colloid oncotic pressure, coupled with increased vascular permeability and the loss of intravascular fluid and protein into interstitial tissues, increases the risk of pulmonary edema.

Hematologic Changes

- Hypercoagulable state (**Table 28.1**)

TABLE 28.1 Changes that Imply Hypercoagulation in Preeclampsia

↑ Common pathway activity
↓ Fibrinogen
↑ Fibrin-degradation products
D-Dimer positive
↑ Fibrinopeptide A

↑ Factor VIII antigen; factor VIII activity
↓ Antithrombin-III
↑ Antithrombin-III/antithrombin complex
↓ Platelets
↑ β-Thromboglobulin
↑ Platelet aggregability
↓ Sensitivity to prostacyclin

↓, decreased; ↑, increased.

Reprinted from Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019. Copyright © 2019 Elsevier. With permission.

- Platelet activation: Thrombocytopenia occurs in 15% to 30% of women with preeclampsia or eclampsia. Preeclampsia may be associated with a significant defect in *both* platelet function and platelet number. Thrombocytopenia without other coagulation abnormalities but with evidence of hemolysis and increased liver enzymes characterizes HELLP syndrome.

Renal Changes

- Glomerular enlargement results in ischemia, leading to decreased glomerular filtration rate.
- Proteinuria occurs as a result of an increased permeability to most large molecular weight proteins.
- Urate clearance decreases and serum uric acid concentrations increase. Hyperuricemia may provide an early indication of preeclampsia.
- Oliguria parallels the severity of preeclampsia.

Endocrine Changes

In women with preeclampsia, a breakdown of the normal balance between vasodilators (PGI_2, NO) and vasoconstrictors (angiotensin II, TXA_2, serotonin, ET-1) occurs. There is also a decrease in plasma renin concentration and suppression of the renin–angiotensin–aldosterone system.

Respiratory Changes

- Pharyngeal and laryngeal edema may make airway management difficult, necessitating the use of smaller endotracheal tubes.
- Pulmonary edema occurs in 3% of cases, with some cases occurring postpartum.

Hepatic Changes

- Serum transaminase levels frequently increase in patients with mild preeclampsia.
- Epigastric or subcostal pain is an ominous symptom that is typically caused by distension of the liver capsule by edema or subcapsular or parenchymal bleeding. Hepatic swelling produces epigastric pain.
- Liver rupture is a rare complication but is associated with more than 80% mortality.

Neurologic Changes

- The classic manifestations of preeclampsia include severe headache, visual disturbances, central nervous system hyperexcitability, and hyperreflexia.
- The occurrence of seizures indicates eclampsia until proven otherwise. Etiologies of seizures include hypertonic encephalopathy, vasospasm, microinfarctions and punctate hemorrhages, thrombosis, and cerebral edema.
- Postpartum eclampsia may occur up to 4 weeks after delivery.

Uteroplacental Perfusion

- Uteroplacental perfusion is decreased in preeclampsia with the potential for intrauterine growth retardation.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:848–851.

Melchiorre K, Sharma R, Thilaganathan B. Cardiovascular implications in preeclampsia: an overview. *Circulation*. 2014;130(8):703–714.

Pineles BL, Romero R, Montenegro D, et al. Distinct subsets of microRNAs are expressed differentially in the human placentas of patients with preeclampsia. *Am J Obstet Gynecol*. 2007;196(3):261.e1–261.e6.

Powe CE, Levine RJ, Karumanchi SA. Preeclampsia, a disease of the maternal endothelium: the role of antiangiogenic factors and implications for later cardiovascular disease. *Circulation*. 2011;123(4):2856–2869.

Yancey LM, Withers E, Bakes K, et al. Postpartum preeclampsia: emergency department presentation and management. *J Emerg Med*. 2011;40(4):380–384.

A.10. What are some of the complications associated with preeclampsia?

Maternal complications include disseminated intravascular coagulation, congestive heart failure with pulmonary edema, placental abruption, postpartum hemorrhage, acute kidney injury, rupture of the liver, cerebrovascular accident, and septic shock. The leading cause of maternal death is intracranial hemorrhage.

Fetal complications include prematurity with respiratory distress, intrauterine growth retardation, oligohydramnios, intracranial hemorrhage, small for gestational age, and aspiration of meconium. The leading cause of intrauterine morbidity and mortality is uteroplacental insufficiency caused by placental infarcts, followed by placental abruption, and chorioamnionitis.

Datta S, ed. *Anesthetic and Obstetric Management of High-Risk Pregnancy*. 3rd ed. New York: Springer; 2004:270–281.

Ghulmiyyah L, Sibai B. Maternal mortality from preeclampsia/eclampsia. *Semin Perinatol*. 2012;36(1):56–59.

B. Preoperative Evaluation and Preparation

B.1. What initial laboratory studies are recommended for patients with preeclampsia?

- Hemoglobin and hematocrit

- Platelet count
- Coagulation assay including activated partial thromboplastin time, prothrombin time, fibrinogen, D-dimer
- Serum electrolytes
- Blood urea nitrogen, creatinine, and uric acid concentration
- Liver function tests
- Urinalysis, microscopy, 24-hour specimen for protein and creatinine clearance
- Type and screen (crossmatch if antibodies present)

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:856–859.

B.2. Discuss bleeding time and platelet count evaluation during preoperative assessment of a patient with preeclampsia requesting epidural analgesia/anesthesia for labor and delivery.

The bleeding time does not specifically measure platelet function, and it can be abnormal in a number of coagulation disorders, such as factor deficiencies. No evidence suggests that the skin bleeding time predicts the potential for bleeding from a traumatized epidural vein in a woman with severe preeclampsia. Therefore, the bleeding time should not be used to measure platelet function. A specific platelet count that predicts the risk of complications from regional anesthesia has not been determined. The *trend* in platelet count is important to note because preeclampsia is a dynamic disorder, and a rapid decrease in platelet count in a short interval may warrant concern.

Many anesthesiologists will place an epidural anesthetic at a platelet count of 80,000 per μL and some at lower platelet counts, especially in otherwise healthy parturients. The preeclamptic patient must be individualized and a thorough

bleeding history, along with the trend in platelet count, should always be considered. If the platelet count is below 100,000 per μL, serial platelet counts as well as the prothrombin time, partial thromboplastin time, and fibrinogen levels should be measured.

Abramovitz S, Beilin Y. Thrombocytopenia, low molecular weight heparin, and obstetric anesthesia. *Anesthesiol Clin North America*. 2003;21:99–109.

Laskin S, Payne B, Hutcheon JA, et al. The role of platelet counts in the assessment of inpatient women with preeclampsia. *J Obstet Gynaecol Can*. 2011;33:900–908.

Lee LO, Bateman BT, Kheterpal S, et al. Risk of epidural hematoma after neuraxial techniques in thrombocytopenic parturients: a report from the multicenter perioperative outcomes group. *Anesthesiology*. 2017;126(6):1053–1063.

B.3. What types of monitoring are important for patients with preeclampsia? When is a central venous pressure (CVP) monitor indicated?

- BP monitoring with noninvasive cuff
- Maternal respiratory function assessment with oxygen saturation
- Foley catheter for assessing urine output
- Monitor deep tendon reflexes and serial magnesium levels
- Tocodynamometer and continuous fetal heart rate monitoring
- Consider invasive BP monitoring with an arterial line when severe refractory hypertension is present; when rapid-acting vasodilators, such as sodium nitroprusside (SNP) or nicardipine, are used; or when noninvasive BP measurement proves difficult (e.g., obesity).
- A CVP monitor or a PA catheter may be indicated for the following conditions:
  - Persistent oliguria
  - Difficulty in fluid management therapy in antepartum and/or postpartum period
  - Presence of pulmonary edema

A survey on the use of invasive hemodynamic monitoring among anesthesiologists who care for patients with preeclampsia indicates that central monitoring is used in 7.5% of patients. When invasive hemodynamic monitoring is used, 56% of anesthesiologists use an arterial line, 26% use an arterial line and central monitoring, and 20% use central monitoring only. Also, 92% of respondents use a CVP monitor, whereas only 8% use a PA catheter. The etiology of pulmonary edema, however, may be due to an increase in capillary permeability as well as from diastolic dysfunction, complicating assessment of cardiac function and volume status. Only in severe forms of preeclampsia is left ventricular systolic function markedly reduced. Furthermore, there may be technical difficulties with placing the PA catheter that are both patient related (awake, anxious, short neck with poorly visible landmarks, coagulopathy) and physician related (inexperience with central venous catheterization), which may alter the balance between benefit and risk of invasive monitoring. Whenever possible, a bedside transthoracic echocardiogram may be obtained; however, there may be limited windows for imaging due to the gravid uterus causing distention of the abdomen.

Birnbach DJ, Gatt SP, Datta S, eds. *Textbook of Obstetric Anesthesia*. New York: Churchill Livingstone; 2000:546.

Ross VH, Moore CH, Fragneto RY, et al. Invasive hemodynamic monitoring in the management of PIH: a survey of practicing anesthesiologists. *Anesthesiology*. 2000;92:A89.

B.4. Discuss the obstetric management of preeclampsia with severe features.

The goal of therapy is to stabilize the mother and to safely deliver the fetus and placenta.

- Administer antihypertensive agents to prevent stroke, myocardial ischemia, or heart failure.

- Administer seizure prophylaxis.
- Determine timing of delivery.

B.5. What are the antihypertensive agents of choice for preeclampsia?

Labetalol is a commonly used antihypertensive agent that decreases maternal SVR without increasing maternal heart rate or decreasing cardiac index, uterine blood flow, or fetal heart rate when it is given in a total dose of less than 1 mg per kg. When given in an initial intravenous bolus dose of 10 to 20 mg, it has a faster onset of action than hydralazine, and, if necessary, the dose may be doubled every 10 minutes. It is useful in the management of refractory hypertension. If a second agent must be administered (e.g., hydralazine, SNP, or nicardipine), labetalol helps to prevent reflex tachycardia. It is important to note that the mechanism of hypertension is mediated greatly by circulating catecholamines, making labetalol a preferred antihypertensive agent that will antagonize the vasoconstrictive effects of norepinephrine, in particular. Other agents may reduce the BP as reflected by a peripheral BP monitor; however, unopposed vasoconstriction at the central and at the microcirculatory levels may cause end-organ injury. Labetalol should be avoided in women with asthma due to risk of bronchospasm.

Hydralazine is another antihypertensive agent that can be used because of its direct vasodilating effect. The full extent of its effect is evident in 20 minutes; therefore, if sufficient time is not allowed between injections, severe hypotension will be seen. It is used in 5- to 10-mg increments intravenously every 20 to 30 minutes until the diastolic BP is decreased, with a cumulative dose of 20 mg. Hydralazine directly decreases peripheral vascular resistance. Reflex sympathetic activity can result in tachycardia and increased stroke volume and cardiac output.

Tachycardia can be treated with labetalol, 10 to 20 mg intravenously. The patient may complain of headache and flushing of the face during therapy.

Nitroglycerin (NTG) causes vascular smooth muscle relaxation by means of its intracellular degradation to NO. The primary effect of NTG is venodilation, but it is less effective in prehydrated patients. NTG readily crosses the placenta. The drug is most useful for short-term treatment (e.g., to control the response to tracheal intubation). Small doses, 50 to 100 μg, may be given intravenously, or NTG may be given sublingually in a 400 μg metered spray.

SNP relaxes the arterial vessels, thereby reducing afterload. However, SNP also reduces venous return. The drug is most useful for short-term treatment, similar to NTG. Cyanide toxicity is proposed to be more likely with prolonged infusion rates that exceed 4 μg/kg/min over several hours to days. However, Naulty et al. demonstrated that intravenous infusion of nitroprusside solution in pregnant ewes, maintained at a rate sufficient to decrease mean maternal arterial pressure by 20% for 1 hour, resulted in equilibration of maternal and fetal levels of nitroprusside at the 20-minute sample. Five of the eight animals exhibited tachyphylaxis to nitroprusside, and their fetuses died in utero with lethal levels of cyanide. No significant changes were observed in uterine blood flow. There have been attempts to counteract the cyanide toxicity of nitroprusside by coadministration of sodium thiosulfate. Curry et al. administered sodium thiosulfate and nitroprusside to pregnant ewes and only nitroprusside to a control group. Although control ewes and fetuses suffered progressive increases in red cell cyanide concentrations into the toxic range, experimental ewes and fetuses never developed toxic red cell cyanide levels. These results suggest that coadministration of sodium thiosulfate with SNP to pregnant women at doses currently in use for

nonpregnant patients will prevent fetal, as well as maternal, cyanide toxicity. Unfortunately, it is not known whether these findings are transferable to humans, raising major concern over ongoing clinical use of nitroprusside in obstetrics when safer drugs such as nicardipine and labetalol are available.

Nifedipine is a calcium entry blocker that affects predominantly arterial and arteriolar smooth muscle. Common maternal side effects include facial flushing, headache, and tachycardia. Nifedipine rapidly lowers BP after oral or sublingual administration. After an initial dose of 10 mg sublingually, it may be repeated in 30 minutes and subsequently given in a maintenance dose of 10 to 20 mg every 3 to 6 hours. Caution must be exercised in the patient receiving both magnesium sulfate and calcium entry blockers because of the risk of myocardial depression and resultant pulmonary edema.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:853–854.

Committee on Obstetric Practice. Committee Opinion No. 692: emergent therapy for acute-onset, severe hypertension during pregnancy and the postpartum period. *Obstet Gynecol*. 2017;129(4):e90–e95.

Curry SC, Carlton MV, Raschke RA. Prevention of fetal and maternal cyanide toxicity from nitroprusside with coinfusion of sodium thiosulfate in gravid ewes. *Anesth Analg*. 1997;84(5):1121–1126.

Duley L, Meher S, Jones L. Drugs for treatment of very high blood pressure during pregnancy. *Cochrane Database Syst Rev*. 2013;(7):CD001449.

Naulty J, Cefalo RC, Lewis PE. Fetal toxicity of nitroprusside in the pregnant ewe. *Am J Obstet Gynecol*. 1981;139(6):708–711.

B.6. What drug therapy is the treatment of choice for seizure prophylaxis?

Magnesium sulfate is the initial therapy for seizure prophylaxis. The Eclampsia Trial Collaborative Group compared magnesium sulfate, phenytoin, and diazepam administration for the prevention of recurrent seizures in women with preeclampsia.

They found that magnesium sulfate was more effective in preventing recurring seizures than either phenytoin or diazepam.

An initial bolus of 4 to 6 g of magnesium sulfate is administered over 20 minutes and followed with an intravenous infusion of 1 to 2 g per hour. Urine output, respiratory rate, and patellar reflexes are monitored during magnesium therapy. The serum magnesium sulfate concentration should be measured at least 4 hours after initiation of therapy. The therapeutic range for serum magnesium sulfate concentrations is between 4 and 6 mEq per L. Loss of deep tendon reflexes occurs at 7 mEq per L with evidence of prolonged PQ intervals and widening QRS complexes. Respiratory depression occurs at 10 mEq per L, and asystole or cardiac arrest occurs at 25 mEq per L.

American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 202: gestational hypertension and preeclampsia. *Obstet Gynecol*. 2019;133(1):e1–e25.

Pauli JM, Repke JT. Preeclampsia: short-term and long-term implications. *Obstet Gynecol Clin North Am*. 2015;42(2):299–313.

The Eclampsia Trial Collaborative Group. Which anticonvulsant for women with eclampsia? Evidence from the collaborative eclampsia trial. *Lancet*. 1995;345(8963):1455–1463.

B.7. Discuss the mechanism of action of magnesium sulfate.

Magnesium has the following effects:

- It is a central nervous system depressant and anticonvulsant.
- It may protect the blood–brain barrier, decrease cerebral edema, or act centrally at *N*-methyl-D-aspartate receptors to raise the seizure threshold.
- It inhibits the release of acetylcholine at the neuromuscular junction, decreases the sensitivity of the motor end plate to acetylcholine, and decreases muscle membrane excitability, thereby potentiating the effects of nondepolarizing and depolarizing muscle relaxants.

- It decreases uterine hyperactivity by its mild relaxant effect on vascular and uterine smooth muscle; it may improve uterine blood flow. Postpartum, it may lead to uterine atony and increased hemorrhage risk.
- It is a mild vasodilator in vascular beds (including small-diameter cerebral vessels) by a direct or indirect (calcium-competing) effect, and it has a mild antihypertensive effect.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:854–855.

Euser AG, Cipolla MJ. Magnesium sulfate treatment for the prevention of eclampsia: a brief review. *Stroke*. 2009;40(4):1169–1175.

B.8. What are the fetal effects of magnesium sulfate therapy?

Magnesium sulfate crosses the placenta. There can be evidence of decreased beat-to-beat variability in the fetal heart rate. Neonatal depression (e.g., respiratory depression and hyporeflexia) also can occur.

Pauli JM, Repke JT. Preeclampsia: short-term and long-term implications. *Obstet Gynecol Clin North Am*. 2015;42(2):299–313.

B.9. Discuss the treatment of magnesium sulfate toxicity.

Magnesium sulfate is excreted by the kidneys. Therefore, urine output must be followed closely and serial serum concentrations of magnesium sulfate must be checked, especially in women with renal dysfunction. If magnesium sulfate toxicity is suspected, the magnesium sulfate infusion should be immediately discontinued. Intravenous calcium gluconate, 1 g, or calcium chloride, 300 mg, should be administered if needed to antagonize the effects of magnesium sulfate along with intravenous furosemide to accelerate urinary excretion. If respiratory distress occurs, the patient may require endotracheal intubation and mechanical ventilation.

American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 202: gestational hypertension and preeclampsia. *Obstet Gynecol*. 2019;133(1):e1–e25.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:854–855.

Curry SC, Carlton MV, Raschke RA. Prevention of fetal and maternal cyanide toxicity from nitroprusside with coinfusion of sodium thiosulfate in gravid ewes. *Anesth Analg*. 1997;84(5):1121–1126.

Naulty J, Cefalo RC, Lewis PE. Fetal toxicity of nitroprusside in the pregnant ewe. *Am J Obstet Gynecol*. 1981;139(6):708–711.

B.10. What conditions mandate immediate delivery, regardless of the gestational age?

- Severe hypertension that is unresponsive to antihypertensive medications
- HELLP syndrome
- Epigastric or right upper quadrant (RUQ) pain that is unresponsive to analgesics
- Persistent headache or other neurologic sequela of preeclampsia (including seizure or stroke)
- New or worsening renal dysfunction (including severe oliguria)
- Pulmonary edema
- Evidence of deteriorating fetal status

American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 202: gestational hypertension and preeclampsia. *Obstet Gynecol*. 2019;133(1):e1–e25.

Datta S, ed. *Anesthetic and Obstetric Management of High-Risk Pregnancy*. 3rd ed. New York: Springer; 2004:407–408.

Sibai BM. Evaluation and management of severe preeclampsia before 34 weeks' gestation. *Am J Obstet Gynecol*. 2011;205(3):191–198.

Uzan J, Carbonnel M, Piccone O, et al. Pre-eclampsia: pathophysiology, diagnosis, and management. *Vasc Health Risk Manag*. 2011;7:467–474.

B.11. Discuss the management of eclampsia.

- Turn patient to the left side; apply jaw thrust.

- Administer oxygen.
- Apply pulse oximeter and monitor.
- Secure intravenous access.
- Check BP at frequent intervals.
- Monitor electrocardiogram (ECG) recordings.
- Secure airway with aspiration precautions if necessary.
- Administer magnesium sulfate to prevent recurrent seizures.
- Deliver the baby expeditiously after maternal stabilization.

American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 202: gestational hypertension and preeclampsia. *Obstet Gynecol*. 2019;133(1):e1–e25.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:866–868.

C. Intraoperative Management

C.1. What is your choice of labor analgesia for patients with preeclampsia?

Most anesthesiologists and obstetricians consider epidural analgesia the safe and preferred form of pain relief for labor and delivery in preeclamptic women. Epidural analgesia provides the following advantages:

- Pain relief that is superior to other analgesic methods
- Attenuation of the exaggerated hypertensive response to pain in preeclamptic women
- Decrease in circulating levels of catecholamines and stress-related hormones, which facilitate BP control
- Improvement of intervillous blood flow in preeclamptic women
- Stable cardiac output
- Preeclamptic women are at increased risk for cesarean delivery compared with other parturients, and early administration of epidural analgesia for labor facilitates the

subsequent administration of epidural anesthesia for emergent cesarean delivery while avoiding the risks of general anesthesia.

Abboud T, Artal R, Sarkis F, et al. Sympathoadrenal activity, maternal, fetal, and neonatal responses after epidural anesthesia in the preeclamptic patient. *Am J Obstet Gynecol*. 1982;144(8):915–918.

Pauli JM, Repke JT. Preeclampsia: short-term and long-term implications. *Obstet Gynecol Clin North Am*. 2015;42(2):299–313.

C.2. What is the advantage of prehydration prior to initiation of neuraxial analgesia?

Prehydration helps compensate for reductions in preload and afterload during the administration of neuraxial analgesia. Two studies have investigated the effects of intravenous volume loading with crystalloid on atrial natriuretic peptide (ANP) secretion in preeclamptic women. ANP is a vasodilator secreted from the cardiac atria in response to an acute volume load, and this response is more pronounced in preeclamptic women. ANP has properties that counteract vasospasm and improve renal elimination of excess extracellular fluid. These studies support the use of volume expansion before administration of neuraxial analgesia in preeclamptic women.

However, in current practice, lower concentrations of local anesthetics combined with an opioid are used for labor analgesia, and fluid preloading is of less clinical relevance. One still needs to be vigilant to the risk of pulmonary edema in the severely preeclamptic patient because the incidence of global diastolic dysfunction, although usually mild, is about 40%.

Melchiorre K, Sutherland GR, Baltabaeva A, et al. Maternal cardiac dysfunction and remodeling in women with preeclampsia at term. *Hypertension*. 2011;57(1):85–93.

C.3. What sensory level of analgesia is required for labor and delivery?

- First stage of labor: T10–L1
- Second stage of labor: S2–S4

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:241.

C.4. Discuss the commonly used local anesthetics for labor analgesia.

Bupivacaine, ropivacaine, and levobupivacaine (amide local anesthetics) are commonly used because they provide potent analgesia with a longer duration but less motor block compared to lidocaine.

Bupivacaine is four times more potent than lidocaine. However, it is also known to be more cardiotoxic. The mechanism relates to its action on cardiac sodium channels. Bupivacaine is a "fast-in, slow-out" agent. While bupivacaine and lidocaine both rapidly block sodium channels to the nerves and to the heart, bupivacaine takes five times longer. This delayed recovery may precipitate arrhythmias.

Ropivacaine is a homolog of mepivacaine and bupivacaine, but it is formulated as a single levorotatory isomer rather than as a racemic mixture. It appears to be less cardiotoxic than bupivacaine.

Levobupivacaine is also a single levorotatory isomer formulation of a local anesthetic. Levobupivacaine appears to be less cardiotoxic than bupivacaine.

2-Chloroprocaine is an ester type of local anesthetic. It is hydrolyzed by plasma cholinesterase, and it has a rapid metabolism, allowing for a very quick onset of action.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:271–274.

C.5. Is the addition of epinephrine to local anesthetics advisable in preeclamptic patients?

Clinical evidence supports the safety of epidural administration of an epinephrine-containing local anesthetic in preeclamptic women. However, care must be taken when using epinephrine-containing local anesthetic solutions in severe preeclamptic women because inadvertent intravascular injection may result in acute severe hypertension.

Dror A, Abboud TK, Moore J, et al. Maternal hemodynamic responses to epinephrine-containing local anesthetics in mild pre-eclampsia. *Reg Anesth*. 1988;13:107–111.

Heller PJ, Goodman C. Use of local anesthetics with epinephrine for epidural anesthesia in preeclampsia. *Anesthesiology*. 1986;65(2):224–226.

C.6. What is the treatment for the abnormal fetal heart rate pattern seen with maternal hypotension after neuraxial analgesia is instituted?

- Administration of oxygen with face mask
- Left uterine displacement
- Administration of intravenous fluids
- Elevation of lower extremities to facilitate venous return
- Administration of small increments of phenylephrine, 50 to 100 μg, or ephedrine, 5 to 10 mg, intravenously, if the BP falls more than 20% of baseline

Vercauteren M. Obstetric spinal analgesia and anesthesia. *Curr Opin Anesthesiol*. 2003;16(5):503–507.

C.7. What would you do after an accidental dural puncture? How do you treat postdural puncture headache?

Accidental dural puncture can be managed with one of two options. First, the epidural needle can be removed and the placement of the epidural catheter may be reattempted in another interspace. Local anesthetic must be administered slowly because now, there is a direct communication with the

intrathecal space through the dural hole, and thereby, a more profound analgesic/anesthetic block may occur. Alternatively, a catheter can be threaded into the intrathecal space and maintained for continuous spinal labor analgesia. This approach may be prudent when the initial placement of the epidural catheter was difficult, allowing for faster pain relief and eliminating the risk of a second dural puncture.

The incidence of a postdural puncture headache after an accidental wet tap with an epidural needle is more than 50%. The headache occurs within 5 days of dural puncture and symptoms may include nausea or vomiting, tinnitus, blurry vision, and neck pain. The only effective treatment is epidural blood patch. Immediate relief occurs in almost 90% of patients on first attempt. Transient side effects include backache and neck pain.

Gaiser R. Postdural puncture headache: an evidence-based approach. *Anesthesiol Clin*. 2017;35(1):157–167.

C.8. How would you manage total spinal anesthesia?

- High spinal anesthesia may occur several minutes after an epidural injection of local anesthetic, especially if the injection is into the subarachnoid or subdural space. It is vitally important to communicate with the patient. Agitation, dyspnea, and difficulty speaking may indicate the onset of total spinal anesthesia.
- Avoid aortocaval compression.
- Administer 100% oxygen.
- Provide positive pressure ventilation if necessary, preferably through an endotracheal tube.
- Monitor maternal BP, ECG recordings, and fetal heart rate.
- Support maternal circulation with intravenous fluids and vasopressors as needed. Give epinephrine if needed.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:263–264.

C.9. Should methylergonovine be given to preeclamptic patients?

Preeclampsia is a relative contraindication to the use of ergot alkaloids because of the risk of inducing a hypertensive crisis. In preeclamptic patients, uterine atony unresponsive to oxytocin may be treated with 15-methylprostaglandin $F_{2\alpha}$.

Suresh M, Segal BS, Preston RL, et al, eds. *Shnider and Levinson's Anesthesia for Obstetrics*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:159–163.

C.10. When and how would you give spinal anesthesia?

Spinal anesthesia may be used for cesarean delivery in patients with preeclampsia. Hyperbaric bupivacaine 0.75% in a dose of 11.25 to 12 mg with or without fentanyl, 15 to 20 μg, and morphine, 100 to 200 μg, may be given.

Advantages of spinal anesthesia in patients with preeclampsia with severe features include the following:

- Avoidance of general anesthesia and risks of difficulty with an edematous airway
- Elimination of risk of severe hypertensive response to laryngoscopy and endotracheal intubation, which can result in intracranial hemorrhage
- More reliable anesthesia than with an epidural anesthetic technique
- Smaller needle size than an epidural and therefore possibly less risk of trauma to epidural veins

One study by Aya et al. noted that the risk of hypotension was almost six times less in severely preeclamptic women than in healthy pregnant women receiving spinal anesthesia for elective cesarean section. In these preeclamptic patients, spinal anesthesia may cause a higher incidence than epidural

anesthesia; however, this hypotension is typically easily treatable and short-lived and has not been linked to clinically significant differences in maternal or neonatal outcomes.

Aya AG, Mangin R, Vialles N, et al. Patients with severe preeclampsia experience less hypotension during spinal anesthesia for elective cesarean delivery than healthy parturients: a prospective cohort comparison. *Anesth Analg*. 2003;97(3):867–872.

Henke VG, Bateman BT, Leffert LR. Focused review: spinal anesthesia in severe preeclampsia. *Anesth Analg*. 2013;117(3):686–693.

C.11. Discuss a general anesthesia technique for the patient with preeclampsia presenting for cesarean delivery.

- Aspiration prophylaxis. Acceptable methods include 30 mL of an oral nonparticulate antacid, and/or an H_2-blocker intravenously, and possibly metoclopramide, 10 mg intravenously.
- Consider arterial line placement before induction in patients with preeclampsia with severe features for continuous BP measurement. The transient but severe hypertension that accompanies tracheal intubation in preeclamptic women can significantly increase maternal intracranial pressure, with the attendant risks of cerebrovascular accident.
- Prepare for possible difficult airway, with available equipment such as a video laryngoscope.
- Preoxygenation and denitrogenation with 100% oxygen through face mask
- Induction of anesthesia with cricoid pressure and either propofol and/or etomidate
- Succinylcholine, 1.5 mg per kg, for rapid sequence intubation
- Use a smaller endotracheal tube (6.0 or 6.5 mm internal diameter) because of airway edema.
- Continue magnesium sulfate administration during the intraoperative and postoperative periods; magnesium sulfate

potentiates the effects of both depolarizing and nondepolarizing muscle relaxants.

- Administer volatile anesthetics until delivery to prevent awareness under anesthesia.
- Consider adding nitrous oxide (N_2O) and reducing volatile anesthetic to 0.5 to 0.75 minimum alveolar concentration (MAC) after delivery to minimize uterine atony and bleeding.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:862–864.

C.12. What agents can you use to prevent hypertension during the induction of general anesthesia for cesarean delivery?

Before induction, labetalol, 5- to 10-mg increments; NTG, 50- to 100-μg increments; or SNP, 50-μg increments, can be used to attenuate the pressor response to laryngoscopy and intubation. The short-acting opioid remifentanil or lidocaine 1.5 mg per kg can also be used.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:862–864.

Pant M, Fong R, Scavone B. Prevention of peri-induction hypertension in preeclamptic patients: a focused review. *Anesth Analg*. 2014;119(6):1350–1356.

D. Postoperative Management

D.1. Discuss the postpartum management of preeclamptic patients.

- Provide adequate analgesia.
- Continue magnesium sulfate for at least 24 hours after delivery, regardless of mode of delivery.
- Maintain strict intake/output during magnesium infusion.
- Maintain hemodynamic control with antihypertensives if

necessary.

- Continue to monitor for symptoms of eclampsia, stroke, and pulmonary edema in the postpartum period.

American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 202: gestational hypertension and preeclampsia. *Obstet Gynecol*. 2019;133(1):e1–e25.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:865.

D.2. Can nonsteroidal anti-inflammatory drugs (NSAIDs) be used to treat postpartum pain in preeclamptic patients?

Increasing concerns surrounding the opioid epidemic as well as narcotic use in breastfeeding women have led to a preference for administration of NSAIDs over opioids for postpartum pain. NSAIDs do not cause a significant elevation of BP in nonpregnant, normotensive individuals but can lead to increased BP in patients with chronic hypertension. However, data suggest NSAID use in hypertensive postpartum patients is safe. For example, one retrospective study by Viteri et al. including 399 patients with preeclampsia found that NSAID use was not associated with persistent postpartum hypertension or adverse outcomes. Also, a randomized controlled trial found that administration of ibuprofen, compared to acetaminophen, did not prolong the duration of severe BP elevations in patients with preeclampsia. In light of this research, the American College of Obstetricians and Gynecologists recommends use of NSAIDs over opioid analgesics in this patient population.

American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 202: gestational hypertension and preeclampsia. *Obstet Gynecol*. 2019;133(1):e1–e25.

Blue NR, Murray-Krezan C, Drake-Lavelle S, et al. Effect of ibuprofen vs acetaminophen on postpartum hypertension in preeclampsia with severe features: a double-masked, randomized controlled trial. *Am J Obstet Gynecol*.

2018;218(6):616.e1–616.e8.

Viteri OA, England JA, Alrais MA, et al. Association of nonsteroidal antiinflammatory drugs and postpartum hypertension in women with preeclampsia with severe features. *Obstet Gynecol*. 2017;130(4):830–835.

Wasden SW, Ragsdale ES, Chasen ST, et al. Impact of non-steroidal anti-inflammatory drugs on hypertensive disorders of pregnancy. *Pregnancy Hypertens*. 2014;4(4):259–263.

29 Breech Presentation, Fetal Distress, and Mitral Stenosis

Jill Fong and Jaime Aaronson

A 24-year-old primigravida at 37 weeks of gestation with fetal breech position presents to the labor and delivery unit for external cephalic version (ECV). The patient has a history of rheumatic fever with no subsequent medical follow-up. On physical examination, she has an opening snap and a diastolic murmur. She reports having shortness of breath when climbing two flights of stairs. Prior to attempting ECV, an epidural catheter is placed without event. After adequate analgesia is achieved, the obstetrician begins to rotate the fetus. Several minutes into the attempted ECV, the fetal heart rate (FHR) decreases to 60 beats per minute. Despite intrauterine resuscitative efforts, the FHR remains at 60 beats per minute. The patient is rushed to the operating room for an emergency cesarean section. Her blood pressure is 100/60 mmHg; pulse rate, 100 beats per minute; and respiratory rate, 18 breaths per minute.

A. Medical Disease and Differential Diagnosis

1. How are fetal lie, presentation, and position defined and determined?
2. What is the approximate frequency of the various lies and

presentations at or near term?

3. What are the different types of breech presentation, and what is their incidence?
4. What is the cause of breech presentation?
5. What are the delivery problems associated with breech presentation?
6. What is the usual obstetrical management for patients with breech presentation?
7. What is the incidence of heart disease in pregnancy and the mortality rate associated with maternal cardiac disease?
8. How is peripartum cardiomyopathy defined?
9. What classifications help predict an individual pregnant woman's cardiac risk?
10. What are the cardiovascular changes of pregnancy?
11. What changes normally occur in heart sounds during pregnancy?
12. What are the normal electrocardiographic and echocardiographic changes seen during pregnancy?
13. What causes rheumatic heart disease?
14. What are the physiologic consequences of mitral stenosis?
15. What are the auscultatory findings associated with mitral stenosis?
16. What may be seen on the electrocardiogram (ECG) in patients with mitral stenosis?
17. What are the echocardiographic findings associated with mitral stenosis?
18. What is the effect of the physiologic changes of pregnancy on patients with mitral stenosis?
19. If mitral stenosis is first recognized during pregnancy and symptoms develop, how would you treat the patient?
20. What are the determinants of fetal oxygenation?
21. What are the determinants of uterine blood flow?

B. Preoperative Evaluation and Preparation

1. How is fetal well-being assessed during labor?
2. How are FHR and maternal contractions monitored?
3. What is the normal FHR with beat-to-beat variability?
4. What are FHR decelerations?
5. How accurate is FHR monitoring in predicting fetal well-being?
6. In a fetus with minimal FHR variability, what other modalities can be used to assess fetal well-being?
7. What is the significance of meconium-stained amniotic fluid?
8. What is meconium aspiration syndrome?
9. What are the usual noninvasive tests used to evaluate the pregnant cardiac patient?
10. What preoperative medications, if any, would you give this patient?

C. Intraoperative Management

1. What monitors would you use in this functional New York Heart Association (NYHA) class II patient during her cesarean section?
2. When would you use invasive monitoring in a pregnant patient with cardiac disease?
3. What are the hemodynamic goals of intraoperative management of the pregnant patient with mitral stenosis?
4. What anesthetic technique would you use for this emergency cesarean section?
5. How would you manage local anesthetic systemic toxicity (LAST) in this patient?
6. If cardiac arrest were to occur prior to delivery, how would you proceed?
7. What technique could you use for general anesthesia in this patient?
8. If you are unexpectedly unable to intubate this patient, how

would you manage the airway?
9. Would this patient benefit from the use of β-blockers?
10. What is the effect of the inhalation agents on uterine contractility?
11. What is the Apgar scoring system?
12. What is the significance of Apgar scores?
13. At birth, what should be done to minimize an infant's risk of meconium aspiration syndrome?
14. If the Apgar score of the newborn is 3 at 1 minute, how would you treat the newborn?
15. Blood gases are sent immediately after delivery. What are the normal values for umbilical vein and artery blood gases?

D. Postoperative Management

1. Immediately after the baby is delivered, the mother's oxygen saturation decreases. What is the differential diagnosis?
2. Additional bleeding occurs in the postanesthesia care unit, and the obstetrician diagnoses retained placenta. What, if any, antibiotics are indicated to prevent endometritis after manual extraction of retained placenta?

A. Medical Disease and Differential Diagnosis

A.1. How are fetal lie, presentation, and position defined and determined?

- Fetal lie—longitudinal, transverse, or oblique—describes the position of the long axis of the fetus relative to the long axis of the mother. Longitudinal lies are either cephalic or pelvic (breech) depending on which fetal structure enters the maternal pelvis. Transverse lies are either back up or back down with the long axis of the fetus perpendicular to the mother's long axis. An oblique lie results when the long axis of the fetus is at an acute angle to that of the mother; it is

usually transitory and converts to transverse or longitudinal when labor begins.

- Presentation describes the part of the fetus that is lowermost in the pelvis: cephalic or breech if the lie is longitudinal, or shoulder if the lie is transverse. Cephalic presentations are further subdivided into vertex, sinciput (anterior fontanel), brow, and face.
- Position describes the relationship of the presenting part to either side (right or left) of the birth canal. For vertex, face, and breech presentations, the determining points are the fetal occiput, chin (mentum), and sacrum, respectively.
- Fetal lie, presentation, and position are determined by manual pelvic and abdominal examination. Ultrasonography is also useful, particularly, when palpation is inconclusive, as can occur with maternal obesity, multiple gestations, placenta previa, and/or polyhydramnios.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 25th ed. New York: McGraw-Hill; 2018:422.

A.2. What is the approximate frequency of the various lies and presentations at or near term?

Longitudinal lie, >99%, which includes cephalic (97%) and breech (3% to 4%); transverse lie, 0.3%. Frequencies of the various presentations are as follows: compound (an extremity prolapses alongside the presenting part), 0.1%; face, 0.05%; and brow, 0.01%.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 25th ed. New York: McGraw-Hill; 2018:422.

A.3. What are the different types of breech presentation, and what is their incidence?

- *Frank breech*: Both fetal lower extremities are flexed at the hips and extended at the knees; the incidence is

approximately 60% (48% to 73%).

- *Complete breech*: One or both knees are flexed; the incidence is approximately 10% (4.6% to 11.5%).
- *Incomplete or footling breech*: One or both hips are extended and one or both feet or knees hangs below the breech; the incidence is approximately 30% (12% to 38%).

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 25th ed. New York: McGraw-Hill; 2018:539.

A.4. What is the cause of breech presentation?

Although the etiology of breech presentation is unknown, certain factors are associated with it; these include prematurity, polyhydramnios, uterine relaxation secondary to high parity, multiple fetuses, oligohydramnios, hydrocephaly, anencephaly, uterine anomalies (e.g., uterine septum), pelvic tumors, placenta previa, cornual–fundal placenta implantation, and previous breech delivery. Ford et al. found the rate of breech recurrence after a previous breech pregnancy to be 9.9% and after two prior breech pregnancies to be 27.5%. After a prior cesarean delivery, a twofold increase in the incidence of breech presentation has been reported.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 25th ed. New York: McGraw-Hill; 2018:422.

Ford JB, Roberts CL, Nassar N, et al. Recurrence of breech presentation in consecutive pregnancies. *BJOG*. 2010;117(7):830–836.

A.5. What are the delivery problems associated with breech presentation?

There is an increased incidence of both maternal and fetal morbidity with breech presentation. For the mother, the mode of delivery—vaginal versus cesarean—correlates with the nature of the morbidity. With vaginal delivery, for example, genital tract laceration is a concern, whereas with cesarean delivery,

extraction of the head may require extension of the hysterotomy. Fetal morbidity occurs in the way of birth trauma, prolapsed umbilical cord, preterm delivery, and fetal anomalies.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 25th ed. New York: McGraw-Hill; 2018:542–550.

A.6. What is the usual obstetrical management for patients with breech presentation?

ECV is a procedure whereby a breech fetus is rotated to vertex position before the onset of labor. The American College of Obstetricians and Gynecologists (ACOG) recommends that ECV be offered to patients with a term singleton breech fetus who desire a planned vaginal delivery (of a vertex-presenting fetus) and have no contraindications. The reported success rate of ECV varies from 35% to 86% and is associated with multiparity, abundant amniotic fluid, a nonengaged presenting part, fetal size ranging from 2,500 to 3,000 g, a posterior placenta, and non-obesity. Tocolysis is variably effective in improving version success rates, and there is more evidence to support betamimetic tocolysis versus, for example, oral nifedipine (10 to 20 mg) or IV nitroglycerin (50 to 100 μg). The use of neuraxial techniques increases the success rate of ECV and reduces cesarean delivery rates for fetal malpresentation. There is no consensus, however, regarding the optimal dose of local anesthetic to facilitate ECV. According to available data, anesthetic doses of neuraxial blockade are better than analgesic doses.

According to ACOG, the decision regarding mode of delivery depends on the experience of the health care provider. To this end, planned vaginal delivery of a term singleton breech fetus may be reasonable under hospital-specific protocol guidelines. Cesarean delivery is commonly performed in the following circumstances: lack of operator experience, incomplete or

footling breech, hyperextended fetal head, fetal macrosomia, unfavorable pelvic shape, severe fetal growth restriction, fetal anomaly incompatible with vaginal delivery, healthy preterm fetus with maternal labor or indicated delivery, previous perinatal death/trauma, maternal cesarean section request, and possibly previous cesarean delivery. The availability of skilled operators to perform safe vaginal delivery of breech fetuses seems to be declining. This trend is likely related to publication of the Term Breech Trial in 2000—a large, international, multicenter, randomized clinical trial that compared planned, breech vaginal delivery to planned cesarean delivery and found perinatal mortality, neonatal mortality, and serious neonatal morbidity to be significantly lower in the planned cesarean group.

American College of Obstetricians and Gynecologists. ACOG Committee Opinion No. 745: mode of term singleton breech delivery. *Obstet Gynecol*. 2018;132(2):e60–e63.

American College of Obstetricians and Gynecologists, Society for Maternal-Fetal Medicine. Obstetric Care Consensus No. 1: safe prevention of the primary cesarean delivery. *Obstet Gynecol*. 2014;123(3):693–711.

Chalifoux LA, Bauchat JR, Higgins, N et al. Effect of intrathecal bupivacaine dose on the success of external cephalic version for breech presentation: a prospective, randomized, blinded clinical trial. *Anesthesiology*. 2017;127(4):625–632.

Goetzinger KR, Harper LM, Tuuli MG, et al. Effect of regional anesthesia on the success rate of external cephalic version: a systematic review and meta-analysis. *Obstet Gynecol*. 2011;118(5):1137–1144.

Hannah ME, Hannah WJ, Hewson SA, et al. Planned caesarean section versus planned vaginal birth for breech presentation at term: a randomised, multicentre trial. Term Breech Trial Collaborative Group. *Lancet*. 2000;356:1375–1383.

Weiniger, CF. Analgesia/anesthesia for external cephalic version. *Curr Opin Anaesthesiol*. 2013;26:278–287.

A.7. What is the incidence of heart disease in pregnancy and the mortality rate associated with maternal

cardiac disease?

Cardiac disease occurs in 1% to 4% of pregnancies and is the leading cause of indirect (i.e., non-obstetric) maternal deaths (15% to 20%). In developing nations, rheumatic fever remains the main cause of valvular disease in pregnancy, and it also continues to be a problem in immigrants to developed countries. In developed countries, congenital, not rheumatic, heart disease is the major cause of heart disease in pregnancy. Other cardiac conditions encountered in pregnancy include cardiomyopathy (peripartum and non-peripartum), pulmonary hypertension, and even ischemic heart disease.

Centers for Disease Control and Prevention. Pregnancy Mortality Surveillance System. https://www.cdc.gov/reproductivehealth/maternalinfanthealth/pregnancy-mortality-surveillance-system.htm. Accessed February 7, 2019.

Elkayam U, Goland S, Pieper PG, et al. High-risk cardiac disease in pregnancy: part I. *J Am Coll Cardiol*. 2016;68(4):396–410.

Simpson LL. Maternal cardiac disease: update for the clinician. *Obstet Gynecol*. 2012;119:345–359.

Small MJ, James AH, Kershaw T, et al. Near-miss maternal mortality: cardiac dysfunction as the principal cause of obstetric intensive care unit admission. *Obstet Gynecol*. 2012;119(2, pt 1):250–255.

A.8. How is peripartum cardiomyopathy defined?

Peripartum cardiomyopathy is an idiopathic cardiomyopathy that presents toward the end of pregnancy or in the months following delivery with heart failure due to left ventricular systolic dysfunction. Unlike valvular heart disease in pregnancy, peripartum cardiomyopathy is a diagnosis of exclusion, and although the left ventricle may not be dilated, the ejection fraction is almost always less than 45%. Because early symptoms may mimic those of normal pregnancy, the index of suspicion for peripartum cardiomyopathy must be high. The incidence worldwide is thought to be 1 per 1,000 pregnancies.

Cunningham FG, Byrne JJ, Nelson DB. Peripartum cardiomyopathy. *Obstet Gynecol*. 2019;133(1):167–179.

Sliwa K, Hilfiker-Kleiner D, Petrie MC, et al; for Heart Failure Association of the European Society of Cardiology Working Group on Peripartum Cardiomyopathy. Current state of knowledge on aetiology, diagnosis, management, and therapy of peripartum cardiomyopathy: a position statement from the Heart Failure Association of the European Society of Cardiology Working Group on Peripartum Cardiomyopathy. *Eur J Heart Fail*. 2010;12(8):767–778.

A.9. What classifications help predict an individual pregnant woman's cardiac risk?

There are three models for maternal cardiac risk stratification—Cardiac Disease in Pregnancy (CARPREG), Zwangerschap bij Aangeboren Hartafwijkingen I (ZAHARA), and World Health Organization (WHO) (**Table 29.1**). The NYHA classification, although not widely used to determine overall risk, is included in each of the models:

TABLE 29.1 World Health Organization (WHO) Risk Classification for Cardiovascular Disease in Pregnancy

WHO class I: no increase mortality risk; no/mild increase morbidity	• Uncomplicated, small or mild – Pulmonary stenosis – Patent ductus arteriosus – Mitral valve prolapse • Successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, anomalous pulmonary venous drainage). • Atrial or ventricular ectopic beats, isolated
WHO class II: small increase mortality risk; moderate increase morbidity	• Unoperated atrial or ventricular septal defect • Repaired tetralogy of Fallot • Most arrhythmias
WHO classes II to III (depends on individual)	• Mild left ventricular impairment • Hypertrophic cardiomyopathy • Native or tissue valvular heart disease not considered WHO class I or IV • Marfan syndrome without aortic dilation • Aorta <45 mm in aortic disease associated with bicuspid aortic valve • Repaired coarctation

WHO class III: significant increase mortality risk; severe increase morbidity	• Mechanical valve • Systemic right ventricle • Fontan circulation • Cyanotic heart disease (unrepaired) • Other complex congenital heart disease • Aortic dilation 40–45 mm in Marfan syndrome • Aortic dilation 45–50 mm in aortic disease associated with bicuspid aortic valve
WHO class IV: extremely high-risk mortality/morbidity; pregnancy contraindicated; discuss termination	• Pulmonary arterial hypertension of any cause • Severe systemic ventricular dysfunction (LVEF <30%, NYHA III–IV) • Severe mitral stenosis, severe symptomatic aortic stenosis • Marfan syndrome with aorta dilated >45 mm • Aortic dilation >50 mm in aortic disease associated with bicuspid aortic valve • Native severe coarctation

LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.
Modified from Thorne S, MacGregor A, Nelson-Piercy C. Risks of contraception and pregnancy in heart disease. *Heart*. 2006;92(10):1520–1525; with permission from BMJ Publishing Group Ltd.; Regitz-Zagrosek V, Blomstrom Lundqvist C, Borghi C, et al. ESC guidelines on the management of cardiovascular diseases during pregnancy: the Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). *Eur Heart J*. 2011;32(24):3147–3197.

- *Class I*: no limitation of physical activity
- *Class II*: slight limitation of physical activity; symptoms with ordinary activity
- *Class III*: marked limitation of physical activity; symptoms with less than ordinary activity
- *Class IV*: unable to carry out any physical activity without discomfort; symptoms may be present at rest

According to the American College of Cardiology, the WHO model best predicts cardiovascular risk in pregnant patients with congenital heart disease. The Task Force for the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology recommends disease-specific risk be assessed using the modified WHO classification and that risk estimation should be further refined by CARPREG, ZAHARA, and Registry of Pregnancy and Cardiac Disease (ROPAC).

Neonatal and maternal adverse events are highly correlated; specifically, maternal cardiac disease is associated with neonatal complications, which include small for gestational age, prematurity, and death. In women with cardiac disease, maternal predictors of increased neonatal adverse events include baseline NYHA class >II, cyanosis, smoking during pregnancy, left-sided heart obstruction, multiple gestations, oral anticoagulation during pregnancy, and presence of a mechanical valve prosthesis.

Drenthen W, Boersma E, Balci A, et al. Predictors of pregnancy complications in women with congenital heart disease. *Eur Heart J*. 2010;31(17):2124–2132.

Furenäs E, Eriksson P, Wennerholm UB, et al. Effects of maternal age and cardiac disease severity on outcome of pregnancy in women with congenital heart disease. *Int J Cardiol*. 2017;243:197–203.

Owens A, Yang J, Nie L, et al. Neonatal and maternal outcomes in pregnant women with cardiac disease. *J Am Heart Assoc*. 2018;7(21):e009395.

Regitz-Zagrosek V, Blomstrom Lundqvist C, Borghi C, et al. ESC guidelines on the management of cardiovascular diseases during pregnancy: the Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). *Eur Heart J*. 2011;32(24):3147–3197.

Siu SC, Sermer M, Colman JM, et al. Prospective multicenter study of pregnancy outcomes in women with heart disease. *Circulation*. 2001;104(5):515–521.

Stangl V, Schad J, Gossing G, et al. Maternal heart disease and pregnancy outcome: a single-centre experience. *Eur J Heart Fail*. 2008;10(9):855–860.

A.10. What are the cardiovascular changes of pregnancy?

During the first trimester of pregnancy, cardiac output increases 40% to 50% above the normal nonpregnant level and plateaus at approximately 28 weeks of gestation. It remains fairly stable until the stresses imposed by labor increase it further. The increase in cardiac output is due to a 30% increase in stroke volume and a 15% increase in heart rate. Blood pressure, however, is not elevated because peripheral vascular resistance decreases. Central venous pressure, pulmonary capillary wedge

pressure, pulmonary artery diastolic pressure, and left ventricular stroke work index are unchanged when compared to nonpregnant values.

During labor, cardiac output increases approximately 15% with uterine contractions during the latent phase, 30% in the active phase, and 45% in the expulsive phase when compared to prelabor values. The greatest increase in cardiac output occurs immediately postpartum when it increases an average of 80% above prelabor values. Cardiac output and heart rate decline to prelabor values within 1 hour of delivery, and by approximately 24 hours, mean blood pressure and stroke volume return to prelabor baseline. The cardiovascular changes of pregnancy resolve in the first 3 to 6 months after delivery. It can take up to a year, however, for the residual effects of cardiovascular remodeling to subside.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:13–20.

A.11. What changes normally occur in heart sounds during pregnancy?

It is normal for changes in heart sounds to occur in pregnancy. There may be, for example, an exaggerated splitting of the first heart sound and increased loudness of both components. There may also be a loud third heart sound. Soft diastolic murmurs occur, as do continuous murmurs arising from the breast vasculature.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 25th ed. New York: McGraw-Hill; 2018:61.

A.12. What are the normal electrocardiographic and echocardiographic changes seen during pregnancy?

It is also normal for changes in the ECG and echocardiogram to occur in pregnancy. Commonly seen electrocardiographic

changes include slight left axis deviation as well as Q waves in leads II, III, and avF. Flat or inverted T waves may also occur. ST elevations, however, do not occur normally and should be considered pathologic. Normal echocardiographic findings include an increase in both left ventricular wall mass and the atrial diameters bilaterally, whereas left ventricular function may be unchanged or slightly improved. The annuli of the pulmonary, tricuspid, and mitral valves dilate progressively, and term pregnant women may have mild tricuspid, pulmonic, and/or (but much more infrequently) mitral regurgitation. A small pericardial effusion may develop as well.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:987–1033.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 25th ed. New York: McGraw-Hill; 2018:61.

A.13. What causes rheumatic heart disease?

Rheumatic heart disease occurs in patients who have had acute rheumatic fever (ARF)—an immune-mediated illness that develops after an untreated group A streptococcal infection. It predominantly affects the heart and joints and may lead to chronic heart disease. ARF occurs most commonly in the winter and spring in children between the ages of 5 and 15 years old. In developed countries, ARF is much less common than it was a few decades ago.

The pathogenetic mechanism of ARF is unknown. The manifestations are extremely variable, and specific laboratory tests to confirm the diagnosis do not exist. The diagnosis is clinical and made using the Jones criteria, revised by the American Heart Association in 1992, and again in 2000. Diagnosis of ARF requires evidence of a preceding group A streptococcal infection in conjunction with two major or one major plus two minor manifestations (**Table 29.2**).

TABLE 29.2 Revised Jones Criteria

For all patients with a preceding GAS infection	
• Diagnosis: initial ARF	Two major or one major plus two minor manifestations
• Diagnosis: recurrent ARF	Two major or one major and two or three minor manifestations
Major criteria—low-risk populations	Major criteria—moderate-/high-risk populations
• Carditis (clinical and/or subclinical)	• Carditis (clinical and/or subclinical)
• Arthritis (polyarthritis only)	• Arthritis (mono- or polyarthritis; polyarthralgia)
• Chorea	• Chorea
• Erythema marginatum	• Erythema marginatum
• Subcutaneous nodules	• Subcutaneous nodules
Minor criteria—low risk populations	Minor criteria—moderate/high risk populations
• Polyarthralgia	• Monoarthralgia
• Fever (≥38.5°C)	• Fever (≥38°C)
• ESR ≥60 mm in first hr and/or CRP ≥3.0 mg/dL (or upper limit of normal for laboratory; use peak value)	• ESR ≥30 mm/hr and/or CRP ≥3.0 mg/dL (or upper limit of normal for laboratory; use peak value)
• Prolonged PR interval (after accounting for age (unless carditis is a major criterion)	• Prolonged PR interval (after accounting for age (unless carditis is a major criterion)

ARF, acute rheumatic fever; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; GAS, group A streptococcus.

Reprinted with permission from Gewitz MH, Baltimore RS, Tani LY, et al. Revision of the Jones Criteria for the diagnosis of acute rheumatic fever in the era of Doppler echocardiography: a scientific statement from the American Heart Association. *Circulation*. 2015;131(20):1806–1818. Copyright © 2018 American Heart Association, Inc.

Of note, rheumatic heart disease is the only long-term sequelae of ARF. With improved ability to prevent recurrent attacks, prognosis has improved and is related directly to the severity of cardiac involvement during the acute phase. More widespread use of echocardiography has revealed the prevalence of rheumatic heart disease in developing countries to be about 10-fold greater than that recognized by conventional screening.

In almost all adults, mitral stenosis is caused by previous rheumatic carditis, although approximately 60% of patients with rheumatic mitral valve disease do not report a history of rheumatic fever or chorea. In about 40% of all patients with

rheumatic heart disease, isolated mitral stenosis occurs. Mitral valve insufficiency and aortic valve stenosis and insufficiency can also occur in these patients.

Gewitz MH, Baltimore RS, Tani LY, et al. Revision of the Jones Criteria for the diagnosis of acute rheumatic fever in the era of Doppler echocardiography: a scientific statement from the American Heart Association. *Circulation*. 2015;131(20):1806–1818.

Karthikeyan G, Guilherme L. Acute rheumatic fever. *Lancet*. 2018;392(10142):161–174.

Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Thorac Cardiovasc Surg*. 2014;148(1):e1–e132.

A.14. What are the physiologic consequences of mitral stenosis?

The normal mitral valve orifice area is 4 to 6 cm^2, but with mitral stenosis, the valve area is reduced to varying degrees. When it reaches 2 cm^2, cardiovascular hemodynamics are impaired. A valve area of ≤1.5 cm^2 is considered moderate mitral stenosis, and as the cross-sectional area decreases further to 1 cm^2 and mean left atrial pressure increases to at least 25 mmHg to maintain an adequate cardiac output, it is considered severe. The pathophysiology of mitral stenosis results from obstruction of blood flow from the left atrium into the left ventricle.

The increase in heart rate, cardiac output, red blood cell mass, and plasma volume that occurs with pregnancy can lead to increased atrial pressure and cardiac decompensation in patients with mitral stenosis. Specifically, cardiac consequences include a decline in functional capacity, atrial arrhythmias, and pulmonary edema. Pulmonary hypertension can also result due to elevated left atrial pressure and pulmonary arteriolar constriction. If severe pulmonary hypertension develops, right-

sided heart failure can ensue.

Elkayam U, Goland S, Pieper PG, et al. High-risk cardiac disease in pregnancy: part I. *J Am Coll Cardiol*. 2016;68(4):396–410.

Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Thorac Cardiovasc Surg*. 2014;148(1):e1–e132.

A.15. What are the auscultatory findings associated with mitral stenosis?

The first heart sound is accentuated, whereas the second heart sound is normal or accentuated. There may be an opening snap, which is usually loudest at the apex. A diastolic rumbling murmur is best heard at the apex with the patient in left lateral decubitus position and usually starts with or shortly after the opening snap and may continue through the entire diastolic phase. The presence of pulmonary hypertension may, however, alter the auscultatory findings associated with mitral stenosis; the first heart sound may be normal or only slightly accentuated, and the opening snap and diastolic murmur may be absent.

Dack S, Bleifer S, Grishman A, et al. Mitral stenosis: auscultatory and phonocardiographic findings. *Am J Cardiol*. 1960;5:815–835.

A.16. What may be seen on the electrocardiogram (ECG) in patients with mitral stenosis?

Broadened, diphasic P waves in lead V_1 are a common finding. There may be signs of right ventricular hypertrophy if pulmonary hypertension is marked. Atrial fibrillation may be present.

Walsh RA, Fang JC, Fuster V, eds. *Hurst's The Heart: Manual of Cardiology*. 13th ed. New York: McGraw-Hill; 2013:383.

A.17. What are the echocardiographic findings associated with mitral stenosis?

Mitral stenosis is characterized by both thickening and shortening of the leaflets and chordae and fusion of the commissures, which results in doming of the leaflets in diastole. Together, these changes restrict valve opening, leading to varying degrees of mitral stenosis. On echocardiogram, the anterior leaflet is commonly described as having a "hockey stick" appearance (**Fig. 29.1**).

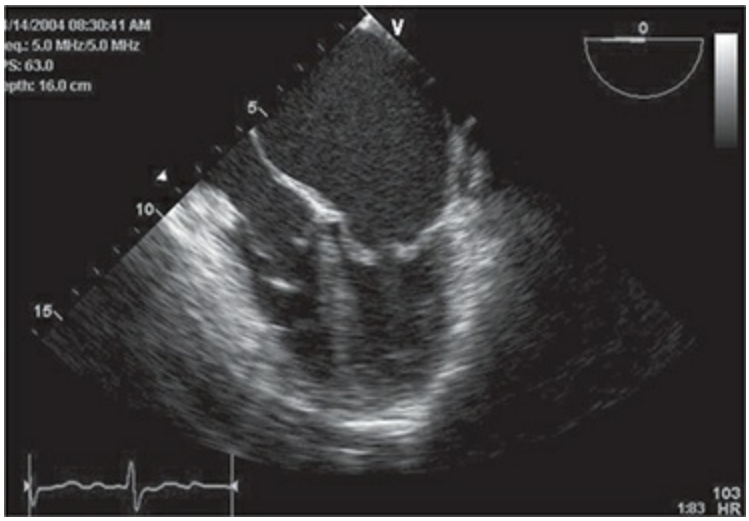


FIGURE 29.1. Two-dimensional echocardiography of the mitral valve showing severe mitral stenosis with the typical "hockey-stick" appearance.

With mitral stenosis, diastolic filling of the left ventricle is compromised, and in turn, left atrial pressure increases and the left atrium may become dilated. Long-standing mitral stenosis leads to pulmonary hypertension by way of increased pulmonary vascular resistance. Two-dimensional echocardiography is used to evaluate mitral valve area and morphology. Three-dimensional echocardiography, however, enhances the ability to examine mitral valve morphology and allows for complete assessment in a single-imaging plane. Continuous Doppler across the mitral valve best measures the severity of the lesion.

Wunderlich NC, Beigel R, Siegel RJ. Management of mitral stenosis using 2D and 3D echo-Doppler imaging. *JACC Cardiovasc Imaging*. 2013;6(11):1191–1205.

A.18. What is the effect of the physiologic changes of pregnancy on patients with mitral stenosis?

The increased cardiovascular load of pregnancy can cause patients to deteriorate and even advance from one NYHA classification to another. Increased cardiac output, tachycardia, and fluid retention increase the pressure gradient across the stenotic valve, which explains why more than half of NYHA class I and II patients with mitral stenosis, therefore, have worsening clinical symptomatology during pregnancy. A decline in functional capacity, atrial fibrillation, and/or pulmonary edema, for example, may occur. The incidence of maternal and fetal complications is related to the severity of stenosis, and maternal and perinatal outcomes depend largely on maternal functional status during pregnancy. Maternal mortality and morbidity is, not surprisingly, increased in parturients with NYHA III and IV disease.

Hameed A, Karaalp IS, Tummala PP, et al. The effect of valvular heart disease on maternal and fetal outcome of pregnancy. *J Am Coll Cardiol*. 2001;37(3):893–899.

Nanna M, Stergiopoulos K. Pregnancy complicated by valvular heart disease: an update. *J Am Heart Assoc*. 2014;3(3):e000712.

Silversides CK, Colman JM, Sermer M, et al. Cardiac risk in pregnant women with rheumatic mitral stenosis. *Am J Cardiol*. 2003;91(11):1382–1385.

A.19. If mitral stenosis is first recognized during pregnancy and symptoms develop, how would you treat the patient?

Heart rate reduction and decreased left atrial pressure are the standard therapeutic goals for women with moderate to severe mitral stenosis. Therefore, β-adrenergic receptor blockade is the cornerstone of medical therapy in the symptomatic patient. It is useful in preventing tachycardia and prolonging diastolic filling time, which can result in marked improvement of symptoms.

Atrial fibrillation or flutter should be treated aggressively; a rapid ventricular response compromises diastolic flow time and can lead to pulmonary edema. For rate control, digoxin or a β-adrenergic receptor blocker should be given. Calcium channel blockers are also thought to be safe in pregnancy, although there is less data to support their use. If, on the other hand, the patient is unstable, synchronized cardioversion should be used. Atrial fibrillation not only increases the risk of pulmonary edema but also increases the likelihood of a thromboembolic event, which is why patients with persistent atrial fibrillation should be anticoagulated. There is some data to suggest that patients with severe mitral stenosis should receive antithrombotic therapy even if they are in sinus rhythm because of the potential for thrombotic events.

If symptoms of pulmonary congestion develop, salt restriction and cautious use of diuretics decrease left atrial pressure by decreasing blood volume. Avoidance of both hypovolemia and decreased uteroplacental perfusion are essential. If symptoms are uncontrolled by medical therapy, the mitral valve should be repaired or replaced. Percutaneous balloon valvuloplasty can be done using echocardiography or, if radiographic imaging is required, with appropriate shielding of the fetus. It has a low morbidity rate for both the mother and fetus and has favorable long-term results when performed in NYHA functional class III and IV patients. If a contraindication to balloon valvuloplasty exists, surgical commissurotomy or valve replacement should be done, although it is usually well tolerated by the mother (i.e., comparable to nonpregnant women), fetal loss of over 20% has been reported.

Esteves CA, Munoz JS, Braga S, et al. Immediate and long-term follow-up of percutaneous balloon mitral valvuloplasty in pregnant patients with mitral stenosis. *Am J Cardiol*. 2006;98(6):812–816.

Hameed A, Akhter M, Bitar F, et al. Left atrial thrombosis in pregnant women

with mitral stenosis and sinus rhythm. *Am J Obstet Gynecol*. 2005;193(2):501–504.

Katsi V, Georgiopoulos G, Marketou M, et al. Atrial fibrillation in pregnancy: a growing challenge. *Curr Med Res Opin*. 2017;33(8):1497–1504.

Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Thorac Cardiovasc Surg*. 2014;148(1):e1–e132.

Sutton SW, Duncan MA, Chase VA, et al. Cardiopulmonary bypass and mitral valve replacement during pregnancy. *Perfusion*. 2005;20(6):359–368.

A.20. What are the determinants of fetal oxygenation?

Oxygen delivery to the fetal circulation occurs via the placenta. The factors that affect oxygen exchange across the placenta include blood flow (maternal placental and fetal placental), maternal blood oxygen capacity, maternal and fetal blood oxygen affinity, and both placental oxygen diffusion capacity and oxygen consumption.

Carter AM. Evolution of factors affecting placental oxygen transfer. *Placenta*. 2009;30(suppl A):S19–S25.

A.21. What are the determinants of uterine blood flow?

Uterine blood flow is derived from Ohm's law, which states that pressure equals flow multiplied by resistance. It is shown as follows:

$$\text{Uterine blood flow} = \frac{\text{uterine artery pressure} - \text{uterine venous pressure}}{\text{uterine artery resistance}}$$

At term, 10% to 15% of maternal cardiac output goes to the uterus (i.e., approximately 750 mL per minute). Uterine blood flow is directly related to maternal blood pressure because the uterine vessels do not autoregulate.

Datta S, Kodali BS, Segal S. *Obstetric Anesthesia Handbook*. 5th ed. New York: Springer; 2010:69.

Gabbe SG, Niebyl JR, Simpson JL, et al, eds. *Obstetrics: Normal and*

Problem Pregnancies. 7th ed. Philadelphia, PA: Elsevier; 2017:23.

B. Preoperative Evaluation and Preparation

B.1. How is fetal well-being assessed during labor?

Fetal well-being is dependent on an intact uteroplacental unit. Simultaneous monitoring of FHR and uterine contractions aids in the detection of fetal distress.

American College of Obstetricians and Gynecologists. Practice Bulletin No. 106: intrapartum fetal heart rate monitoring: nomenclature, interpretation, and general management principles. *Obstet Gynecol*. 2009;114(1):192–202.

B.2. How are FHR and maternal contractions monitored?

FHR can be monitored noninvasively using the Doppler technique or invasively using a fetal scalp electrode. Uterine contractions may be monitored noninvasively by a tocodynamometer, which measures the tightening of maternal abdominal muscles, or invasively by a transcervical pressure catheter connected to a strain gauge.

American College of Obstetricians and Gynecologists. Practice Bulletin No. 106: intrapartum fetal heart rate monitoring: nomenclature, interpretation, and general management principles. *Obstet Gynecol*. 2009;114(1):192–202.

Bakker JJ, Janssen PF, van Halem K, et al. Internal versus external tocodynamometry during induced or augmented labor. *Cochrane Database Syst Rev*. 2013;(8):CD006947.

B.3. What is the normal FHR with beat-to-beat variability?

In the third trimester, the normal baseline FHR is between 110 and 160 beats per minute with beat-to-beat variability (6 to 25 beats per minute). A baseline FHR <110 beats per minute is termed *bradycardia* and >160 beats per minute is *tachycardia*.

American College of Obstetricians and Gynecologists. Practice Bulletin No. 116: management of intrapartum fetal heart rate tracings. *Obstet Gynecol*.

2010;116(5):1232–1240.

B.4. What are FHR decelerations?

A deceleration is a decrease in FHR from baseline. Decelerations fall into three categories—early, late, or variable—depending on their shape and timing with respect to maternal contractions (Fig. 29.2).

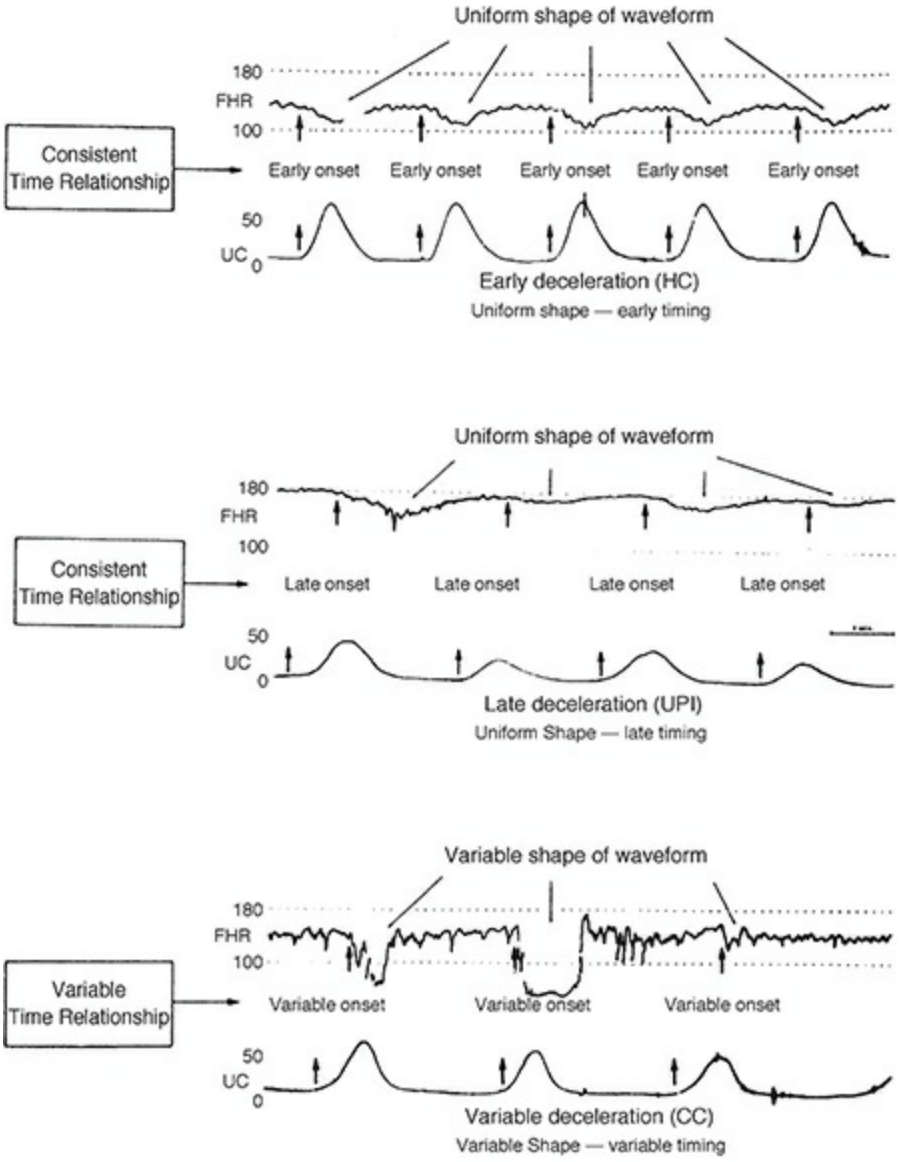


FIGURE 29.2. Fetal heart rate (FHR) decelerations in relation to the time of onset of uterine contractions (UCs). CC, cord compression; HC, head compression; UPI, uteroplacental insufficiency. (*From Hon EH.* An Atlas of Fetal Heart Rate Patterns. *New Haven, CT: Harty Press; 1968, with permission.*)

- Early deceleration—symmetrical, gradual decrease and return of FHR that coincides with the onset, peak, and end of a uterine contraction. They are thought to be a vagal response caused by fetal head compression and are not associated with fetal hypoxia, acidemia, or low Apgar scores.
- Late deceleration—symmetrical, gradual decrease and return of FHR that begins after the onset of a contraction and lasts beyond the end. They indicate uteroplacental insufficiency and require prompt evaluation and treatment.
- Variable deceleration—abrupt decrease in FHR with an onset, depth, and duration that varies with successive uterine contractions. The decrease in FHR is 15 beats per minute or greater, and lasts between 15 seconds and 2 minutes. They are FHR reflexes that reflect fetal blood pressure changes due to umbilical cord compression or changes in fetal oxygenation.

A prolonged deceleration is a decrease from baseline that is 15 beats per minute or more and lasts 2 or more minutes but less than 10 minutes.

American College of Obstetricians and Gynecologists. Practice Bulletin No. 116: management of intrapartum fetal heart rate tracings. *Obstet Gynecol*. 2010;116(5):1232–1240.

B.5. How accurate is FHR monitoring in predicting fetal well-being?

FHR monitoring is used to determine fetal oxygenation (i.e., fetal well-being). This is because the fetal brain, via a combination of sympathetic and parasympathetic pathways, modulates the FHR. The accuracy of FHR monitoring is thought to be limited, however, by various factors, which include questions about its overall efficacy as well as clinician reliability.

At the present time, a three-tiered system is used to evaluate

and manage intrapartum electronic FHR patterns. Category I FHR tracings are normal and include a baseline heart rate of 110 to 160 beats per minute, moderate beat-to-beat variability, and no late or variable decelerations; early decelerations and accelerations may or may not be present. Category I tracings are not associated with fetal acidemia. Category III FHR tracings are abnormal and are characterized by the absence of variability and either recurrent late decelerations, recurrent variable decelerations, bradycardia, or a sinusoidal pattern. Unlike category I FHR tracings, category III tracings are associated with an increased risk for fetal acidemia (at the time of interpretation). Category II FHR tracings are considered to be indeterminate and include all those not categorized as either category I or III. They are not predictive of abnormal fetal acid–base status but require evaluation, intervention when applicable, and continuous surveillance. Of interest, Cahill et al. conducted a retrospective cohort study of more than 5,000 term births and found that none of the three categories had a significant association with neonatal blood acidemia (pH ≤7.10) when considered in the last 10 or 30 minutes prior to delivery. *Minimal variability without an identifiable cause or that does not resolve with appropriate resuscitative measures may indicate fetal acidemia.*

American College of Obstetricians and Gynecologists. Practice Bulletin No. 106: intrapartum fetal heart rate monitoring: nomenclature, interpretation, and general management principles. *Obstet Gynecol*. 2009;114(1):192–202.

American College of Obstetricians and Gynecologists. Practice Bulletin No. 116: management of intrapartum fetal heart rate tracings. *Obstet Gynecol*. 2010;116(5):1232–1240.

Cahill AG, Roehl KA, Odibo AO, et al. Association and prediction of neonatal acidemia. *Am J Obstet Gynecol*. 2012;207(3):206.e1–206.e8.

Macones GA, Hankins GD, Spong CY, et al. The 2008 National Institute of Child Health and Human Development workshop report on electronic fetal monitoring: update on definitions, interpretations, and research guidelines.

Obstet Gynecol. 2008;112(3):661–666.

B.6. In a fetus with minimal FHR variability, what other modalities can be used to assess fetal well-being?

There are four techniques that can be used to elicit or improve FHR variability—fetal scalp sampling, Allis clamp scalp stimulation, vibroacoustic stimulation, and digital scalp stimulation. The latter two options are preferred given the invasiveness of the former. In a parturient with a breech fetus, any technique that requires access to the fetal head would, of course, not be applicable.

American College of Obstetricians and Gynecologists. Practice Bulletin No. 106: intrapartum fetal heart rate monitoring: nomenclature, interpretation, and general management principles. *Obstet Gynecol*. 2009;114(1):192–202.

Skupski DW, Rosenberg CR, Eglinton GS. Intrapartum fetal stimulation tests: a meta-analysis. *Obstet Gynecol*. 2002;99(1):129–134.

B.7. What is the significance of meconium-stained amniotic fluid?

Meconium-stained amniotic fluid occurs in 4% to 22% of births. In and of itself, it does not indicate an adverse outcome. In fact, it has been suggested that meconium becomes an environmental hazard when fetal acidemia occurs rather than meconium release being a marker of preexisting fetal compromise.

American College of Obstetricians and Gynecologists Committee on Obstetric Practice. ACOG Committee Opinion Number 346, October 2006: amnioinfusion does not prevent meconium aspiration syndrome. *Obstet Gynecol*. 2006;108(4):1053.

Blackwell SC, Moldenhauer J, Hassan SS, et al. Meconium aspiration syndrome in term neonates with normal acid-base status at delivery: is it different? *Am J Obstet Gynecol*. 2001;184(7):1422–1426.

Greenwood C, Lalchandani S, MacQuillan K, et al. Meconium passed in labor: how reassuring is clear amniotic fluid? *Obstet Gynecol*. 2003;102(1):89–93.

Ramin KD, Leveno KJ, Kelly MA, et al. Amniotic fluid meconium: a fetal

environmental hazard. *Obstet Gynecol*. 1996;87(2):181–184.

B.8. What is meconium aspiration syndrome?

Meconium aspiration syndrome is a respiratory condition that occurs in neonates born through meconium-stained amniotic fluid. The degree of respiratory distress is variable, but severe cases are associated with perinatal mortality. The pathophysiology of meconium aspiration is incompletely understood and complex, with a number of contributing factors —airway obstruction, surfactant dysfunction, chemical pneumonitis, and persistent pulmonary hypertension of the newborn. Treatment is mainly supportive in nature, although infants who fail conventional ventilation strategies appear to benefit from extracorporeal membrane oxygenation.

Chettri S, Bhat BV, Adhisivam B. Current concepts in the management of meconium aspiration syndrome. *Indian J Pediatr*. 2016;83(10):1125–1130.

Swarnam K, Soraisham AS, Sivanandan S. Advances in the management of meconium aspiration syndrome. *Int J Pediatr*. 2012;2012:359571.

Vain NE, Batton DG. Meconium "aspiration" (or respiratory distress associated with meconium-stained amniotic fluid?). *Semin Fetal Neonatal Med*. 2017;22(4):214–219.

B.9. What are the usual noninvasive tests used to evaluate the pregnant cardiac patient?

Physical examination, exercise tolerance, ECG, pulse oximetry, Holter monitoring, and echocardiography with Doppler flow studies may all be useful to evaluate these patients. Cardiac magnetic resonance imaging is safe in pregnant women, but the use of contrast dye should be limited to those situations in which its use will improve diagnostic performance. Tests using radiation should be avoided unless absolutely necessary, and it is best to delay radiologic exams until as late as possible in the pregnancy and to use protective fetal radiation shielding. The risk of fetal anomalies is low, however, with less than 50 mGy

of radiation exposure. Radiation exposure with a chest radiograph is, for example, less than 0.1 mGy, whereas the fetal exposure is between 0.0005 and 0.01 mGy.

Brent RL. Saving lives and changing family histories: appropriate counseling of pregnant women and men and women of reproductive age, concerning the risk of diagnostic radiation exposures during and before pregnancy. *Am J Obstet Gynecol*. 2009;200(1):4–24.

Jain C. ACOG Committee Opinion No. 723: guidelines for diagnostic imaging during pregnancy and lactation. *Obstet Gynecol*. 2019;133(1):186.

B.10. What preoperative medications, if any, would you give this patient?

Prophylactic antibiotics to prevent endocarditis are not recommended for women with acquired (or congenital) heart disease for either vaginal or cesarean delivery in the absence of infection. According to the American Heart Association, it is reasonable to consider antibiotic prophylaxis only for those women at highest risk of an adverse outcome from infective endocarditis (e.g., prosthetic cardiac valve or material, previous endocarditis, unrepaired cyanotic heart disease, during the first 6 months after complete repair of congenital heart disease, presence of residual defects after repair of congenital heart disease, and valvulopathy after heart transplant). When prophylactic antibiotics are indicated, the regimens are as follows: amoxicillin (2 g orally), or in patients unable to take anything by mouth, ampicillin (2 g intravascular [IV]), or cefazolin (1 g IV), or ceftriaxone (1 g IV) should be given 30 to 60 minutes before the procedure. If the patient is allergic to ampicillin or penicillin, cefazolin (1 g IV), or ceftriaxone (1 g IV), or clindamycin (600 mg IV) should be given.

Prophylactic antibiotics are indicated for patients undergoing cesarean section to prevent endometritis, febrile morbidity, and wound infections. ACOG recommends that a prophylactic antibiotic, namely a first-generation cephalosporin (i.e.,

cefazolin) be given within 1 hour of surgical incision. This time frame is known to decrease postcesarean section maternal infections without adverse neonatal effects.

Pregnant patients are considered to be at increased risk for aspiration of gastric contents. Gastric fluid volume, though, is not different in pregnant patients versus their nonpregnant counterparts, and pregnancy itself does not decrease gastric emptying (except during labor). The increased risk for aspiration is thought to be due to a decrease in lower esophageal sphincter tone as well as an increased risk of difficult intubation. Although the exact time at which the risk increases is unclear, it is prudent to consider pregnant patients to be at increased risk for aspiration of gastric contents after 16 to 20 weeks of gestation.

In this patient for emergency cesarean delivery, an oral nonparticulate antacid, such as 15 to 30 mL of 0.3 M sodium citrate, given immediately before induction reduces the risk of developing aspiration pneumonitis. H_2-receptor antagonists (ranitidine and famotidine), as well as metoclopramide may also decrease the risk, but require more time (at least 30 to 40 minutes) to be effective. These drugs may be given after the anesthetic induction if time does not allow for dosing before. Avoiding general anesthesia is the most effective way to prevent the risk of aspiration.

American College of Obstetricians and Gynecologists Committee on Practice Bulletins—Obstetrics. ACOG Practice Bulletin No. 199: use of prophylactic antibiotics in labor and delivery. *Obstet Gynecol*. 2018;132(3):e103–e119.

Apfelbaum J, Hawkins J, Madhulika A, et al. Practice guidelines for obstetric anesthesia: an updated report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia and the Society for Obstetric Anesthesia and Perinatology. *Anesthesiology*. 2016;124(2):270–300.

Bedson R. Physiology of pregnancy: clinical anesthetic implications. *Contin Educ Anaesth Critic Care Pain*. 2013;14(2):69–72.

Tita AT, Rouse DJ, Blackwell S, et al. Emerging concepts in antibiotic prophylaxis for cesarean delivery: a systematic review. *Obstet Gynecol*.

2009;113(3):675–682.

Van de Putte P, Vernieuwe L, Perlas A. Term pregnant patients have a similar gastric volume to non-pregnant females: a single-centre cohort study. *Br J Anaesth*. 2019;122(1):79–85.

Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Circulation*. 2007;116:887–896.

C. Intraoperative Management

C.1. What monitors would you use in this functional New York Heart Association (NYHA) class II patient during her cesarean section?

Heart rate (via ECG), blood pressure, oxygen saturation, and temperature need to be monitored throughout the anesthetic. A urinary catheter should also be used. For patients undergoing general anesthesia, continuous end-tidal carbon dioxide monitoring is needed. Assessment of neuromuscular function using a peripheral nerve stimulator, although not mandated by the American Society of Anesthesiologists, is critical. In addition, electroencephalogram-processing monitors may be used, although they probably do not reduce the incidence of intraoperative awareness during general anesthesia for cesarean section when end-tidal gas monitoring is used.

Standards for Basic Anesthetic Monitoring. Committee of Origin: standards and practice parameters (approved by the ASA House of Delegates on October 21, 1986, last amended on October 20, 2010, and last affirmed on October 28, 2016). https://www.asahq.org/~/media/Sites/ASAHQ/Files/Public/Resources/standardguidelines/standards-for-basic-anesthetic-monitoring.pdf. Accessed May 6, 2016.

C.2. When would you use invasive monitoring in a pregnant patient with cardiac disease?

NYHA class I and II patients do not routinely require invasive hemodynamic monitoring. In the past, parturients in class III or IV were often monitored with a pulmonary artery catheter; routine use of this modality, however, has fallen out of favor given the invasiveness required for its use. Echocardiography, on the other hand, is far less invasive, yet both safe and effective—a combination that has led to its increasing popularity in the perioperative period. An arterial line is warranted if serial blood gas determinations and/or continuous blood pressure monitoring are needed. Hemodynamic monitoring should be continued for at least 24 hours postdelivery because the sudden increase in preload can precipitate pulmonary edema.

Canobbio MM, Warnes CA, Aboulhosn J, et al. Management of pregnancy in patients with complex congenital heart disease: a scientific statement for healthcare professionals from the American Heart Association. *Circulation*. 2017;135(8):e50–e87.

C.3. What are the hemodynamic goals of intraoperative management of the pregnant patient with mitral stenosis?

- Avoid tachycardia.
- Maintain sinus rhythm.
- Avoid marked decreases in systemic vascular resistance.
- Avoid marked increases in blood volume.
- Avoid increases in pulmonary vascular resistance.

Increased heart rates should be avoided because decreasing the amount of diastolic time for blood to flow across the stenotic mitral valve can lead to pulmonary edema and decreased cardiac output. Atrial fibrillation with a rapid ventricular response, similarly, can result in cardiac decompensation, and the loss of atrial contraction is detrimental. Marked decreases in systemic

vascular resistance should be avoided because a compensatory increase in heart rate can result. Elevation of pulmonary vascular resistance, which can occur with hypercarbia, hypoxia, and acidosis, is poorly tolerated by these patients.

Kannan M, Vijayanand G. Mitral stenosis and pregnancy: current concepts in anaesthetic practice. *Indian J Anaesth*. 2010;54(5):439–444.

C.4. What anesthetic technique would you use for this emergency cesarean section?

The choices of anesthetic techniques for cesarean section are neuraxial (spinal, epidural, combined spinal epidural) or general anesthesia. In this case, the patient's epidural catheter should be dosed with additional local anesthetic to provide surgical anesthesia to a T4 level. If an adequate level of anesthesia cannot be achieved via an existing epidural catheter, conversion to general anesthesia is needed, especially in the setting of an abnormal FHR tracing.

In the non-emergent setting, patients with mitral stenosis are good candidates for epidural anesthesia for cesarean (or vaginal) delivery. Combined spinal–epidural analgesia, particularly when an opioid only spinal dose is used, is also a reasonable option. Spinal anesthesia, on the other hand, may lead to a sudden and profound decrease in systemic vascular resistance with hypotension and reflex tachycardia, which can exacerbate fetal distress and lead to maternal decompensation in patients with mitral stenosis.

Cohen K, Minehart R, Leffert L. Anesthetic treatment of cardiac disease during pregnancy. *Curr Treat Options Cardiovasc Med*. 2018;20(8):66.

C.5. How would you manage local anesthetic systemic toxicity (LAST) in this patient?

LAST is a serious and potentially fatal complication of regional/neuraxial anesthesia. It is caused by a high plasma

concentration of local anesthetic, either as a result of direct IV injection or from delayed absorption at the injection site. Pregnancy increases the risk for LAST, and it appears that epidural conversion from labor analgesia to surgical anesthesia puts patients at particular risk. Management of LAST includes the use of lipid emulsion according to the most current practice advisory by the American Society of Regional Anesthesia and Pain Medicine in conjunction with advanced cardiovascular life support (ACLS) guidelines, although there have been no randomized controlled trials to determine differences in either timing or dosing in pregnancy (**Fig. 29.3**).

AMERICAN SOCIETY OF REGIONAL ANESTHESIA AND PAIN MEDICINE

CHECKLIST FOR TREATMENT OF LOCAL ANESTHETIC SYSTEMIC TOXICITY (LAST)

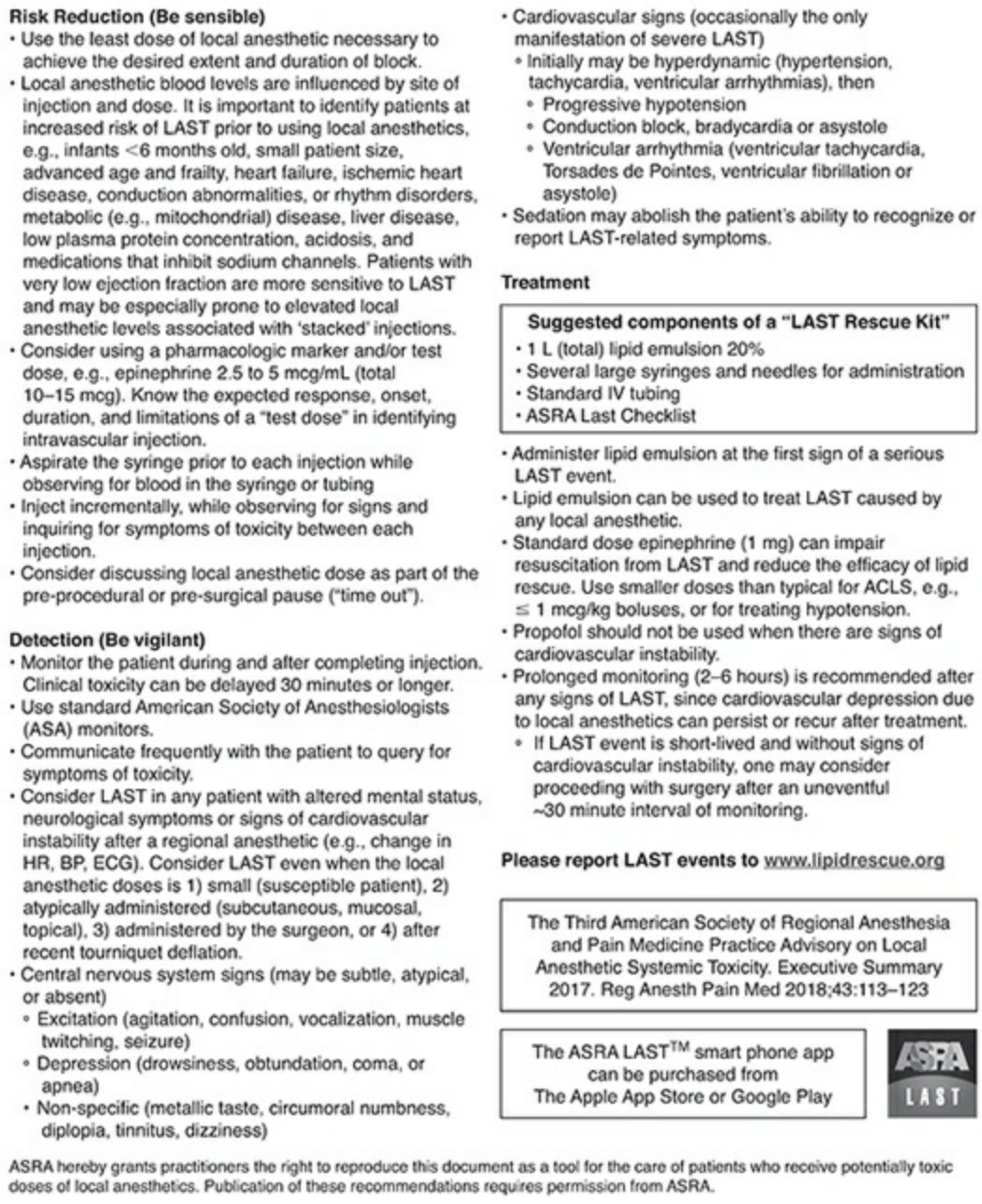
The Pharmacologic Treatment of LAST is Different from Other Cardiac Arrest Scenarios

- **Reduce** individual **epinephrine** boluses to ≤ 1 mcg/kg
- **Avoid** vasopressin, calcium channel blockers, beta blockers, or other local anesthetics

- Stop injecting local anesthetic
- Get help
  - Consider lipid emulsion therapy at the first sign of a serious LAST event
  - Call for the LAST Rescue Kit
  - Alert the nearest cardiopulmonary bypass team – resuscitation may be prolonged
- Airway management
  - Ventilate with 100% oxygen / avoid hyperventilation / advanced airway device if necessary
- Control seizures
  - Benzodiazepines preferred
  - **Avoid** large doses of **propofol**, especially in hemodynamically unstable patients
- Treat hypotension and bradycardia – **If pulseless, start CPR**

Lipid Emulsion 20% (Precise volume and flow rate are not crucial)	
Greater than 70 kg patient	Less than 70 kg patient
Bolus 100 mL Lipid Emulsion 20% Rapidly over 2–3 minutes • Lipid emulsion infusion 200–250 mL over 15–20 minutes	**Bolus 1.5 mL/kg Lipid Emulsion 20%** Rapidly over 2–3 minutes • Lipid emulsion infusion ~0.25 mL/kg/min (ideal body weight)
If patient remains unstable: • Re-bolus once or twice at the same dose and double infusion rate; be aware of dosing limit (12 mL/kg) • Total volume of lipid emulsion can approach 1 L in a prolonged resuscitation (e.g., > 30 minutes)	

- Continue monitoring
  - At least 4–6 hours after a cardiovascular event
  - Or, at least 2 hours after a limited CNS event
- Do not exceed 12 mL/kg lipid emulsion (particularly important in the small adult or child)
  - Much smaller doses are typically needed for LAST treatment
- See reverse side of this checklist for further details



Risk Reduction (Be sensible)

- Use the least dose of local anesthetic necessary to achieve the desired extent and duration of block.
- Local anesthetic blood levels are influenced by site of injection and dose. It is important to identify patients at increased risk of LAST prior to using local anesthetics, e.g., infants <6 months old, small patient size, advanced age and frailty, heart failure, ischemic heart disease, conduction abnormalities, or rhythm disorders, metabolic (e.g., mitochondrial) disease, liver disease, low plasma protein concentration, acidosis, and medications that inhibit sodium channels. Patients with very low ejection fraction are more sensitive to LAST and may be especially prone to elevated local anesthetic levels associated with 'stacked' injections.
- Consider using a pharmacologic marker and/or test dose, e.g., epinephrine 2.5 to 5 mcg/mL (total 10–15 mcg). Know the expected response, onset, duration, and limitations of a "test dose" in identifying intravascular injection.
- Aspirate the syringe prior to each injection while observing for blood in the syringe or tubing
- Inject incrementally, while observing for signs and inquiring for symptoms of toxicity between each injection.
- Consider discussing local anesthetic dose as part of the pre-procedural or pre-surgical pause ("time out").

Detection (Be vigilant)

- Monitor the patient during and after completing injection. Clinical toxicity can be delayed 30 minutes or longer.
- Use standard American Society of Anesthesiologists (ASA) monitors.
- Communicate frequently with the patient to query for symptoms of toxicity.
- Consider LAST in any patient with altered mental status, neurological symptoms or signs of cardiovascular instability after a regional anesthetic (e.g., change in HR, BP, ECG). Consider LAST even when the local anesthetic doses is 1) small (susceptible patient), 2) atypically administered (subcutaneous, mucosal, topical), 3) administered by the surgeon, or 4) after recent tourniquet deflation.
- Central nervous system signs (may be subtle, atypical, or absent)
  - Excitation (agitation, confusion, vocalization, muscle twitching, seizure)
  - Depression (drowsiness, obtundation, coma, or apnea)
  - Non-specific (metallic taste, circumoral numbness, diplopia, tinnitus, dizziness)
- Cardiovascular signs (occasionally the only manifestation of severe LAST)
  - Initially may be hyperdynamic (hypertension, tachycardia, ventricular arrhythmias), then
    - Progressive hypotension
    - Conduction block, bradycardia or asystole
    - Ventricular arrhythmia (ventricular tachycardia, Torsades de Pointes, ventricular fibrillation or asystole)
- Sedation may abolish the patient's ability to recognize or report LAST-related symptoms.

Treatment

Suggested components of a "LAST Rescue Kit"

- 1 L (total) lipid emulsion 20%
- Several large syringes and needles for administration
- Standard IV tubing
- ASRA Last Checklist

- Administer lipid emulsion at the first sign of a serious LAST event.
- Lipid emulsion can be used to treat LAST caused by any local anesthetic.
- Standard dose epinephrine (1 mg) can impair resuscitation from LAST and reduce the efficacy of lipid rescue. Use smaller doses than typical for ACLS, e.g., ≤ 1 mcg/kg boluses, or for treating hypotension.
- Propofol should not be used when there are signs of cardiovascular instability.
- Prolonged monitoring (2–6 hours) is recommended after any signs of LAST, since cardiovascular depression due to local anesthetics can persist or recur after treatment.
  - If LAST event is short-lived and without signs of cardiovascular instability, one may consider proceeding with surgery after an uneventful ~30 minute interval of monitoring.

Please report LAST events to www.lipidrescue.org

The Third American Society of Regional Anesthesia and Pain Medicine Practice Advisory on Local Anesthetic Systemic Toxicity. Executive Summary 2017. Reg Anesth Pain Med 2018;43:113–123

The ASRA LAST™ smart phone app can be purchased from The Apple App Store or Google Play

ASRA LAST

ASRA hereby grants practitioners the right to reproduce this document as a tool for the care of patients who receive potentially toxic doses of local anesthetics. Publication of these recommendations requires permission from ASRA.

FIGURE 29.3. Checklist for treatment of LAST. (*Reprinted from Neal JM, Barrington MJ, Fettiplace MR, et al. The third American Society of Regional Anesthesia and Pain Medicine practice advisory on local anesthetic systemic toxicity: executive summary 2017.* Reg Anesth Pain Med. *2018;43:113–123; with permission from BMJ Publishing Group Ltd.*)

Bern S, Weinberg G. Local anesthetic toxicity and lipid resuscitation in pregnancy. *Curr Opin Anaesthesiol*. 2011;24(3):262–267.

Neal JM, Bernards CM, Butterworth JF IV, et al. ASRA practice advisory on local anesthetic systemic toxicity. *Reg Anesth Pain Med*. 2010;35(2):152–161.

C.6. If cardiac arrest were to occur prior to delivery, how would you proceed?

High-quality chest compressions and oxygenation must be performed along with manual left lateral uterine displacement; this is true for all pregnant patients when the uterine size is ≥20 weeks. When the rhythm is shockable, defibrillation is appropriate (without risk to the fetus) in pregnancy. If return of spontaneous circulation fails to occur within 4 minutes of resuscitation efforts, perimortem cesarean delivery is advised. Of note, IV access should be obtained above the diaphragm because compression of the inferior vena cava by the gravid uterus prevents both fluids and medications from reaching the heart.

Jeejeebhoy FM, Zelop CM, Lipman S, et al. Cardiac arrest in pregnancy: a scientific statement from the American Heart Association. *Circulation*. 2015;132(18):1747–1773.

Zelop CM, Einav S, Mhyre JM, et al. Cardiac arrest during pregnancy: ongoing clinical conundrum. *Am J Obstet Gynecol*. 2018;219(1):52–61.

C.7. What technique could you use for general anesthesia in this patient?

- Induction
  - Crystalloid hydration through a large-bore, peripheral cannula
  - Supine position with left lateral tilt to avoid aortocaval compression
  - Preoxygenation with 100% inspired concentration of oxygen (F_{IO_2}) by face mask for 3 to 5 minutes if time permits, or four maximally deep inspirations (vital capacity breaths) if time is limited
  - Rapid sequence induction (after a team "time-out" and abdominal preparation and draping) with thiopental sodium (4 mg per kg; not available in the United States)

or etomidate (0.2 to 0.3 mg per kg) and succinylcholine (1 mg per kg)

- Although propofol (2 mg per kg) is most often used for induction of general anesthesia for cesarean delivery, it may cause hypotension, making it a less ideal choice in this patient.
- Ketamine should also be avoided because it increases heart rate.
- Because pregnant women tend not to experience severe fasciculations, a defasciculating dose of nondepolarizing muscle relaxant is not recommended.
- Depending on the severity of the lesion, patients with mitral stenosis may benefit from use of a β-adrenergic receptor antagonist, such as esmolol, or a modest dose of opioid (e.g., remifentanil) during induction of general anesthesia.
- If hypotension occurs, phenylephrine, not ephedrine, is the vasopressor of choice because it does not cause tachycardia in the mother (and is less likely than ephedrine to cross the placenta and increase concentrations of lactate, glucose, and catecholamines in fetal circulation).

– It is important to inform the neonatologist in the delivery room about medications given to the mother.
– Mucosal swelling and capillary engorgement in pregnancy may make intubation more difficult. Using a smaller endotracheal tube, such as one with a 7-mm internal diameter, may increase the likelihood of successful endotracheal intubation on the first attempt. The value of cricoid pressure—traditionally maintained until the endotracheal tube cuff is inflated and the position of the tube verified—is unknown. In human cadavers, it seems to effectively prevent regurgitation with gastric pressures

as high as 50 to 94 cm H_2O. Rice et al. showed that cricoid pressure compresses the hypopharynx leading to effective compression of the conduit between the stomach and the pharynx. Smith et al. found, however, that cricoid pressure in awake volunteers leads to airway displacement and does not reliably produce midline esophageal compression. In practice, its protective effect against passive reflux may actually be limited and even make intubation more difficult.

- Maintenance—prior to delivery of the neonate
  - N_2O with 50% oxygen and volatile anesthetic (e.g., 1% sevoflurane)
    - If pulmonary hypertension is present, N_2O should, however, be avoided because it increases pulmonary vascular resistance.
    - No more than 0.5 minimum alveolar concentration (MAC) should be used because halogenated anesthetic agents promote uterine atony. In this patient, both isoflurane and desflurane are best avoided because they cause tachycardia.
  - Muscle relaxant (vecuronium, cisatracurium, or rocuronium), as needed
  - Attention to maintenance of eucapnia is also important.
  - As always, the anesthetic technique should be tailored to the severity of the patient's underlying condition.
- Maintenance—after delivery of the neonate
  - Use of midazolam, fentanyl (or other opioid), muscle relaxant, and oxygen (usually with N_2O and 0.5 MAC of volatile agent, as earlier)
  - It is important to remember that the MAC of volatile agents is decreased by up to 40% in pregnant patients. MAC is a spinal nociceptive reflex involving both sensory

and motor components; the decrease in MAC has been interpreted to mean that pregnant patients have a decreased inhalational anesthetic requirement. In a small study of 30 patients, however, there was no difference in bispectral index (BIS) values between cesarean section patients and nonpregnant gynecologic patients undergoing general anesthesia with sevoflurane. According to Zand et al., BIS is not reliable for monitoring depth of anesthesia during cesarean section. Regardless of the anesthetic agents chosen, the aim is to achieve a satisfactory balance between hemodynamic stability, maternal amnesia, adequate uterine tone, and minimal neonatal depression.

- IV oxytocin infusion—begin immediately after delivery of the neonate
  - Bolus administration of oxytocin, methylergonovine, or 15-methyl prostaglandin $F_{2\alpha}$ should be avoided.
- Tracheal extubation—after protective laryngeal reflexes have returned and the patient has regained consciousness

de Souza DG, Doar LH, Mehta SH, et al. Aspiration prophylaxis and rapid sequence induction for elective cesarean delivery: time to reassess old dogma? *Anesth Analg*. 2010;110(5):1503–1505.

Norris MC, Dewan DM. Preoxygenation for cesarean section: a comparison of two techniques. *Anesthesiology*. 1985;62:827–829.

Rice MJ, Mancuso AA, Gibbs C, et al. Cricoid pressure results in compression of the postcricoid hypopharynx: the esophageal position is irrelevant. *Anesth Analg*. 2009;109(5):1546–1552.

Schulte-Sasse U, Hess W, Tarnow J. Pulmonary vascular response to nitrous oxide in patients with normal and high pulmonary vascular resistance. *Anesthesiology*. 1982;57(1):9–13.

Smith KJ, Dobranowski J, Yip G, et al. Cricoid pressure displaces the esophagus: an observational study using magnetic resonance imaging. *Anesthesiology*. 2003;99(1):60–64.

Ueyama H, Hagihira S, Takashina M, et al. Pregnancy does not enhance volatile anesthetic sensitivity on the brain: an electroencephalographic analysis study. *Anesthesiology*. 2010; 113:577–584.

Zand F, Hadavi SM, Chohedri A, et al. Survey on the adequacy of depth of anaesthesia with bispectral index and isolated forearm technique in elective caesarean section under general anaesthesia with sevoflurane. *Br J Anaesth*. 2014;112(5):871–878.

C.8. If you are unexpectedly unable to intubate this patient, how would you manage the airway?

Figure 29.4 illustrates management of failed intubation in the obstetric patient with an unrecognized difficult airway. In the case of failed intubation when delivery of the neonate must occur, it is of utmost importance to maintain maternal oxygenation either via facemask or supraglottic airway device. The mother's life should not be endangered to deliver a distressed fetus. Calling for help promptly when difficulties arise is essential.

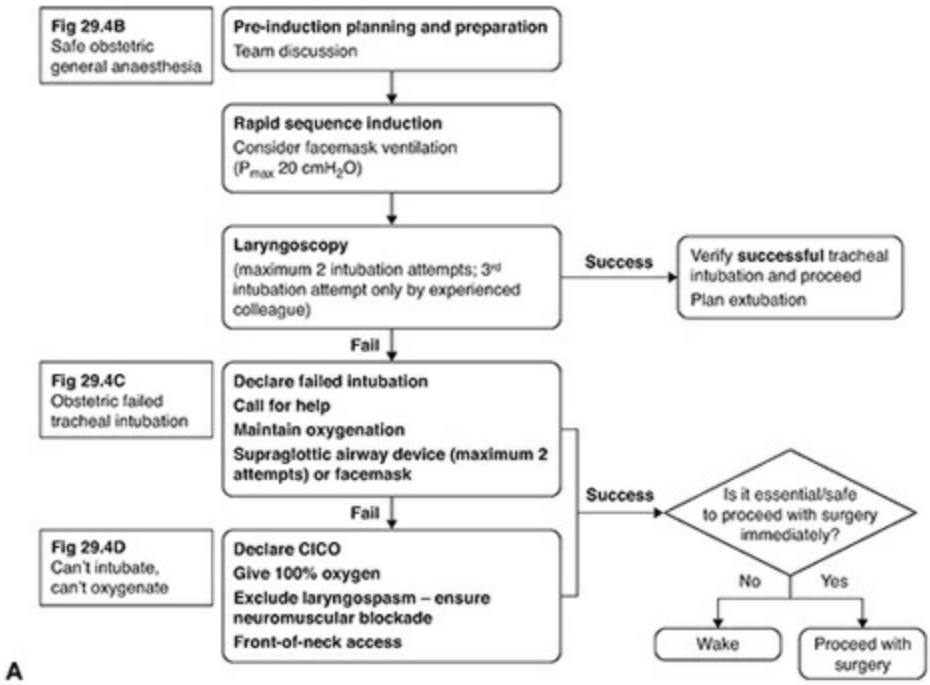
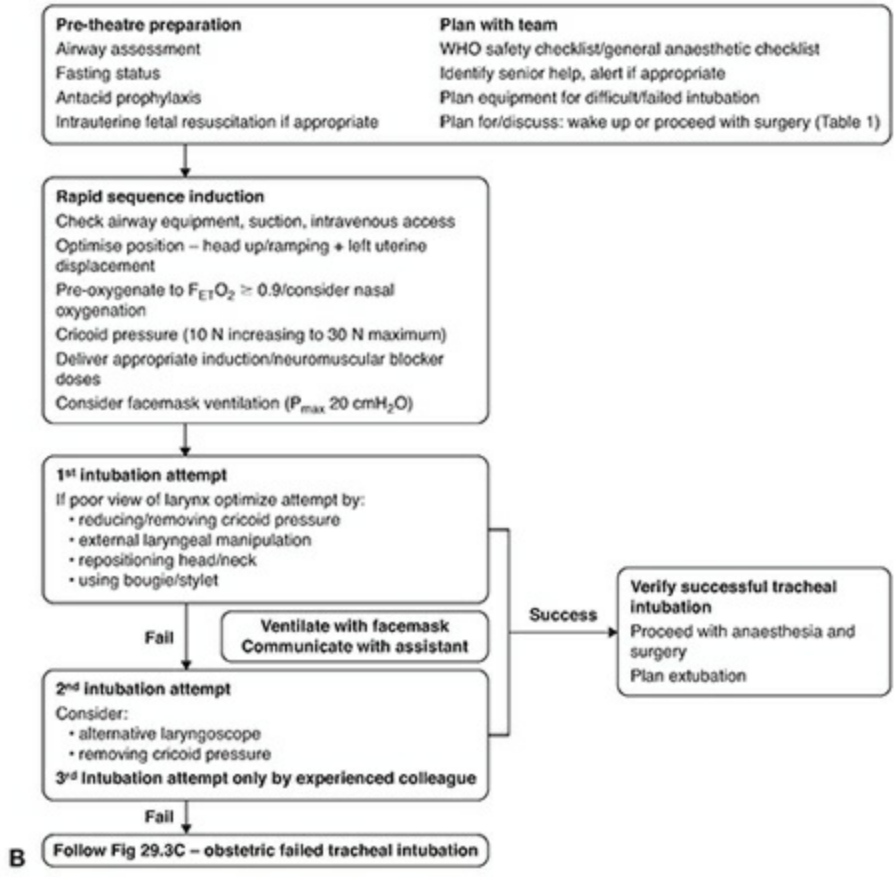


Fig 29.4B
Safe obstetric general anaesthesia
Pre-induction planning and preparation
Team discussion
Rapid sequence induction
Consider facemask ventilation
(P_{max} 20 cmH_2O)
Laryngoscopy
(maximum 2 intubation attempts; 3rd intubation attempt only by experienced colleague)
Success
Verify successful tracheal intubation and proceed
Plan extubation
Fail
Fig 29.4C
Obstetric failed tracheal intubation
Declare failed intubation
Call for help
Maintain oxygenation
Supraglottic airway device (maximum 2 attempts) or facemask
Success
Fail
Fig 29.4D
Can't intubate, can't oxygenate
Declare CICO
Give 100% oxygen
Exclude laryngospasm – ensure neuromuscular blockade
Front-of-neck access
Is it essential/safe to proceed with surgery immediately?
No
Yes
Wake
Proceed with surgery
A


Pre-theatre preparation
Airway assessment
Fasting status
Antacid prophylaxis
Intrauterine fetal resuscitation if appropriate
Plan with team
WHO safety checklist/general anaesthetic checklist
Identify senior help, alert if appropriate
Plan equipment for difficult/failed intubation
Plan for/discuss: wake up or proceed with surgery (Table 1)
Rapid sequence induction
Check airway equipment, suction, intravenous access
Optimise position – head up/ramping + left uterine displacement
Pre-oxygenate to $F_{ET}O_2 \geq 0.9$/consider nasal oxygenation
Cricoid pressure (10 N increasing to 30 N maximum)
Deliver appropriate induction/neuromuscular blocker doses
Consider facemask ventilation (P_{max} 20 cmH_2O)
1st intubation attempt
If poor view of larynx optimize attempt by:
• reducing/removing cricoid pressure
• external laryngeal manipulation
• repositioning head/neck
• using bougie/stylet
Fail
Ventilate with facemask
Communicate with assistant
Success
Verify successful tracheal intubation
Proceed with anaesthesia and surgery
Plan extubation
2nd intubation attempt
Consider:
• alternative laryngoscope
• removing cricoid pressure
3rd intubation attempt only by experienced colleague
Fail
Follow Fig 29.3C – obstetric failed tracheal intubation
B

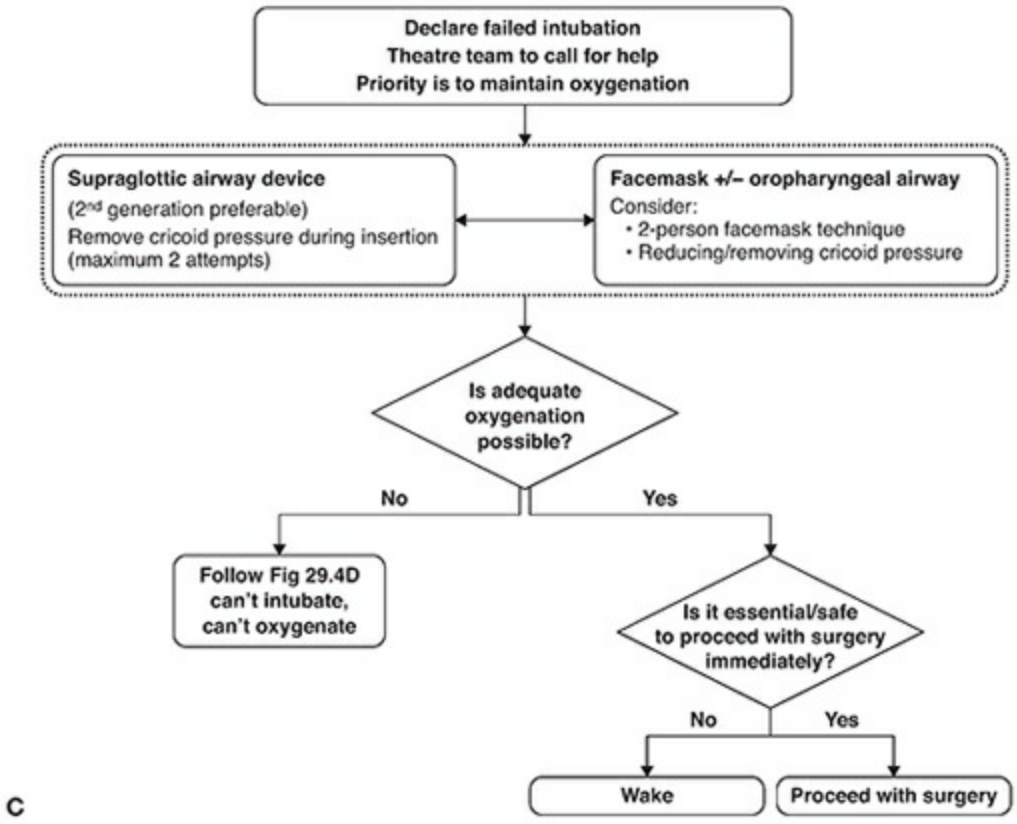


FIGURE 29.4. Algorithms for management of failed tracheal intubation in obstetric patients. A. Master algorithm. **B.** Safe obstetric general anesthesia. **C.** Obstetric failed tracheal intubation. **D.** Can't intubate, can't oxygenate (CICO). ENT, ear, nose, and throat. (*Reproduced from Mushambi MC,*

Kinsella SM, Popat M, et al. Obstetric Anaesthetists' Association and Difficult Airway Society guidelines for the management of difficult and failed tracheal intubation in obstetrics. Anaesthesia. *2015;70:1286–1306, with permission from Obstetric Anaesthetists' Association/Difficult Airway Society.*)

American Society of Anesthesiologists Task Force on Obstetric Anesthesia. Practice guidelines for obstetric anesthesia: an updated report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia. *Anesthesiology*. 2007;106(4):843–863.

Apfelbaum JL, Hagberg CA, Caplan RA, et al; for American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Practice guidelines for the management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. *Anesthesiology*. 2013;118(2):251–270.

Frerk C, Mitchell VS, McNarry AF, et al. Difficult Airway Society 2015 guidelines for management of unanticipated difficult intubation in adults. *Br J Anaesth*. 2015;115:827–848. http://m.bja.oxfordjournals.org/content/early/2015/11/05/bja.aev371.full.pdf. Accessed December 15, 2015.

Mushambi MC, Kinsella SM, Popat M, et al. Obstetric Anaesthetists' Association and Difficult Airway Society guidelines for the management of difficult and failed tracheal intubation in obstetrics. *Anaesthesia*. 2015;70(11):1286–1306.

C.9. Would this patient benefit from the use of *β*-blockers?

Because this patient is asymptomatic, *β*-blockade is unnecessary. Should tachycardia occur, *β*-blockade with drugs such as propranolol, atenolol, or esmolol may be useful, as may digoxin, and/or cardioversion depending on the dysrhythmia. Al Kasab et al. have shown that pregnant patients with symptomatic mitral stenosis who receive *β*-blockade with propranolol or atenolol to attenuate tachycardia have a significant decrease in the incidence of pulmonary edema with no adverse neonatal side effects.

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al Kasab SM, Sabag T, al Zaibag M, et al. Beta-adrenergic receptor blockage in the management of pregnant women with mitral stenosis. *Am J Obstet Gynecol*. 1990;163:37–40.

C.10. What is the effect of the inhalation agents on uterine contractility?

At less than one MAC, there is no decrease in uterine contractility (or increase in blood loss) because the uterus still responds to oxytocin. At higher concentrations, uterine contractility is decreased, and as a result, blood loss is increased.

Tjeuw MT, Yao FS, van Poznak A. Depressant effects of anesthetics on isolated human gravid and non-gravid uterine muscle. *Chinese Med J (Engl)*. 1986;99(3):235–242.

Warren TM, Datta S, Ostheimer GW, et al. Comparison of the maternal and neonatal effects of halothane, enflurane, and isoflurane for cesarean delivery. *Anesth Analg*. 1983;62:516–520.

C.11. What is the Apgar scoring system?

The Apgar scoring system is used to assess the neonate's condition at 1 minute and 5 minutes of life. Each of five categories is given a rating of 0 to 2, and the final score at each time is the sum of the individual category scores. Ten points is the best possible score (**Table 29.3**).

TABLE 29.3 Apgar Scoring System

		Score		
Mnemonic	**Sign**	**0**	**1**	**2**
A	Appearance (color)	Blue, pale	Body pink, extremities blue	Pink
P	Pulse	Absent	<100/min	>100/min
G	Grimace (reflex irritability; response to catheter in the nose)	Absent	Grimace	Cough, sneeze
A	Activity (muscle tone)	Limp	Some extremity flexion	Active motion
R	Respiratory effect	Absent	Slow, irregular	Good cry

Apgar V. A proposal for a new method of evaluation of the newborn infant. *Curr Res Anesth Analg*. 1953;32:260–267.

C.12. What is the significance of Apgar scores?

The Apgar score is a standardized assessment of neonates at the time of delivery. It is measured at 1 and 5 minutes of life for all infants and then every 5 minutes up to 20 minutes for those with a score less than 7. The Apgar score provides information about the response to resuscitation but does not predict mortality or neurologic outcome.

American Academy of Pediatrics Committee on Fetus and Newborn, American College of Obstetricians and Gynecologists Committee on Obstetric Practice. The Apgar score. *Pediatrics*. 2015;136(4):819–822.

Casey BM, McIntire DD, Leveno KJ. The continuing value of the Apgar score for the assessment of newborn infants. *N Engl J Med*. 2001;344(7):467–471.

Silverman F, Suidan J, Wasserman J, et al. The Apgar score: is it enough? *Obstet Gynecol*. 1985;66(3):331–336.

C.13. At birth, what should be done to minimize an infant's risk of meconium aspiration syndrome?

For many years, obstetricians suctioned the mouth and nose of the newborn before its first breath and delivery of the shoulders. At the present time, neither routine suctioning (oropharyngeal/nasopharyngeal), nor tracheal intubation, even in the presence of meconium-stained fluid is recommended. In the case of neonatal depression, it is recommended that emphasis be placed on initiating positive pressure ventilation; routine intubation, even in this situation, is not supported.

American College of Obstetricians and Gynecologists Committee on Obstetric Practice. ACOG Committee Opinion No. 379: management of delivery of a newborn with meconium-stained amniotic fluid. *Obstet Gynecol*. 2007;110(3):739.

American Heart Association, American Academy of Pediatrics. 2005 American Heart Association (AHA) guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiovascular care (ECC) of pediatric and neonatal patients: neonatal resuscitation guidelines. *Pediatrics*. 2006;117(5):e1029–e1038.

Polin RA, Carlo WA. Surfactant replacement therapy for preterm and term neonates with respiratory distress. *Pediatrics*. 2014;133(1):156–163.

Vain NE, Szyld EG, Prudent LM, et al. Oropharyngeal and nasopharyngeal suctioning of meconium-stained neonates before delivery of their shoulders: multicentre, randomised controlled trial. *Lancet*. 2004;364(9434):597–602.

Wyckoff MH, Aziz K, Escobedo MB, Kapadia VS, et al. Part 13: neonatal resuscitation: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2015;132:S543–S560.

C.14. If the Apgar score of the newborn is 3 at 1 minute, how would you treat the newborn?

Positive pressure ventilation and preductal pulse oximetry (right upper extremity) should be initiated at 1 minute of life when the heart rate is <100 beats per minute or the infant is gasping or apneic. If the heart rate remains below 100 beats per minute, an attempt to correct ventilation should occur; but if it is below 60, chest compressions are indicated. The F_{IO_2} used during the initial resuscitation should be low (21% in term infants and 21% to 30% in infants ≤35 weeks) because hyperoxia may lead to tissue and organ injury. If, however, chest compressions are needed, then the F_{IO_2} can be increased. For term infants born at sea level, target preductal SpO_2 levels based on the time after delivery are as follows:

- 1 minute, 60% to 65%
- 2 minutes, 65% to 70%
- 3 minutes, 70% to 75%
- 4 minutes, 75% to 80%
- 5 minutes, 80% to 85%
- 10 minutes, 85% to 95%

Target data on SpO_2 levels does not exist for preterm or term infants born at different altitudes, but the above levels are thought to be reasonably usable in both of these patient populations.

Medications are rarely needed during neonatal resuscitation. However, if the heart rate remains below 60 beats per minute

despite adequate ventilation and chest compressions, IV epinephrine (0.01 to 0.03 mg per kg) should be given. Umbilical vein catheterization is the quickest way to gain IV access.

Dawson JA, Vento M, Finer NN, et al. Managing oxygen therapy during delivery room stabilization of preterm infants. *J Pediatr*. 2012;160(1):158–161.

Perlman JM, Wyllie J, Kattwinkel J, et al. Part 7: neonatal resuscitation: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. *Circulation*. 2015;132(16 suppl 1):S204–S241.

Rook D, Schierbeek H, Vento M, et al. Resuscitation of preterm infants with different inspired oxygen fractions. *J Pediatr*. 2014;164(6):1322.e3–1326.e3.

C.15. Blood gases are sent immediately after delivery. What are the normal values for umbilical vein and artery blood gases?

In term infants, normal blood gases are as follows:

Umbilical artery

- pH, 7.27 ± 0.069
- P_{CO_2}, 50.3 ± 11.1 mmHg
- P_{O_2}, 22.0 ± 3.6 mmHg
- Bicarbonate, 22.3 ± 2.5 mEq per L

Umbilical vein

- pH, 7.35 ± 0.05
- P_{CO_2}, 38.2 ± 5.6 mmHg
- P_{O_2}, 29.2 ± 5.9 mmHg
- Bicarbonate, 20.4 ± 2.1 mEq per L

Umbilical artery blood gas values reflect fetal conditions, whereas umbilical vein blood gas values represent those of the uteroplacental unit and mother. ACOG recommends that cord blood gas measurements be obtained in the following circumstances: cesarean section for fetal compromise, low 5-minute Apgar score, severe fetal growth restriction, abnormalities in the FHR tracing, maternal thyroid disease,

intrapartum maternal fever, and/or multiple gestation. In 2003, the American Academy of Pediatrics and ACOG defined metabolic acidosis as umbilical arterial pH <7.0 and a base deficit of at least 12 mmol per L. Umbilical cord blood gas and pH measurements alone, however, are poorly predictive of immediate or long-term adverse neurologic outcome, but they do provide objective evidence of the fetal metabolic state at birth.

American College of Obstetricians and Gynecologists Committee on Obstetric Practice. ACOG Committee Opinion No. 348, November 2006: umbilical cord blood gas and acid-base analysis. *Obstet Gynecol*. 2006;108(5):1319–1322.

American College of Obstetricians and Gynecologists' Task Force on Neonatal Encephalopathy. Executive summary: neonatal encephalopathy and neurologic outcome, second edition. Report of the American College of Obstetricians and Gynecologists' Task Force on Neonatal Encephalopathy. *Obstet Gynecol*. 2014;123(4):896–901.

Cunningham FG, Leveno KJ, Bloom SL, et al, eds. *Williams Obstetrics*. 24th ed. New York: McGraw-Hill; 2014:628–631, 639–640.

Phelan JP, Korst LM, Martin GI. Application of criteria developed by the Task Force on Neonatal Encephalopathy and Cerebral Palsy to acutely asphyxiated neonates. *Obstet Gynecol*. 2011;118(4):824–830.

D. Postoperative Management

D.1. Immediately after the baby is delivered, the mother's oxygen saturation decreases. What is the differential diagnosis?

The following are possible causes of hypoxemia in this patient:

- Mechanical problems with the endotracheal tube (e.g., kinking)
- Cardiac decompensation with pulmonary edema
- Pulmonary venous embolism: air, amniotic, or thrombotic

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2019:937–955.

Fong J, Gadalla F, Pierri MK, et al. Are Doppler-detected venous emboli during cesarean section air emboli? *Anesth Analg*. 1990;71(3):254–257.

D.2. Additional bleeding occurs in the postanesthesia care unit, and the obstetrician diagnoses retained placenta. What, if any, antibiotics are indicated to prevent endometritis after manual extraction of retained placenta?

Manual extraction of the placenta is indicated when excessive bleeding occurs and/or when part of the placenta is retained after delivery. There is conflicting data regarding the risk for endometritis after manual extraction of the placenta, and the need for antibiotic prophylaxis, therefore, remains in question. Despite a lack of consensus regarding the need for routine antibiotics, the WHO recommends one IV dose of ampicillin or a first-generation cephalosporin. In a retrospective cohort study of more than 400 women who delivered vaginally, there was not a statistically significant difference in the rate of postpartum endometritis after manual extraction of the placenta between those who had or had not received prophylactic antibiotics.

Safrai M, Kabiri D, Haj-Yahya R, et al. The effect of prophylactic antibiotic treatment for manual removal of the placenta on frequency of postpartum endometritis. *Int J Gynaecol Obstet*. 2017;139(1):45–49.

World Health Organization. *WHO Recommendations for the Prevention and Treatment of Postpartum Haemorrhage*. Geneva, Switzerland: World Health Organization. https://www.who.int/reproductivehealth/publications/maternal_perinatal_healtl Accessed February 7, 2019.

30 Appendectomy for a Pregnant Patient

Robert S. White and Farida Gadalla

A 25-year-old woman at 32 weeks' gestation presented to the emergency room with vague right-sided abdominal pain. She had lost her appetite and experienced two episodes of emesis. Her temperature was 37.5°C (99.5°F); pulse rate, 100 beats per minute; hematocrit, 34%; and white blood cell (WBC) count, 15,000 per μL.

A. Medical Disease and Differential Diagnosis

1. What is the differential diagnosis for acute abdomen in the pregnant patient?
2. How would you make the clinical diagnosis of acute appendicitis?
3. What is the incidence of surgery during pregnancy? What is the incidence of appendicitis during pregnancy?
4. What is the incidence of gangrenous appendix/peritonitis during pregnancy, and is this incidence higher in pregnant than in nonpregnant women?
5. What are the main concerns associated with nonobstetric surgery in the pregnant patient?
6. What are the factors influencing teratogenicity from anesthetic

agents in humans?

7. Are there any specific concerns regarding neurotoxicity and cognitive development in the developing fetus?
8. What factors influence fetal oxygenation, and how would you prevent intrauterine fetal asphyxia?
9. What is the incidence of trauma during pregnancy, and what are the risks to the mother and the fetus secondary to trauma?
10. What are other common surgeries performed during pregnancy?

B. Preoperative Evaluation and Preparation

1. Preoperatively, what would you discuss with this patient? Are any additional medical consultations warranted?
2. Is there a difference in the goal of anesthesia for delivery and for nonobstetric surgery in a pregnant patient?
3. How would you premedicate this patient?

C. Intraoperative Management

1. What factors would alter your anesthetic technique from that used for a nonpregnant patient?
2. If you choose epidural anesthesia, describe your technique and dosage.
3. If the patient needs supplemental analgesia, what would be your choice?
4. What vasopressor would you choose to improve uteroplacental perfusion?
5. When this patient arrived in the operating room, she desired a general anesthetic. Describe your technique.
6. Does any controversy exist surrounding the use of nitrous oxide?
7. Does any controversy exist surrounding operating room personnel, anesthetic exposure, and pregnancy outcomes?
8. What is the impact of nonobstetric surgery on maternal mortality, birth defects, and fetal loss? What factors influence

it?

9. Should intraoperative fetal heart rate (FHR) monitoring be used? What would you expect to see on the electronic fetal monitor during anesthesia?
10. How would your anesthetic management differ if the patient were having upper extremity surgery?
11. The surgeon schedules the procedure to be performed laparoscopically. Does this pose any additional problems?

D. Postoperative Management

1. When would you extubate this patient?
2. Postoperatively, what monitors would you use?
3. What other postoperative precautions would you take? What is the incidence of preterm delivery following nonobstetric surgery during pregnancy?
4. The next day, the patient went into premature labor and now needs a cesarean section for prematurity and breech presentation. She requires another general anesthetic. In what way would your technique differ from your previous anesthetic technique?

A. Medical Disease and Differential Diagnosis

A.1. What is the differential diagnosis for acute abdomen in the pregnant patient?

The differential diagnosis for acute abdomen in the pregnant patient includes appendicitis, cholecystitis, and intestinal obstruction as the most common nonobstetric surgical emergencies.

Medical Conditions

- Sickle cell disease
- Porphyria

- Glomerulonephritis
- Inflammatory bowel disease
- Pyelonephritis
- Pneumonia
- Splenic disorders
- Withdrawal from drug addiction

Obstetric Conditions

- Ectopic pregnancy
- Hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome
- Labor
- Abruptio placentae
- Chorioamnionitis

Gynecologic Conditions

- Fibroid degeneration
- Salpingitis
- Degenerating myoma
- Ovarian cyst or tumor, either torted or ruptured
- Tubo-ovarian abscess

Surgical Conditions

- Appendicitis
- Cholecystitis
- Pancreatitis
- Mesenteric adenitis
- Intestinal obstruction
- Maternal trauma

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2020:368–391.

Tase A, Kamarizan MF, Swarnkar K. Appendicitis in pregnancy: difficulties in diagnosis and management. Guidance for the emergency general surgeon: a systematic review. *Int J Surg Open*. 2017;6:5–11.

A.2. How would you make the clinical diagnosis of acute appendicitis?

The diagnosis is based on a detailed history, physical exam, imaging, and the following symptoms:

- Vague abdominal pain (right flank or upper quadrant): The position is variable because of the cephalad displacement of appendix due to the growing uterus, but the most common presenting symptom is right lower quadrant pain.
- Gastrointestinal distress: anorexia, nausea, vomiting
- Abdominal tenderness, guarding, rebound pain, rectal tenderness
- Mildly elevated temperature, 37°C to 38°C (98.6°F to 100.4°F)
- Mildly elevated pulse rate
- An increase in WBC count: Because pregnant patients normally have a higher WBC count, a physiologic leukocytosis, than nonpregnant patients, an increased WBC count may not be a reliable marker.

Ultrasonography is the most frequently used imaging modality, is not associated with risk, and allows for the exclusion of other causes of acute abdominal pain and for the assessment of the fetal condition. Use is operator dependent, and acute appendicitis may have normal abdominal findings. When the ultrasound is equivocal, magnetic resonance imaging (MRI) has lower rates of nonvisualization. Gadolinium-based contrast during pregnancy is controversial with restricted use. Computed tomography (CT) scan has limited role in pregnancy because of radiation and contrast risks; however, radiation exposure is at dose much lower than the exposure associated with fetal harm and clinically necessary imaging should not be withheld.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2020:368–391.

Committee on Obstetric Practice. Committee Opinion No. 723: guidelines for diagnostic imaging during pregnancy and lactation. *Obstet Gynecol*. 2017;130(4):e210–e216.

Walker HG, Al Samaraee A, Mills SJ, et al. Laparoscopic appendicectomy in pregnancy: a systematic review of the published evidence. *Int J Surg*. 2014;12:1235–1241.

A.3. What is the incidence of surgery during pregnancy? What is the incidence of appendicitis during pregnancy?

Between 0.75% and 2% or approximately 75,000 pregnant women will yearly require emergency nonobstetric surgery—mostly for acute appendicitis, cholecystitis (6:1,000 pregnancies), maternal trauma, and cancer. Gastrointestinal surgery accounts for 45% of the nonobstetric surgery in the pregnant patient and orthopedic procedures account for 24%. Appendicitis is the most common surgical emergency with varying incidence between 1:500 and 1:635 and has been reported as low as 1:2,000. It occurs more frequently in the second (45%) than in the first (30%) or third trimesters (25%). In epidemiologic studies, the reduced incidence of appendicitis in pregnant women compared to matched controls suggests a protective effect of pregnancy.

Prodromidou A, Machairas N, Kostakis ID, et al. Outcomes after open and laparoscopic appendectomy during pregnancy: a meta-analysis. *Eur J Obstet Gynecol Reprod Biol*. 2018;225:40–50.

Tolcher MC, Fisher WE, Clark SL. Nonobstetric surgery during pregnancy. *Obstet Gynecol*. 2018;132(2):395–403.

Walker HG, Al Samaraee A, Mills SJ, et al. Laparoscopic appendicectomy in pregnancy: a systematic review of the published evidence. *Int J Surg*. 2014;12:1235–1241.

A.4. What is the incidence of gangrenous appendix/peritonitis during pregnancy, and is this incidence higher in pregnant than in nonpregnant

women?

During pregnancy, the gravid uterus pushes the appendix cephalically away from the omentum (**Fig. 30.1**), thereby causing the diseased appendix to produce little pain typically in the right lower quadrant and obfuscating the classic symptoms with flank pain. MRI studies have confirmed that the appendix is displaced upward to a mean distance of 45 mm above the iliac crest at term. This delays diagnosis and surgical intervention, allowing the appendix to become gangrenous. Also, contributing to diagnostic delay is postponement in diagnostic procedures such as radiography and laparoscopy for fetal concern. A 24-hour surgical delay can cause a 66% increase in perforation rate. The incidence of perforation of the appendix is approximately 15%. The perforation rates for first, second, and third trimesters tend to be 8.7%, 12.1%, and 26.1%, respectively. Epidemiologic data, however, show no higher incidence of perforated appendix in pregnant women compared to matched controls.

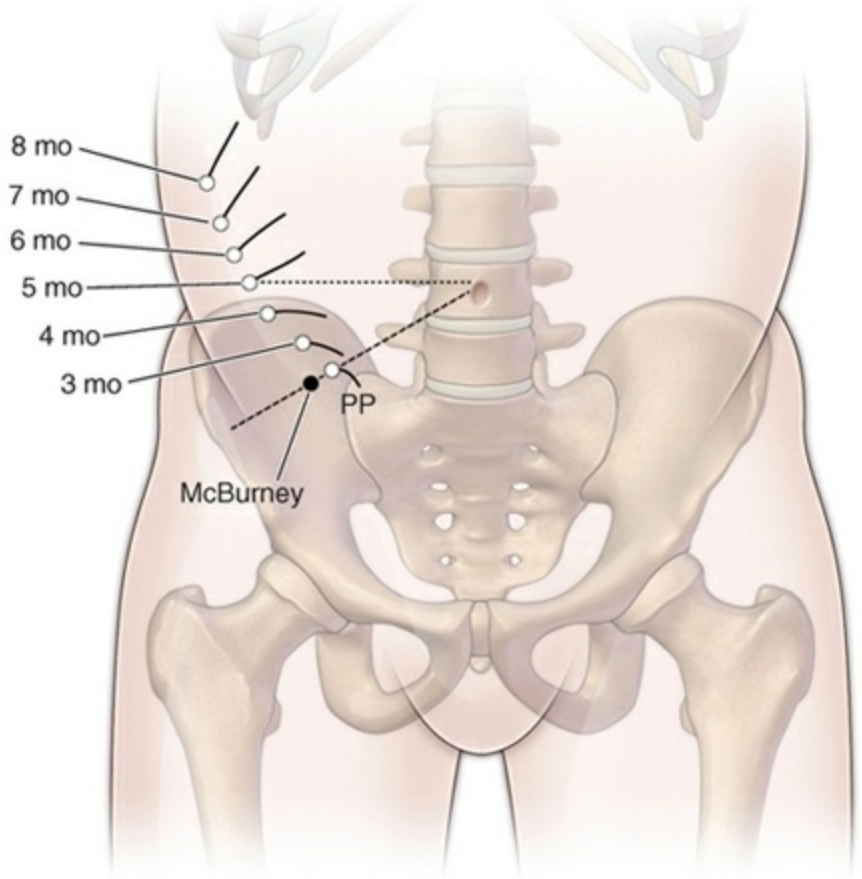

FIGURE 30.1. Changes in position and direction of the appendix during pregnancy. McBurney, McBurney's point; PP, prepregnancy. (*Adapted from Baer JL, Reis RA, Arens RA. Appendicitis in pregnancy with changes in position and axis of the normal appendix in pregnancy*. JAMA. *1932;98:1359*.)

Andersson RE, Lambe M. Incidence of appendicitis during pregnancy. *Int J Epidemiol*. 2001;30(6):1281–1285.

Kumamoto K, Imaizumi H, Hokama N, et al. Recent trend of acute appendicitis during pregnancy. *Surg Today*. 2015;45:1521–1526.

Pates JA, Avendiano TC, Zaretsky MV, et al. The appendix in pregnancy: confirming historical observations with a contemporary modality. *J Reprod Med*. 2008;53:711–713.

A.5. What are the main concerns associated with nonobstetric surgery in the pregnant patient?

Abdominal surgeries during pregnancy have an increased risk of poor pregnancy outcomes—premature delivery, spontaneous

abortion, premature labor, and perinatal morbidity and mortality. Maternal mortality rate is very low, and to ensure maternal safety, awareness of the physiologic changes of the parturient is of great importance. Special care should be taken to prevent aspiration pneumonitis especially after midgestation. Failed intubation is increased. Faster uptake of anesthetics and a decrease in minimum alveolar concentration (MAC) for volatile anesthetics may rapidly render patients unconscious at lower doses.

As early as 8 weeks of gestation, most of the increases in cardiac output and stroke volume and decreases in vascular resistance are apparent. There is the risk of supine hypotensive syndrome (aortocaval compression). For fetal safety, it is essential to avoid teratogenic anesthetic agents and intrauterine fetal asphyxia. Maintenance of adequate maternal oxygenation, oxygen-carrying capacity, and uteroplacental perfusion are critical to fetal well-being.

American College of Obstetricians and Gynecologists (ACOG)/American Society of Anesthesiologists (ASA) have recommended that indicated surgery should never be denied to a pregnant woman, regardless of trimester; elective surgery should be postponed until after delivery; and, if possible, nonurgent surgery should be performed in the second trimester when preterm contractions and spontaneous abortion are least likely.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2020:368–391.

Committee on Obstetric Practice, American Society of Anesthesiologists. Committee Opinion No. 696: nonobstetric surgery during pregnancy. *Obstet Gynecol*. 2017;129(4):777–778.

Reitman E, Flood P. Anaesthetic considerations for non-obstetric surgery during pregnancy. *Br J Anaesth*. 2011;107(suppl 1):i72–i78.

A.6. What are the factors influencing teratogenicity from anesthetic agents in humans?

An ACOG/ASA committee opinion states the following generalization: “No currently used anesthetic agents have been shown to have any teratogenic effects in humans when using standard concentrations at any gestational age.” Nevertheless, most anesthesiologists adhere to the use of only time-tested anesthetics with the goal of minimizing anesthetic exposures and exposure time. The factors influencing teratogenicity are genetic predisposition, inherent toxicity of the administered drug, drug dosage used and duration, placental transfer to the fetus, and fetal developmental stage at time of exposure.

Almost all anesthetics are teratogenic in some animals, but no animal model is perfectly applicable to humans. The most susceptible time for human teratogenicity is during organogenesis between days 31 and 71 after the last menstrual period. Before implantation of the ovum, teratogenicity leads to abortion. Later, malformation, functional deficiencies, and even death can occur. There are no documented reports of teratogenicity, congenital anomalies, or increase in birth defects in humans ascribed to any anesthetic agent used during pregnancy. Associations between the use of benzodiazepines and cleft palate and cardiac anomalies have been refuted; no evidence exists that a single dose of a benzodiazepine is harmful.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut’s Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2020:368–391.

Committee on Obstetric Practice, American Society of Anesthesiologists. Committee Opinion No. 696: nonobstetric surgery during pregnancy. *Obstet Gynecol*. 2017;129(4):777–778.

Reitman E, Flood P. Anaesthetic considerations for non-obstetric surgery during pregnancy. *Br J Anaesth*. 2011;107(suppl 1):i72–i78.

Tolcher MC, Fisher WE, Clark SL. Nonobstetric surgery during pregnancy. *Obstet Gynecol*. 2018;132(2):395–403.

A.7. Are there any specific concerns regarding

neurotoxicity and cognitive development in the developing fetus?

Concern exists regarding exposure to anesthesia and potential neurotoxicity impacting neurodevelopment. A single and relatively brief exposure to general anesthesia is not associated with detectable deficits in most cognitive domains or academic achievement. In December 2016, the U.S. Food and Drug Administration (FDA) released a Drug Safety Communications warning and medication labelling changes that stated "repeated or lengthy use of general anesthetic and sedation drugs during surgeries or procedures in children younger than 3 years or in pregnant women during their third trimester may affect the development of children's brains." The response to this FDA rule change from concerned medical societies has been critical for the poor quality of scientific evidence used, lack of involvement of stakeholder medical societies, and its untoward impact on appropriate medical care with possible patient reluctance to undergo medically necessary procedures.

O'Leary JD, Warner DO. What do recent human studies tell us about the association between anaesthesia in young children and neurodevelopmental outcomes? *Br J Anaesth*. 2017;119(3):458–464.

Tolcher MC, Fisher WE, Clark SL. Nonobstetric surgery during pregnancy. *Obstet Gynecol*. 2018;132(2):395–403.

U.S. Food and Drug Administration. FDA drug safety communication: FDA review results in new warnings about using general anesthetics and sedation drugs in young children and pregnant women. https://www.fda.gov/Drugs/DrugSafety/ucm532356.htm. Accessed December 2, 2018.

A.8. What factors influence fetal oxygenation, and how would you prevent intrauterine fetal asphyxia?

Maintaining maternal homeostasis (i.e., prevention of hypoxemia, hypotension, acidosis, and hyperventilation) is essential to fetal well-being. Fetal oxygenation is directly

dependent on maternal oxygen tension, oxygen saturation, hemoglobin content, oxygen affinity, and uteroplacental perfusion. Maternal hypoxia will result in fetal hypoxia; if uncorrected, fetal abnormalities or death can occur. Uterine blood flow is determined by uterine vascular resistance and uterine perfusion pressure (relative passive perfusion); factors that decrease uterine blood flow must be avoided. Uterine blood flow may be decreased by the following: maternal hypotension; stress, pain, or anxiety (due to the release of maternal catecholamines); hypoxia; hypercarbia, which also directly results in fetal respiratory acidosis; hyperventilation (hypocapnia); positive pressure ventilation; and pressor agents. Overall, one should attach greater importance to anesthetic management than to the agents used, and fluid administration should be appropriate for estimated or anticipated blood loss.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2020:368–391.

Mhuireachtaigh RN, O'Gorman DA. Anesthesia in pregnant patients for nonobstetric surgery. *J Clin Anesth*. 2006;18:60–66.

Reitman E, Flood P. Anaesthetic considerations for non-obstetric surgery during pregnancy. *Br J Anaesth*. 2011;107(suppl 1):i72–i78.

A.9. What is the incidence of trauma during pregnancy, and what are the risks to the mother and the fetus secondary to trauma?

Trauma occurs in 6% to 8% of all pregnancies and is the leading cause of nonobstetric maternal death. Most common causes of trauma during pregnancy are motor vehicle accidents (207:100,000 live births), falls and slips (48.9:100,000), and domestic violence (8,307:100,000). Maternal mortality and fetal mortality due to trauma are 1.4 per 100,000 and 3.7 per 100,000 pregnancies, respectively. Death rates and complications are higher in mothers at term compared to nonpregnant women.

Maternal complications are due to uterine rupture, placental abruption, and premature rupture of membranes. Fetal complications are due to these factors as well as to premature and stillbirths. Fetal viability should be assessed.

The primary goal of treatment is to stabilize the mother with an aggressive resuscitation. Uterine displacement is used and initial evaluation should be based on standard trauma guidelines. Emergent delivery may be necessary. Radiographic studies, if indicated, should be done. CT imaging is at a radiation exposure dose lower than that associated with fetal harm.

Cheek TG, Baird E. Anesthesia for nonobstetric surgery: maternal and fetal considerations. *Clin Obstet Gynecol*. 2009;52:535–545.

Committee on Obstetric Practice. Committee Opinion No. 723: guidelines for diagnostic imaging during pregnancy and lactation. *Obstet Gynecol*. 2017;130(4):e210–e216.

Mendez-Figueroa H, Dahlke JD, Vrees RA, et al. Trauma in pregnancy: an updated systematic review. *Am J Obstet Gynecol*. 2013;209(1):1–10.

A.10. What are other common surgeries performed during pregnancy?

Cardiac surgery: The physiologic changes of pregnancy (i.e., the increases in blood volume, cardiac output, and the decrease in systemic vascular resistance) can exacerbate preexisting heart disease, leading to congestive heart failure, particularly in patients with stenotic mitral or aortic valvular disease and pulmonary hypertension. Two periods are especially associated with cardiac decompensation—at 24 to 28 weeks when cardiac output reaches a maximum and immediately after delivery when uterine auto transfusion increases venous return causing volume overload. Procedures consist of surgical repair and percutaneous balloon valvuloplasty. Considerations include the use and type of cardiopulmonary bypass.

Neurosurgical procedures: The physiologic changes of pregnancy resulting in cardiac and hormonal (i.e., softening of

vascular connective tissue) system changes can theoretically increase the risk of hemorrhaging from intracranial saccular aneurysms or arteriovenous malformations. Other common conditions encountered include brain tumors, traumatic brain injury, and spinal surgery. Specific considerations include the use of "controlled hypotension," prone positioning, and intraoperative maternal hypothermia.

In these unique surgical situations, the importance of a multidisciplinary approach involving the anesthesia, obstetric, and surgical services cannot be overstated.

Cheek TG, Baird E. Anesthesia for nonobstetric surgery: maternal and fetal considerations. *Clin Obstet Gynecol*. 2009;52:535–545.

Reitman E, Flood P. Anaesthetic considerations for non-obstetric surgery during pregnancy. *Br J Anaesth*. 2011;107(suppl 1):i72–i78.

Tolcher MC, Fisher WE, Clark SL. Nonobstetric surgery during pregnancy. *Obstet Gynecol*. 2018;132(2):395–403.

B. Preoperative Evaluation and Preparation

B.1. Preoperatively, what would you discuss with this patient? Are any additional medical consultations warranted?

The pregnant patient undergoing nonobstetric surgery requires a standard anesthesia preoperative assessment and reevaluation with a frank discussion regarding anesthetic and surgical risks to the pregnancy and fetus. Obstetric consultation before surgery is essential as is utilization of a multidisciplinary team approach to provide for optimal safety of the woman and the fetus. The primary obstetric care provider should be notified and an obstetrician with hospital privileges should be involved. Use of fetal monitoring should also be discussed, again emphasizing communication, coordination, and planning between the different physician services. Decisions regarding preterm labor

and tocolysis should be delineated.

It is important to discuss her options concerning regional versus general anesthesia, emphasizing that the fetal outcome is statistically similar, but regional anesthesia is the technique of choice for the mother whenever possible (avoid fetal exposure to drugs and need for airway protection). In this specific case, if the appendectomy is planned laparoscopically, general anesthesia with airway control is preferred. Outcome studies show that woman who undergo surgery during pregnancy deliver earlier and have smaller babies than those who do not. Any increase in miscarriage or preterm birth are mostly attributable to surgical concerns.

Cheek TG, Baird E. Anesthesia for nonobstetric surgery: maternal and fetal considerations. *Clin Obstet Gynecol*. 2009;52:535–545.

Committee on Obstetric Practice, American Society of Anesthesiologists. Committee Opinion No. 696: nonobstetric surgery during pregnancy. *Obstet Gynecol*. 2017;129(4):777–778.

Reitman E, Flood P. Anaesthetic considerations for non-obstetric surgery during pregnancy. *Br J Anaesth*. 2011;107(suppl 1):i72–i78.

B.2. Is there a difference in the goal of anesthesia for delivery and for nonobstetric surgery in a pregnant patient?

The aim of obstetric anesthesia is to permit pain-free labor and delivery without interfering with the progress of child birth. Obstetric anesthesia should provide maternal analgesia without fetal neurologic depression and delayed neonatal breathing. Conversely, the aim of surgical anesthesia is to provide maternal anesthesia without stimulating uterine activity and precipitating premature labor. Surgical anesthesia is designed to maintain uteroplacental perfusion without consideration for fetal neurologic or respiratory depression.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia:*

Principles and Practice. 6th ed. Philadelphia, PA: Elsevier; 2020:368–391, 568–626.

B.3. How would you premedicate this patient?

Premedication has traditionally been avoided in favor of verbal anxiolysis, reassurance, and support. If necessary, benzodiazepines can be given for sedation. Glycopyrrolate, which does not cross the placental barrier, can be used as a vagolytic and antisialagogue. For general anesthesia, a nonparticulate antacid, such as 30 mL of 0.3 M sodium citrate, is given about 30 minutes before surgery to prevent aspiration pneumonitis; an H_2-receptor antagonist may also be given.

Cheek TG, Baird E. Anesthesia for nonobstetric surgery: maternal and fetal considerations. *Clin Obstet Gynecol*. 2009;52:535–545.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2020:368–391, 568–626.

C. Intraoperative Management

C.1. What factors would alter your anesthetic technique from that used for a nonpregnant patient?

The maternal anatomic and physiologic changes of pregnancy have anesthetic implications.

Cardiovascular System

- Increased blood volume by 40% to 50% (20% reduction in hematocrit due to physiologic anemia of pregnancy with more increase in plasma volume than in red blood cell count)
- Increased cardiac output (stroke volume and heart rate) by 40% to 50%
- Decreased peripheral resistance
- Decreased mean arterial blood pressure
- Aortocaval compression in the supine position secondary to

growing uterus as shown in **Figure 30.2**. This can reduce venous return and cardiac output by 30%. Left uterine displacement (supine patient tilted by wedge under her right hip) should be used.

- Lower extremity venous stasis can lead to pedal edema and deep venous thrombosis (also caused by hypercoagulable state of pregnancy).

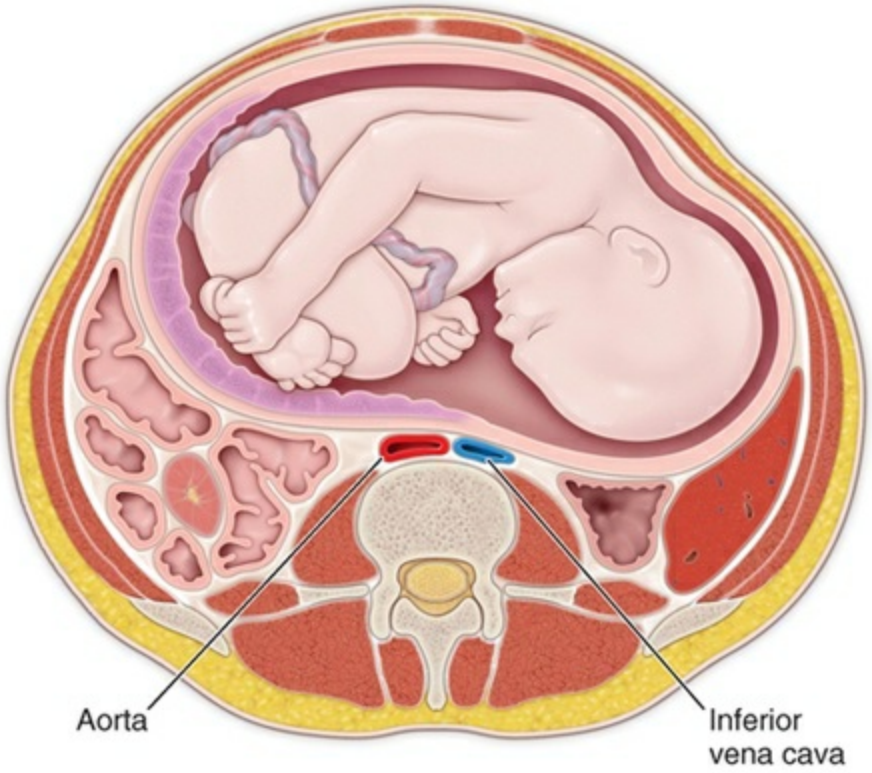

FIGURE 30.2. The pregnant uterus compressing the aorta and the inferior vena cava (aortocaval compression) in supine position. (*Adapted from Ostheimer GW*. Regional Anesthesia Techniques in Obstetrics. *New York: Breon Laboratories; 1980*.)

Respiratory System

- Increased minute ventilation (hyperventilation from progesterone shifting $Paco_2$ curve); chronic respiratory alkalosis with subsequent decrease in bicarbonate buffering capacity
- Increased oxygen consumption by 20%
- Decreased functional residual capacity (FRC) by 20% as

shown in **Figure 30.3**

- Both factors contribute to a rapid decrease in Pa_{O_2} during apneic periods.
- Inhalational induction occurs more rapidly secondary to alveolar hyperventilation and decreased FRC.

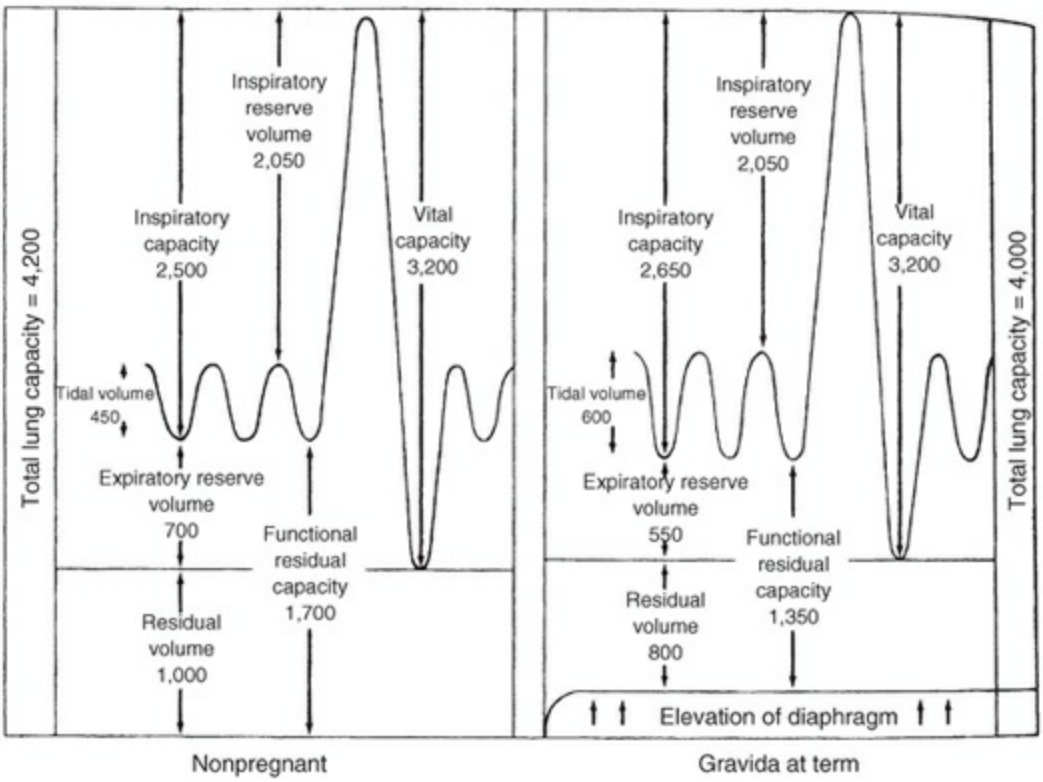

FIGURE 30.3. Pulmonary volumes and capacities during pregnancy. (*From Bonica JJ*. Principles and Practice of Obstetric Analgesia and Anesthesia. *1st ed. Philadelphia, PA: FA Davis; 1967, with permission*.)

Gastrointestinal System

- Decreased esophageal and intestinal motility
- Gastric emptying time is normal except in laboring patient.
- Decreased volume of gastrointestinal secretions
- Distortion of gastric anatomy secondary to growing uterus
- Increased gastric acidity
- Decreased lower esophageal (gastroesophageal) sphincter tone secondary to increased progesterone level. Increased incidence of heartburn/reflux. A pregnant patient beyond the

first trimester should always be considered as having a full stomach and must be considered at risk for regurgitation and aspiration (cautious use of mask ventilation or laryngeal mask airway [LMA]).

Central Nervous System

- Decreased MAC of inhaled anesthetics (30% to 40%)
- Increased sensitivity to local anesthesia
- Decreased volume of epidural anesthetic required because of engorgement of epidural veins and consequent decrease in size of epidural space; also increases risk of intravascular injection

Airway, Skin, and Mucous Membranes

- Swelling of oropharyngeal tissues with decreased caliber of glottis opening (difficulty performing mask ventilation and intubation; increased risk of failed intubation)
- More friable mucous membranes and engorged mucosal capillaries (Avoid nasal manipulation—insertion of nasal airways, nasotracheal, and nasogastric tubes.)
- Mallampati classification maybe more predictive of difficult intubation

Cheek TG, Baird E. Anesthesia for nonobstetric surgery: maternal and fetal considerations. *Clin Obstet Gynecol*. 2009;52:535–545.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2020:13–37.

Reitman E, Flood P. Anaesthetic considerations for non-obstetric surgery during pregnancy. *Br J Anaesth*. 2011;107(suppl 1):i72–i78.

C.2. If you choose epidural anesthesia, describe your technique and dosage.

The patient is placed either in the sitting position or on her side for epidural placement at L2–L3 or L3–L4. Adequate hydration is achieved with intravenous fluids. After testing for inadvertent

spinal or intravascular placement, the local anesthetic is given in divided doses to attain a T4 level. An inadvertent spinal injection is detected by the rapid onset of a solid motor block; an intravascular injection is evidenced by signs of systemic toxicity (dizziness, tinnitus, circumoral numbness, metallic taste). Local anesthetics used are 2% lidocaine, 0.5% bupivacaine, or 0.5% or 0.75% ropivacaine. These agents provide good analgesia with a degree of motor blockade for muscular relaxation. Epidural fentanyl promotes quicker onset and more solid block. The patient is once again placed with left uterine wedge, oxygen is delivered by nasal cannula, and her blood pressure is monitored closely.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2020:238–270.

C.3. If the patient needs supplemental analgesia, what would be your choice?

Morphine and fentanyl are narcotics that have been time tested. Small doses of ketamine (0.25 mg per kg intravenously) may also be given.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2020:368–391.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2036–2041.

Zakowski MI, Geller A. The placenta: anatomy, physiology, and transfer of drugs. In: Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2020:56–76.

C.4. What vasopressor would you choose to improve uteroplacental perfusion?

ASA practice guidelines state that "either IV ephedrine or phenylephrine may be used for treating hypotension during neuraxial anesthesia" and that "in the absence of maternal

bradycardia, consider selecting phenylephrine because of improved fetal acid–base status in uncomplicated pregnancies." Ephedrine was traditionally considered the safest vasopressor because its β-adrenergic effects increase cardiac output, mean arterial pressure, and uterine artery blood flow without a concomitant decrease in uteroplacental perfusion. However, use of ephedrine has been associated with adverse effects on fetal acid–base status (lower neonatal pH and fetal acidosis). Phenylephrine (pure α-agonist) use is now preferred because phenylephrine does not adversely affect neonatal outcome and decreases the incidence of fetal acidosis. This evidence is based on studies conducted in elective cesarean sections, and there is a paucity of evidence on the vasopressor of choice for nonelective cesarean deliveries or other surgical procedures.

Nag DS, Samaddar DP, Chatterjee A, et al. Vasopressors in obstetric anesthesia: a current perspective. *World J Clin Cases*. 2015;3(1):58–64.

Ngan Kee WD, Khaw KS, Tan PE, et al. Placental transfer and fetal metabolic effects of phenylephrine and ephedrine during spinal anesthesia for cesarean delivery. *Anesthesiology*. 2009;111(3):506–512.

Practice guidelines for obstetric anesthesia: an updated report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia and the Society for Obstetric Anesthesia and Perinatology. *Anesthesiology*. 2016;124(2):270–300.

C.5. When this patient arrived in the operating room, she desired a general anesthetic. Describe your technique.

- Apply standard ASA monitors, ensure free flowing intravenous cannula, use of left uterine displacement, and consider blood glucose monitoring for long procedures.
- Preoxygenate for at least 3 minutes to ensure denitrogenation.
- Induction via a rapid sequence induction intubation technique (intubation using a cuffed endotracheal tube with a 7-mm internal diameter or less) with cricoid pressure

- Anesthesia maintenance using time-tested agents: morphine, fentanyl, nondepolarizing muscle relaxants, sevoflurane, and/or desflurane. Inhalation anesthetics additionally relax the uterus and may aid in preventing premature labor.
- Maintain an appropriate maternal oxygenation and a normotensive blood pressure to ensure uteroplacental perfusion and avoid hyper-/hypoventilation.
- Extubate the trachea when the patient is awake and has regained her laryngeal reflexes.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2020:56–76, 368–391.

C.6. Does any controversy exist surrounding the use of nitrous oxide?

Nitrous oxide inhibits methionine synthase, potentially affecting DNA synthesis and myelin deposition, and has been shown to be teratogenic in animals. The neuronal apoptosis and learning impairment observed in animals after exposure to nitrous oxide remain to be determined in humans. As of this writing, no detrimental effects of nitrous oxide on the development of the human fetus have been demonstrated. Nitrous oxide also increases adrenergic tone and decreases uterine blood flow. This can be prevented by the addition of a volatile agent. Nitrous oxide may be used as a component of the inhalational anesthetic.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2020:368–391.

Collins MR, Starr SA, Bishop JT, et al. Nitrous oxide for labor analgesia: expanding analgesic options for women in the United States. *Rev Obstet Gynecol*. 2012;5(3–4):e126–e131.

Tolcher MC, Fisher WE, Clark SL. Nonobstetric surgery during pregnancy. *Obstet Gynecol*. 2018;132(2):395–403.

C.7. Does any controversy exist surrounding operating

room personnel, anesthetic exposure, and pregnancy outcomes?

Case reports and epidemiologic studies from the 1960s and 1970s showed associations between increased spontaneous abortions (increased miscarriage rates) and operating room and dental surgical personnel. Subsequent independent repeat analysis of this work identified methodologic flaws and bias in data collection, causing spurious findings. Prospective studies have found no causal relationships. Additionally, modern volatile anesthetic exposure can be reduced by more than 90% with the use of modern scavenging systems.

Cheek TG, Baird E. Anesthesia for nonobstetric surgery: maternal and fetal considerations. *Clin Obstet Gynecol*. 2009;52:535–545.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2020:368–391.

McGregor DG. Occupational exposure to trace concentrations of waste anesthetic gases. *Mayo Clin Proc*. 2000;75(3):273–277.

C.8. What is the impact of nonobstetric surgery on maternal mortality, birth defects, and fetal loss? What factors influence it?

Meta-analysis including 12,452 pregnant women having surgery estimated maternal death at 0.006% (<1/10,000). Surgery and anesthesia did not increase the risk of major birth defects and were not major risk factors for spontaneous abortion. However, acute appendicitis with peritonitis poses a significant risk for fetal loss. Fetal loss was estimated at less than 5% in cases of uncomplicated acute appendicitis; the rate of fetal loss increased to 20% with perforated appendicitis and 35.7% with generalized peritonitis. In summary, the literature suggests that miscarriage and preterm birth are slightly increased after surgery with the severity of the disease process requiring surgery or the site of surgery having the strongest influence.

Cheek TG, Baird E. Anesthesia for nonobstetric surgery: maternal and fetal considerations. *Clin Obstet Gynecol*. 2009;52:535–545.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2020:368–391.

C.9. Should intraoperative fetal heart rate (FHR) monitoring be used? What would you expect to see on the electronic fetal monitor during anesthesia?

The use of intraoperative FHR monitoring is recommended only if it will alter case management. This decision is individualized and dependent on gestational age, type of surgery, and facilities available. FHR monitoring is practical from 18 to 22 weeks, and heart rate variability can be observed from 25 weeks on. ACOG/ASA guidelines for fetal monitoring state that for a previable fetus, it is generally sufficient to ascertain the FHR by Doppler before and after the procedure. For a viable fetus, simultaneous electronic FHR and contraction monitoring should be performed before and after the procedure to assess fetal well-being and the absence of contractions.

One would expect to see a decrease in beat-to-beat FHR variability during general anesthesia using inhalational agents. FHR slowing (bradycardia) can also be observed, but this could also be secondary to nonbenign situations such as fetal hypoxemia and acidosis. FHR variability is also decreased by the use of opioids and induction agents.

Cheek TG, Baird E. Anesthesia for nonobstetric surgery: maternal and fetal considerations. *Clin Obstet Gynecol*. 2009;52:535–545.

Committee on Obstetric Practice, American Society of Anesthesiologists. Committee Opinion No. 696: nonobstetric surgery during pregnancy. *Obstet Gynecol*. 2017;129(4):777–778.

Reitman E, Flood P. Anaesthetic considerations for non-obstetric surgery during pregnancy. *Br J Anaesth*. 2011;107(suppl 1):i72–i78.

C.10. How would your anesthetic management differ if the patient were having upper extremity surgery?

A brachial plexus block regional technique could be used. Additionally, it is possible to monitor the fetal heart during surgery and to monitor for uterine contractions using a tocodynamometer.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2020:368–391.

Committee on Obstetric Practice, American Society of Anesthesiologists. Committee Opinion No. 696: nonobstetric surgery during pregnancy. *Obstet Gynecol*. 2017;129(4):777–778.

C.11. The surgeon schedules the procedure to be performed laparoscopically. Does this pose any additional problems?

Laparoscopy has been performed during pregnancy both for diagnostic and procedural surgery. Benefits appear similar to those in nonpregnant patients—reduced postoperative pain, postoperative ileus, and other complications and decreased length of hospital stay with faster return to work. Traditionally, there has been concern for direct fetal and uterine trauma and increased intra-abdominal pressure, causing a decrease in maternal cardiac output and uteroplacental perfusion. Carbon dioxide (CO_2) pneumoperitoneum can cause fetal respiratory acidosis. General guidelines are to maintain a low intra-abdominal insufflation pressure of 10 to 15 mmHg, limiting extremes in positioning (Trendelenburg or reverse Trendelenburg), and limiting surgery duration. Intraoperative CO_2 monitoring via capnography is adequate to guide ventilation, and end-tidal CO_2 should be maintained at approximately 32 mmHg. Laparoscopic appendectomy has been shown to be associated with a low rate of intraoperative complications in all three trimesters. Results of multiple meta-analyses, however, have found that fetal loss was statistically significantly higher in those who underwent laparoscopic

compared to open appendectomy. It should be noted that the findings concerning fetal loss were largely dominated by one large study and with study exclusion from pooled meta-analysis, there was no effect of laparoscopy on fetal loss. In summary, the current literature is inconclusive and further larger volume studies are needed to better elucidate the association between fetal loss and laparoscopic appendectomy. The Society of American Gastrointestinal Endoscopic Surgeons states that "laparoscopic appendectomy is the treatment of choice for pregnant patients with acute appendicitis." Furthermore, "Laparoscopy can be safely performed during any trimester of pregnancy when operation is indicated" and "postponing necessary operations until after parturition has been shown in some cases, to increase the rates of complications for both mother and fetus."

Pearl JP, Price RR, Tonkin AE, et al. SAGES guidelines for the use of laparoscopy during pregnancy. *Surg Endosc*. 2017;31(10):3767–3782.

Prodromidou A, Machairas N, Kostakis ID, et al. Outcomes after open and laparoscopic appendectomy during pregnancy: a meta-analysis. *Eur J Obstet Gynecol Reprod Biol*. 2018;225:40–50.

Wilasrusmee C, Sukrat B, McEvoy M, et al. Systematic review and meta-analysis of safety of laparoscopic versus open appendicectomy for suspected appendicitis in pregnancy. *Br J Surg*. 2012;99:1470–1478.

D. Postoperative Management

D.1. When would you extubate this patient?

The patient can be extubated when she is fully awake, in control of her airway reflexes, and able to avoid pulmonary aspiration.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2020:368–391.

D.2. Postoperatively, what monitors would you use?

Postoperative monitors should include electrocardiogram, pulse

oximeter, intermittent blood pressure and temperature monitoring, urinary catheter (to be discontinued within 24 hours, unless specifically indicated), FHR monitor to ensure fetal well-being, and tocodynamometer to detect premature labor.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2020:368–391.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2036–2041.

D.3. What other postoperative precautions would you take? What is the incidence of preterm delivery following nonobstetric surgery during pregnancy?

Postoperative precautions include adequate hydration, supplemental oxygen as needed, continued left uterine displacement, early mobilization, and use of antiembolic massage devices and/or anticoagulation to prevent deep venous thrombosis.

Many obstetricians use intravenous fluids and β-agonist drugs to prevent premature labor. It is recommended that pregnant patients be observed postoperatively on the obstetric floor for a minimum of 12 hours. Magnesium sulfate is given intravenously if preterm labor occurs.

In a study of 778 women who underwent appendectomy while pregnant, 22% delivered during the following week if surgery occurred between 24 and 36 weeks' gestation. There is an increased risk of low birth weight infants (less than 2,500 g) and premature labor before 37 weeks.

Augustin G. *Acute Abdomen during Pregnancy*. New York: Springer; 2014:3–34.

Cheek TG, Baird E. Anesthesia for nonobstetric surgery: maternal and fetal considerations. *Clin Obstet Gynecol*. 2009;52:535–545.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia:*

Principles and Practice. 6th ed. Philadelphia, PA: Elsevier; 2020:368–391.

D.4. The next day, the patient went into premature labor and now needs a cesarean section for prematurity and breech presentation. She requires another general anesthetic. In what way would your technique differ from your previous anesthetic technique?

Magnesium sulfate will both prevent the muscle fasciculations that normally occur following the administration of succinylcholine and will potentiate the effects of nondepolarizing muscle relaxants (use smaller doses). Avoid the use of narcotics until after delivery and then after delivery stop the inhalation agent and begin using a narcotic technique.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2020:368–391, 568–626.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2036–2041.

SECTION 8 The Hematologic System

31 Hemophilia and Disorders of Coagulation

Elizabeth M. Staley

A 46-year-old, HIV-positive man with congenital hemophilia A is scheduled for elective elbow synovectomy with resection of the radial head because of pain with movement and limited range of motion.

A. Medical Disease and Differential Diagnosis

1. Describe the various laboratory tests that evaluate the coagulation cascade and the specific components measured by each.
2. What is the difference between platelet adhesion, activation, and aggregation at sites of vascular injury?
3. Describe the physiologic events that occur following endothelial interruption in the blood vessel.
4. What factors prevent the extension of a clot beyond the site of

injury?

5. Describe the factors involved in the extrinsic, intrinsic, and common coagulation cascade.
6. Describe the typical presentation history and pathophysiology associated with von Willebrand disease (vWD).
7. Explain the pathophysiology, frequency, and treatment of significant rare disorders of coagulation (factor VII [FVII], factor XII [FXII], and fibrinogen).
8. Differentiate between hemophilia A, B, and C.
9. What are the differences in factor replacement therapy between patients with hemophilia A and hemophilia B?
10. What is acquired hemophilia?
11. Which plasma protein is important in maintaining normal levels of factor VIII (FVIII)?
12. How are patients with severe hemophilia managed in the outpatient setting?
13. Describe the levels of FVIII necessary to maintain hemostasis in patients with spontaneous or surgical bleeding.

B. Preoperative Evaluation and Preparation

1. What steps would you take to normalize this patient's coagulation status before surgery?
2. What is meant by 1 unit of FVIII clotting activity, and how much does 1 unit of FVIII clotting activity per kilogram of body weight increase FVIII concentrations?
3. Would you administer FVIII using a bolus or infusion technique?
4. Can hemophiliac patients fail to mount an appropriate coagulation response following FVIII infusion?
5. If a patient with hemophilia does not respond to a bolus injection of FVIII, can an infusion technique be effective?
6. How much FVIII activity is present in plasma? What are the risks associated with plasma administration?

7. What are the indications for the administration of plasma?
8. What is cryoprecipitate, and how is it prepared? How much FVIII activity is present in cryoprecipitate? When is cryoprecipitate indicated?
9. Describe the advantages and disadvantages of the products that are available for repletion of FVIII activity.
10. What is the role of desmopressin (D-amino D-arginine vasopressin [DDAVP]) for hemostatic management in this patient?
11. What is the role of antifibrinolytic therapy in the perioperative period for the patient with hemophilia? What are examples of antifibrinolytics used in the treatment of hemophilia?
12. What are the options for operative treatment of patients with acquired hemophilia? Describe the mechanism of action and dosing considerations for each of these therapies.

C. Intraoperative Management

1. Is it safe to administer an intramuscular injection to this patient before surgery?
2. Would an axillary block be appropriate for this patient?
3. If general anesthesia is used, would it be safe to intubate the patient's trachea?
4. Would you use any special precautions for this patient who is positive for HIV?
5. What special considerations should be taken in choosing anesthetic drugs for this patient?
6. During an operative procedure, if the surgeon indicates that significant blood loss is occurring, would you transfuse this patient with packed red blood cells (RBCs) or whole blood?
7. During the transfusion of the first unit of whole blood, the patient's temperature rose from 36.8°C to 37.9°C (98.2°F to 100.2°F). What immediate steps should be taken by the anesthesiologist at this time?

8. Does giving blood intraoperatively increase the potential for the development of FVIII inhibitors?
9. Can FVIII be safely administered to patients who have developed circulating inhibitors?
10. The surgeon has requested the use of a tourniquet to minimize surgical bleeding. What are the physiologic and hemodynamic responses to tourniquet use?
11. Is it appropriate to suction the endotracheal tube and oropharynx of this patient before extubation?

D. Postoperative Management

1. What special consideration should be given to postoperative pain management for this patient?
2. What steps should be taken to enhance the coagulation status of this patient in the postoperative period while at home?
3. Can this patient be treated with FVIII supplements using home infusion?

A. Medical Disease and Differential Diagnosis

A.1. Describe the various laboratory tests that evaluate the coagulation cascade and the specific components measured by each.

Numerous laboratory tests evaluate specific components of the coagulation cascade.

Routine assessment or monitoring (i.e., pharmacologic anticoagulation) of the coagulation cascade is usually performed with both prothrombin time (PT) and activated partial thromboplastin time (aPTT). Specific factors assessed by different coagulation tests are shown in **Table 31.1**. The PT is measured after recalcification by combining tissue factor (TF) with a plasma specimen and measuring the time to clot formation. This test will detect abnormalities in factor II (FII),

factor V (FV), FVII, and factor X (FX) or the presence of an inhibitor (such as a lupus anticoagulant, or a true antibody-mediate, acquired coagulation factor inhibitor). Clot formation can be measured either mechanically or optically depending on the laboratory method used, the various methods having differential susceptibility to interference from lipemia or icterus and the reagents used have varying sensitivities to factor level depletion (i.e., therefore, cut-offs for abnormal results are set with each reagent). The PT maybe also be prolonged in the setting of hypofibrinogenemia. Typically, fibrinogen (factor I) must be less than 100 mg per dL to affect the PT. The PT is frequently used to monitor warfarin. Results are standardized to accommodate the use of different formulations of thromboplastin activating agents; the international sensitivity index (ISI) rates the sensitivity of a given reagent with respect to a standard with an assigned ISI value of 1. The international normalized ratio (INR) is calculated by determining the ratio of the patient PT to that of the normal/reference population and raising it to the power of the ISI as follows: INR = (patient test result/mean of normal reference population)^{ISI}. The PT is not useful for measuring the effects of other forms of anticoagulant therapy, particularly direct oral anticoagulants (DOACs).

TABLE 31.1 Specific Factors Assessed by Different Coagulation Tests

Laboratory Tests	Components Measured
Prothrombin time	I, II, V, VII, and X
Activated partial thromboplastin time	I, II, V, VII, IX, X, XI, and XII
Thrombin time	I, II
Platelet function analyzer 100 (PFA-100)	vWF, platelet count/function, vascular integrity

vWF, von Willebrand factor.

The aPTT result is determined as the time to clot when partial thromboplastin (no TF) and a negatively charged activating

substance (e.g., celite or kaolin) are added to a test tube of recalcified citrated plasma. Prolongations in the aPTT can be associated with deficiencies in factor I (FI), FII, FV, FVIII, factor IX (FIX), FX, factor XI (FXI), and FXII or the presence of an inhibitor (such as a lupus anticoagulant, or a true antibody-mediated, acquired coagulation factor inhibitor). The aPTT has been used as means of monitoring heparin therapy, with a goal of targeting 1.5 to 2.5 times the mean normal value. However, this practice has fallen in to disuse because the reagents have varying sensitivity to the anti-FXa/anti-FIIa effects of unfractionated heparin. Anti-FXa activity level can be used to monitor heparin anticoagulation when patients have deficiencies of the contact factors, with lupus anticoagulants, or in the setting of DOAC use if the assay is calibrated using the specific DOAC to be monitored. The aPTT is also not useful for measuring the effects of DOACs.

The activated clotting time (ACT) measures the time to clot formation when whole blood is activated by diatomaceous earth (kaolin) or other activators (e.g., celite). This test is used most often to measure the response to large heparin doses (concentrations greater than 1 U per mL and up to 10 U per mL) during percutaneous cardiology interventions, renal dialysis, or cardiopulmonary bypass (CPB). Although the relationship between ACT and heparin level is fairly linear within a given patient, there are substantial differences between patients with regard to the heparin dose-response relationship. The ACT has several limitations: It may be insensitive to specific factor deficiencies; it lacks specificity, and similar to aPTT values, ACT values can be prolonged as related to lupus anticoagulant antibodies or other clinically significant or insignificant inhibitors. Additionally, ACT can be prolonged independent of heparin levels by either hypothermia or hemodilution that are commonly observed with extracorporeal circulation, as during

cardiac surgery.

Thrombin time is an assay that bypasses most of the coagulation cascade and simply measures the conversion of fibrinogen to fibrin. This test can be especially useful to evaluate fibrinogen levels (hypofibrinogenemia) as well as abnormal fibrinogen function (dysfibrinogenemia). The thrombin time is also sensitive to very low concentrations of heparin. The thrombin time can be used to exclude the presence of direct thrombin inhibitors (DTIs) such as bivalirudin or small amounts of residual circulating heparin. A modified (i.e., patient plasma diluted eightfold) version of the thrombin time may be helpful to assess the effects of some of the new oral anti-FIIa inhibitors (e.g., dabigatran).

The thromboelastography (TEG) or rotational thromboelastometry (ROTEM) (**Fig. 31.1**) assesses the viscoelastic properties of blood by measuring the speed of clot formation and clot firmness (i.e., maximum amplitude vs. maximal clot firmness). These tests allow evaluation of a clot from early formation of fibrin strands to clot dissolution through fibrinolysis. The TEG tracings consist of several parameters: reaction time (R value), coagulation time (K value), maximum amplitude (MA value), α angle, and the amplitude 60 degrees after the MA or maximum clot firmness (MCF) (A60) or fibrinolysis indices (MA/A60 ratio). A deviation from a prototypical tracing represents one or more abnormalities in the patient's coagulation profile, and these abnormalities have been shown to be associated with either bleeding (i.e., low MA value) or thrombotic (i.e., with high MA value) complications. Although abnormal TEG or ROTEM tracings can provide useful information, many of the parameters are not necessarily specific for any defined hemostatic abnormality. The MA or MCF can be affected by thrombocytopenia or qualitative platelet abnormalities, fibrinogen deficiencies, or even anemia. More

recent modifications of the TEG and ROTEM devices incorporate the use of various agonists (e.g., kaolin vs. TF) or inhibitors (i.e., of platelets with cytochalasin D or fibrinolysis with aprotinin) that enhance the systematic analysis of intraoperative coagulation defects by increasing specificity with respect to detection of specific defects and can facilitate a more directed approach to therapy. An example of TEG/ROTEM interpretative guidelines is shown in **Table 31.2**.

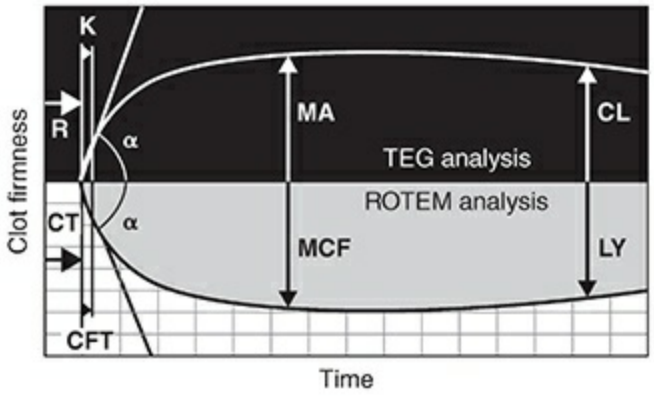

FIGURE 31.1. Tracings of thromboelastography (TEG) and rotational thromboelastometry (ROTEM). Upper side: TEG tracing: *α*, slope between R and K; CL, clot lysis; K, kinetics; MA, maximum amplitude; R, reaction time. Lower side: ROTEM tracing: *α*, slope of tangent at 2-mm amplitude; CFT, clot formation time; CT, clotting time; LY, lysis; MCF, maximal clot firmness.

TABLE 31.2 Interpretation of Thromboelastography (TEG)/Rotational Thromboelastometry (ROTEM) Parameters

TEG	ROTEM	Definition	Etiology	Management
R	CT	Time from the start of test until clot initiation	Prolonged: factor deficiency or anticoagulant	Prolonged: plasma
K	CFT	Time from clot initiation to when curve achieves an amplitude of 20 mm	Prolonged: factor deficiency, hypo-/dysfibrinogenemia, thrombocytopenia, platelet dysfunction	Cryoprecipitate
α	*α*	Angle between the baseline and the tangent to the curve through the starting point of coagulation	Prolonged: factor deficiency, hypo-/dysfibrinogenemia, thrombocytopenia, platelet dysfunction	Cryoprecipitate
MA	MCF	Amplitude measured at the maximum curve width	Prolonged: factor XIII deficiency, hypo-/dysfibrinogenemia,	Platelets. Consider plasma or cryoprecipitate.

			thrombocytopenia, platelet dysfunction	
LY	CL	Reduction in area under the curve (LY) or in amplitude (CL) from the time MA/MCF is achieved until 30–60 min later	Increased: hyperfibrinolysis	Antifibrinolytics

α, alpha angle; CL, clot lysis; CT/R, clotting time/reaction time; K/CFT, kinetics/clot formation time; LY, lysis; MA, maximum amplitude; MCF, maximum clot firmness.
Adapted from Pham HP, Shaz BH. Update on massive transfusion. *Br J Anaesth*. 2013;111(suppl 1):i71–i82. Copyright © 2013 The Author(s). With permission.

Additionally, there are tests available for specifically assessing platelet function; these assays typically use optical density or impedance methods to assess inducible platelet aggregation. The more recently available assays are the VerifyNow and PFA-100. VerifyNow (Accumetrics, San Diego, CA) is a point-of-care instrument that uses light transmission to assess platelet activity and/or inhibition. The test is performed using whole blood and evaluates platelet aggregation of fibrinogen-coated beads in response to stimulation with a potent thrombin receptor agonist. As platelets aggregate/coalesce, there is an increase in light transmittance. Platelets from patients taking antiplatelet therapy will demonstrate impaired aggregation, as demonstrated by reduced light transmission. Much of the data using VerifyNow has focused on assessing the effects of adenosine diphosphate (ADP) $P2Y_{12}$ receptor antagonists such as clopidogrel and prasugrel. However, it may also be used to assess inhibition of platelet aggregation in the setting of glycoprotein (GP) IIb/IIIa receptor antagonists (e.g., abciximab and eptifibatide).

The PFA-100 (Dade Behring, Miami, FL) assesses platelet adhesion and aggregation/activation in response to ADP or epinephrine. This assay draws whole blood through a capillary tube into a chamber through a 150-μm aperture within a collagen membrane coated with one of the two previously mentioned

agonists. Platelet adhesion and aggregation seals the aperture, and the time required for closure or the "closure time" is evaluated. The test is typically used to assess antiplatelet therapy. However, due to the shear forces involved in pulling blood through the aperture, the test is also sensitive to defects in von Willebrand factor (vWF)-mediated platelet adhesion. The test may also be useful in assessing Bernard-Soulier syndrome and/or other congenital and acquired platelet defects. Koscielny et al. studied over 5,500 patients using a standard bleeding history in addition to laboratory screening tests, including PFA-100. The PFA-100 was able to identify patients with impaired clinical hemostasis (history of abnormal bleeding and a defined hemostatic defect with laboratory testing); in a follow-up study, reduced bleeding complications were observed when the PFA-100 was used to direct therapy.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:419–458.

Ferraris VA, Saha SP, Oestreich JH, et al. 2012 Update to the Society of Thoracic Surgeons guideline on use of antiplatelet drugs in patients having cardiac and noncardiac operations. *Ann Thorac Surg*. 2012;94(5):1761–1781.

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Koscielny J, Kiesewetter H, von Tempelhoff GF. More on: platelet function analyzer (PFA)-100 closure time in the evaluation of platelet disorders and platelet function. *J Thromb Haemost*. 2006;4(6):1426–1434.

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Rahe-Meyer N, Solomon C, Hanke A, et al. Effects of fibrinogen concentrate as first-line therapy during major aortic replacement surgery: a randomized, placebo-controlled trial. *Anesthesiology*. 2013;118(1):40–50.

Whiting D, DiNardo JA. TEG and ROTEM: technology and clinical applications. *Am J Hematol*. 2014;89(2):228–232.

A.2. What is the difference between platelet adhesion, activation, and aggregation at sites of vascular

injury?

Platelets are recruited to sites of vascular injury via binding with vWF bound to collagen fibers in the vessel wall and the platelet GP Ib-IX-V receptor. vWF deposits on exposed collagen fibers present at sites of vascular injury and rapidly unfolds in response to vascular shear forces. Conformational changes in the vWF molecule lead to increased exposure of platelet binding sites and adhesion as mediated by platelet surface receptor GP Ib. Platelet activation is mediated via multiple platelet signaling pathways, including initial release of ATP and ADP, and thrombin present as a result of vascular damage, signaling downstream of the GP Ib-IX-V complex and binding of the GP VI collagen receptor. Platelet activation induces conformational changes leading to subsequent interactions between platelet integrin molecules and collagen ($\alpha_2\beta_1$ integrin) and vWF ($\alpha_{IIb}\beta_3$) enhancing adhesion. Activated platelets release alpha and dense granule contents (i.e., thromboxane A2 and ADP), which are agonists for expression of additional surface receptors for further platelet activation and ultimately induce aggregation. Platelet aggregation is the result of platelet cross-linking (clumping) via GP IIb/IIIa receptors that are bound by either vWF or fibrinogen. The degree of platelet aggregation is influenced by varying shear rates in vascular beds and local concentrations of thrombin and other platelet activating agents (e.g., ADP, PAF, epinephrine).

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:419–458.

Furie B, Furie BC. Mechanisms of thrombus formation. *N Engl J Med*. 2008;359(9):938–949.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1579–1603.

Tomaiuolo M, Brass LF, Stalker TJ. Regulation of platelet activation and coagulation and its role in vascular injury and arterial thrombosis. *Interv*

A.3. Describe the physiologic events that occur following endothelial interruption in the blood vessel.

The small size of platelets relative to other blood components, such as red or white blood cells, results in slower transit in the blood vessel with resultant margination. Platelet diffusivity or margination is the process in which the faster moving, larger cellular components within blood push the platelets toward the walls of the blood vessel; accordingly, in the setting of anemia, reduced margination of platelets can result in fewer platelets in close proximity to the vessel wall. Marginated platelets in circulation are in close contact with vascular surfaces and can immediately respond to endothelial defects. Endothelial breaks expose platelets to subendothelial structures, including collagen and other proteins that activate the hemostatic system (e.g., TF). This promotes adhesion of platelets to the subendothelium via platelet GP Ib receptors and induces generation of thrombin. Platelet adhesion promotes platelet activation, resulting in conformational changes to the platelet structure and release of the contents of the cytoplasmic granules. Platelet α and dense granules contain factors such as ADP and serotonin and FVa, which further promote platelet activation and aggregation. The platelet plug formed through this process provides initial hemostasis. The degree of platelet activation, release, and ultimate aggregation is in large part predicated by the concentration of thrombin (FIIa) in the local milieu. The final stage of platelet plug formation is driven by FIIa-mediated expression of platelet IIb/IIIa receptors. Platelet receptor IIb/IIIa facilitates cross-linking of platelets (aggregation) by fibrinogen (fibrin) and vWF. Thrombin converts fibrinogen to fibrin as a means of strengthening the platelet matrix. Finally, activation of factor XIII (FXIII) via thrombin cross-polymerizes the loose

fibrin to produce a firm and stable platelet—coagulation factor cross-linked matrix resulting in a stable clot.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:419–458.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1579–1603.

A.4. What factors prevent the extension of a clot beyond the site of injury?

The localization of coagulation and control of primary/secondary hemostasis results from the interplay/coordination of multiple factors. Circulating heparin (i.e., endogenous or via administration of unfractionated heparin) or endothelial glycosaminoglycans and/or reduced levels of thrombin result in release of tissue factor pathway inhibitor (TFPI). TFPI inhibits TF-mediated activation of FX. Additionally, increased levels of activated thrombin and increased expression of thrombomodulin on the intact endothelial glycocalyx propagate activation of the anticoagulant protein C (along with its cofactor protein S), which subsequently inactivates activated FVa and FVIIIa. The heparin–antithrombin (AT) complex binds and inhibits activated clotting factors, including FXIIa, FXIa, FIXa, FXa, and FIIa. Finally, the intact endothelial surface secretes many mediators that have platelet-inhibiting (e.g., triphosphate dephosphorylases, prostacyclin or prostaglandin I_2 [PGI_2], nitric oxide) or clot-lysing effects. One such mediator, tissue plasminogen activator (tPA), catalyzes conversion of plasminogen to plasmin. Plasmin initiates the physiologic process of fibrinolysis resulting in proteolysis of FV/FVIII, fibrin, and fibrinogen. Fibrin degradation (split) products (fibrin split products [FSPs]) and D-dimers (cross-linked fibrin), respectively, are removed from circulation by the liver via mononuclear phagocyte system. Accumulation of these

by-products (FSPs and D-dimer) in the setting of substantial liver dysfunction can contribute to abnormal hemostasis secondary to platelet dysfunction (perhaps via binding to GP IIb/IIIa receptors).

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:419–458.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1579–1603.

Johnston-Cox HA, Ravid K. Adenosine and blood platelets. *Purinergic Signal*. 2011;7(3):357–365.

A.5. Describe the factors involved in the extrinsic, intrinsic, and common coagulation cascade.

When normal blood is placed in an empty test tube in the absence of any additional agents, a clot will form. The clotting factors involved in this process were originally classified as "intrinsic" factors because everything necessary for blood to clot was "intrinsic" to the test tube. It has also been referred to as the "contact activation pathway" because clotting is initiated via contact with negatively charged surfaces (i.e., glass or subendothelial collagen). In the classical description of this pathway, FXII is converted to FXIIa. FXIIa subsequently converts FXI into FXIa. FXIa activates FIX, which with its cofactor FVIIIa forms the tenase complex that activates FX to FXa. Subsequently, the Va/Xa complex activates thrombin and the common pathway. The laboratory test focusing on assessment of factors characteristic of the intrinsic/common pathways is the aPTT.

The "extrinsic" pathway is so named as the stimulus for thrombin generation involves the binding of tissue thromboplastin or TF to FVIIa. TF and FVIIa form a complex that functions to convert FIX to FIXa, FX to FXa, and, ultimately, FII to FIIa, also resulting in stimulation of the

common pathway. The laboratory test believed to assess the extrinsic/common pathways is the PT.

The extrinsic and intrinsic pathways converge with activation of FX, hence the term “common pathway.” The common pathway proceeds when FXa acting with FVa converts FII (prothrombin) into FIIa (thrombin). Thrombin subsequently cleaves fibrinogen into fibrin, in addition to mediating activation of FV, FVIII, and FXIII.

This classic separation of procoagulant factors into extrinsic, intrinsic, and common coagulation cascades is a convenient framework/reference standard. However, it is now considered by many to be an incredibly limited model of the hemostatic system. This classic paradigm fails to incorporate the cross talk of the multiple factors that play an integral role in coagulation (e.g., endothelium, platelets, and leukocytes). The more current coagulation paradigm uses a cell-based model and emphasizes the contribution of the many localized factors in vivo, perhaps most important the endothelium itself, that are critical for induction of coagulation and the formation of the platelet-rich hemostatic plug. Although the factors represented in the classic intrinsic and extrinsic coagulation pathways propagate the formation and activation of thrombin (and hence the amplification of coagulation), considering their actions in a vacuum can be misleading with respect to an accurate understanding of in vivo mechanisms.

The cell-based theory describes three distinct phases of coagulation: initiation, amplification, and propagation. Each stage represents a different aspect of hemostasis at a cellular level, with pivotal points predicated on a spike or “burst” in the concentration of thrombin that ultimately results in the formation of a stable clot. Thrombin generation is crucial to coagulation, as demonstrated by the fact that the vast majority of anticoagulation strategies involve inhibition of Xa and/or

thrombin. The initiation phase of the cell-based model is notable not only for thrombin generation (secondary to platelet adhesion) but also through exposure of TF to circulating FVIIa, which again leads to generation of thrombin as the essential step. Thrombin generation is amplified by FXIa, ultimately resulting in generation of more thrombin through the amplification and propagation phases. As such, thrombin is crucial for the final two phases of coagulation and serves as a potent catalyst for hemostasis.

The importance of these mechanisms is illustrated by the effectiveness of the hemostatic agent known as recombinant activated FVII or rFVIIa (NovoSeven, Novo Nordisk, Plainsboro, NJ). The effectiveness of rFVIIa is predominately related to its ability to propagate thrombin generation. It has been proposed that rFVIIa is ideally suited for bleeding involving localized sites of injury that express TF (e.g., localized, not traumatic central nervous system [CNS] bleeds). In the setting of high systemic levels of TF (e.g., disseminated intravascular coagulation [DIC], use of extracorporeal devices), administration of rFVIIa can lead to systemic activation of thrombin and intravascular thrombosis. The classic coagulation cascade is depicted in **Figure 31.2**.

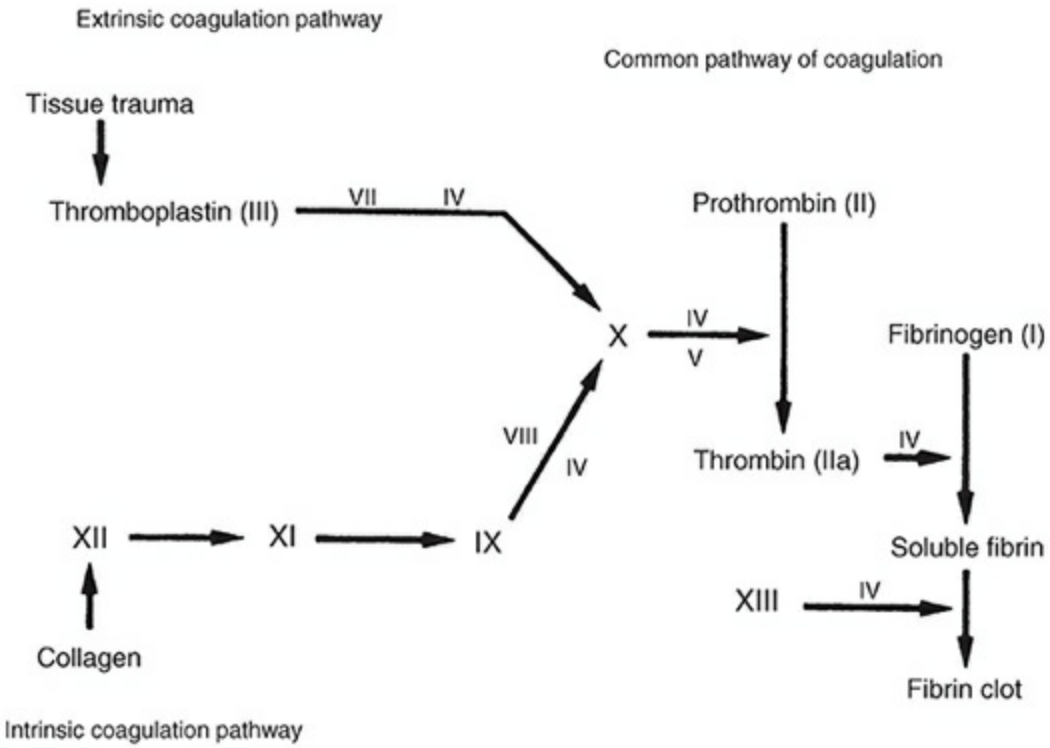

FIGURE 31.2. Schematic diagram of the procoagulant phase of coagulation depicting the cascade sequence in three steps, designated as the intrinsic, extrinsic, and common coagulation pathways. (*Reprinted from Stoelting RK, Dierdorf SF, McCammon RL, eds.* Anesthesia and Co-existing Disease. *2nd ed. New York: Churchill Livingstone; 1988:577. Copyright © 1988 Elsevier. With permission.*)

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:419–458.

Furie B, Furie BC. Mechanisms of thrombus formation. *N Engl J Med*. 2008;359(9):938–949.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1579–1603.

Hoffman M, Monroe DM III. A cell-based model of hemostasis. *Thromb Haemost*. 2001;85:958–965.

A.6. Describe the typical presentation history and pathophysiology associated with von Willebrand disease (vWD).

vWD is the most common inherited bleeding disorder (approximately 0.1% to 1% of the general population); it is characterized by the absence or functional deficiency of vWF. vWF plays a critical role in primary hemostasis, by stimulating

platelet activation via platelet adhesion mediated through binding both platelets (i.e., via GP Ib receptors) and subendothelial matrix components (collagens 1 to 6). vWF can also promote platelet aggregation as a ligand for GP IIb/IIIa receptors. vWF plays an additional role in secondary hemostasis by serving as a carrier/stabilizer for FVIII. vWF is synthesized by endothelial cells, and substantial posttranslational protein modification within the Golgi apparatus leads to high molecular weight (HMW) and very high molecular weight (VHMW) forms of this multimeric protein. These larger forms have the greatest hemostatic functional activity.

vWD manifests clinically as bruising, epistaxis, mucocutaneous bleeding, and menorrhagia in women but can also lead to serious and even life-threatening bleeding with trauma or with high-risk surgical operations. Because vWD is caused by a variety of mutations/types, it manifests along a spectrum of symptoms (see **Table 31.3**) and, as such, there is heterogeneity in its clinical manifestations and relative risk of bleeding. The diagnosis is often suggested by the patient's history of a bleeding diathesis and/or the presence of a prolonged bleeding time (BT) (not often performed), prolonged aPTT (in 50% of patients), or abnormal PFA-100 result despite a normal platelet count and no drug effect. Laboratory analysis is useful for classifying the types and subtypes of vWD and to guide therapy. Interestingly, acquired forms of vWD have been rarely described associated with lymphoproliferative disease, tumors, cardiac valvular lesions, as well as others.

TABLE 31.3 von Willebrand Disease: Diagnosis, Classification, and Response to Desmopressin D-Arginine Vasopressin (DDAVP)

Type	RCoA	vWFAg	Platelet Count	RIPA	FVIII	DDAVP Effective	Multimer Pattern
1	↓	↓	NL	NL or ↓	NL or ↓	Yes	Uniform decrease with all

							multimers present
2A (15%)	↓	NL or ↓	NL	NL or ↓	NL	+/−	Decreased large multimers
2B (5%)	↓	NL or ↓	NL or ↓	↑	NL	No	Decreased large multimers
2M (<1%)	↓	NL or ↓	NL	NL or ↓	NL	No	Uniform decrease with all multimers present
2N (3%)	NL	NL	NL	NL	↓	No	Normal
3 (1%)	↓↓	↓↓	NL	↓↓	↓↓	No	Undetectable

↓, decreased; ↑, increased; FVIII, factor VIII; NL, normal; RCoA, ristocetin cofactor activity; RIPA, ristocetin-induced platelet aggregation; vWFAg, von Willebrand factor antigen.
Adapted from Sadler JE, Budde U, Eikenboom JC, et al. Update on the pathophysiology and classification of von Willebrand disease: a report of the subcommittee on von Willebrand factor. *J Thromb Haemost*. 2006;4(10):2103–2114. Copyright © 2006 John Wiley & Sons, Inc.

Six different vWD types/subtypes exist (type 1, type 2A, type 2B, type 2N, type 2M, and type 3). Type 1 and type 3 represent quantitative deficiency of vWF related to either modest (type 1) or severe (type 3) reductions in vWF expression. Patients with type 2 disease have qualitative defects in vWF and are subdivided based not only on the expression levels of HMW forms of vWF but also on the corresponding mechanistic defects in platelet adhesion, platelet activation/aggregation, or FVIII binding.

vWF type 1 is the most common (85%) and mildest form of the disease. It is inherited as an autosomal dominant trait and has a reported incidence as high as 2% to 3% of northern European populations (approximately 0.1% total population). However, it is believed to be frequently misdiagnosed as a result its mild clinical symptoms (epistaxis, menorrhagia, increased postoperative bleeding) in combination with the variant expression of vWF associated with other factors (i.e., blood type, menstrual cycle, etc.). It is currently recommended that the diagnosis of type 1 vWF be made only when vWF levels are below 30 U per dL, which may require repetitive testing. First-line treatment for type 1 disease is with desmopressin (DDAVP). DDAVP can normalize vWF and FVIII by inducing

release of vWF from the endothelium, with hemostatic regulation being restored in the setting of normal expression of other hemostatic factors (i.e., tPA, prostacyclin, etc.).

Type 3 vWD is both the rarest and the most severe form of the disease. It is inherited in an autosomal recessive fashion and is characterized by a near-complete absence of vWF expression (<2 U per dL). Unfortunately, many cases present as uterine fetal demise or death in the immediate postnatal period. DDAVP is not beneficial in type 3 because patients have little to no endogenous production of vWF. Treatment for vWF type 3 and all forms of type 2 relies on repletion of vWF using factor concentrates.

Type 2A vWD is an autosomal dominant qualitative defect, characterized by normal total expression of vWF in the setting of reduced vWF-mediated platelet adhesion. Decreased activity is the result of reduced expression of the optimally biologically active HMW and VHMW multimers. The deficiency of large multimers is believed to result from defects in multimer assembly or enhanced vWF cleavage by ADAMTS13. Laboratory testing shows normal vWF protein levels in the setting of reduced functional activity. DDAVP has been shown to be beneficial in some patients.

Type 2B vWD is inherited in an autosomal dominant fashion and is characterized by a structural abnormality in the HMW form of vWF resulting in enhanced affinity for platelet GP Ib. This induces heightened platelet activation and spontaneous platelet aggregation. Patients with type 2B can have reduced HMW forms of vWF (selective removal) in the setting of thrombocytopenia. Subtype 2B is diagnosed when patients have an exaggerated response to the ristocetin, an antibiotic that stimulates binding of vWF to platelet GP Ib and induces platelet aggregation and thrombocytopenia. In the absence of HMW forms of vWF, no agglutination will occur during ristocetin

cofactor activity assay. A similar disease entity known as pseudo- or platelet-type von Willebrand disease (pt-vWD) has been described. pt-vWD is also inherited in an autosomal dominant fashion and results from enhanced functionality of the platelet receptor GP Ib. pt-vWD is virtually indistinguishable from vWF type 2B; however, it is believed to be exceedingly rare and is described only in case reports. DDAVP is contraindicated in the setting of both vWF type 2B and pt-vWD because it can aggravate platelet activation/binding and results in clinically significant thrombocytopenia. Repletion of vWF is effective in treating vWF type 2B; however, it would not be effective in the setting of pt-vWD.

Type 2N (Normandy) vWD is an autosomal recessive bleeding disorder that results from a decreased affinity of vWF for FVIII. Patients with type 2 vWD have reduced expression of FVIII binding receptors on vWF. These patients typically have normal levels of vWF and reduced expression of FVIII and thus are often misdiagnosed with hemophilia A. Repletion of vWF is considered optimal therapy.

Type 2M vWD is sometimes described as a diagnosis of exclusion. The condition is inherited in an autosomal dominant fashion and is characterized by reduced vWF-dependent platelet adhesion despite normal expression of vWF and its HMW multimers; however, these HMW multimers may have reduced binding affinity. DDAVP has been shown to be beneficial in some patients; however, treatment usually consists of vWF repletion. The diagnosis and classification of different types of vWD and their response to DDAVP are shown in **Table 31.3**.

Favaloro EJ. Rare forms of von Willebrand disease. *Ann Transl Med*. 2018;6(17):345.

Favaloro EJ, Bodó I, Israels SJ, et al. von Willebrand disease and platelet disorders. *Haemophilia*. 2014;20(suppl 4):59–64.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease*. 7th

ed. Philadelphia, PA: Elsevier Saunders; 2017:477–506.

Lenting PJ, Casari C, Christophe OD, et al. von Willebrand factor: the old, the new and the unknown. *J Thromb Haemost*. 2012;10(12):2428–2437.

Russell SD, Roth GJ. Pseudo-von Willebrand disease: a mutation in the platelet glycoprotein Ib alpha gene associated with a hyperactive surface receptor. *Blood*. 1993;81(7):1787–1791.

A.7. Explain the pathophysiology, frequency, and treatment of significant rare disorders of coagulation (factor VII [FVII], factor XII [FXII], and fibrinogen).

Hemostasis is maintained as a balance between hemostatic and anticoagulant forces, and, as such, the absence of any one of the forces that play a role in maintaining that balance can predispose an individual to bleeding or thrombosis in the various clinical settings. Hemophilia A and B are the most commonly occurring congenital factor deficiencies; however, deficiencies of other key components of the coagulation cascade have been reported, albeit much less commonly. The frequency of hereditary hemostatic disorders is shown in **Table 31.4**. Plasma-derived concentrates are available for fibrinogen, FVII, FVIII, FIX, FX, FXI, and FXIII; additionally, there are recombinant factor replacement products for FVII, FVIII, and FIX. Deficiencies in other coagulation factor products can be accomplished using plasma or cryoprecipitate. Rare coagulation deficiencies (RCDs) typically manifest as mucosal bleeding, excessive bleeding during, and/or following surgical procedures, although severe bleeding and death can occur. The most common RCD is FVII deficiency, reportedly occurring at a frequency of 1:500,000 patients. FVII deficiency may be initially detected due to isolated PT prolongation. Clinical manifestations are heterogeneous, from asymptomatic to severe/fatal bleeding that appears to be unrelated FVII plasma levels. FVII is relatively easily monitored and repleted; the manufacture recommends doses 15–30 μg/kg in the setting of congenital factor deficiency.

Increased dosing maybe recommended in the setting of an acquired factor inhibitor.

TABLE 31.4 The Prevalence of Hereditary Defects of the Hemostatic System

Hemostatic Deficit	Prevalence/Incidence
Platelet disorders (i.e., GP/granule deficits)	8%; 1:250
Coagulation factor deficiencies	
FVIII	1:5,000–1:10,000
FIX	1:30,000
FXI	1:1,000,000 or 1:50 Ashkenazi Jewish births
FVII	1:500,000
FV, FX	1:1,000,000
Afibrinogenemia/dysfibrinogenemia	1:1,000,000
FII, FXIII	1:2,000,000
von Willebrand disease	1.5%; 1:10,000

FII, factor II; FV, factor V; FVII, factor VII; FVIII, factor VIII; FIX, factor IX; FX, factor X; FXI, factor XI; FXIII, factor XIII; GP, glycoprotein.

From Despotis G, Eby C, Lublin DM. A review of transfusion risks and optimal management of perioperative bleeding with cardiac surgery. *Transfusion*. 2008;48(suppl 1):2S–30S. Copyright © 2008 American Association of Blood Banks. Adapted by permission of John Wiley & Sons, Inc.

FXIII deficiency is also very rare, reportedly occurring in 1 in every 2 to 3 million people. FXIII functions to cross-link fibrin monomers and fibronectin, stabilizing fibrin clots rendering them more resistant to mechanical stress and proteolytic degradation. Deficiency is associated with abnormal wound healing, recurrent miscarriages, and excessive bleeding in the postoperative period after operative procedures, with the majority of patients presenting in childhood with umbilical cord bleeding. Patients with FXIII deficiency have an increased incidence of spontaneous intracranial hemorrhage. A FXIII level of <1% is associated with the severe bleeding phenotype, whereas levels between 1% and 4% typically show a moderate bleeding pattern. In the absence of factor concentrates, cryoprecipitate should be used for FXIII repletion.

Congenital fibrinogen disorders can be quantitative (hypo- or afibrinogenemia) or qualitative (dysfibrinogenemia). Afibrinogenemia occurs in 1 in a million people. Hypo- and dysfibrinogenemia are likely more common, but they typically only experience severe bleeding in the setting of trauma or operative interventions and may therefore remain undiagnosed. Congenital afibrinogenemia is typically diagnosed in the setting of prolonged bleeding from an umbilical stump. Afibrinogenemia is associated with spontaneous splenic rupture, poor wound healing, and painful bone cysts. Cryoprecipitate is often used for fibrinogen repletion, although there is now an approved fibrinogen concentrate as well.

de Moerloose P, Schved JF, Nugent D. Rare coagulation disorders: fibrinogen, factor VII and factor XIII. *Hemophilia*. 2016;22(suppl 5):61–65.

NovoSeven® RT. *Coagulation Factor VIIa (Recombinant) [package insert]*. Bgsverd, Denmark: Novo Nordisk A/S; 2016.

Despotis G, Eby C, Lublin DM. A review of transfusion risks and optimal management of perioperative bleeding with cardiac surgery. *Transfusion*. 2008;48(suppl 1):2S–30S.

Sevenet PO, Kaczor DA, Depasse F. Factor VII deficiency: from basics to clinical laboratory diagnosis and patient management. *Clin Appl Thromb Hemost*. 2017;23(7):703–710.

A.8. Differentiate between hemophilia A, B, and C.

Hemophilia, one of the oldest known genetic disorders, can be classified into types A, B, or C. Hemophilia A is the most common form of the disease, accounting for 85% of all patients with hemophilia. Hemophilia A typically presents as a congenitally inherited X-linked recessive bleeding disorder (approximately 1:5,000 male births and rare homozygous females), resulting from absent or decreased activity of coagulation FVIII. It is typically classified as mild (endogenous FVIII levels are >5%), moderate (FVIII between 1% and 5%), and severe (FVIII <1%). However, clinical disease severity (i.e.,

bleeding diathesis) correlates both with the FVIII activity level as well as the presence and efficacy of a neutralizing inhibitor. Severe disease manifests as spontaneous bleeding into joints, muscles, and vital organs and can involve life-threatening bleeding events (e.g., CNS, retroperitoneum). Patients with mild disease may remain undiagnosed until such time as they face a hemostatic stress (i.e., surgery, trauma). The aPTT has been used as a screening test for moderate to severe hemophilia A. The aPTT will be prolonged in hemophilia A with moderate to severe disease, with variable detection of patients with milder forms depending on the sensitivity of the coagulation methods/reagents used. Directly assessing FVIII activity can provide a diagnosis; however, it is important to note that reproducibly normal levels do not exclude carrier status. FVIII is an acute phase reactant and, as such, concentrations can become elevated in times of stress especially when vWF (FVIII carrier protein) is released from endothelium. Genetic testing provides a definitive diagnosis in the setting of an inherited disorder of protein synthesis.

Hemophilia B is the second most common form of disease, representing approximately 14% of known hemophiliacs. Similar to hemophilia A, hemophilia B is a congenital bleeding disorder resulting from impaired functional activity of coagulation FIX. This X-linked genetic disorder has an inheritance pattern and clinical features that are similar to those of hemophilia A. Hemophilia B may be diagnosed by measuring both the concentration and function of FIX. However, it is important to note that FIX is a vitamin K–dependent coagulation factor and is likely to be reduced in the setting of Coumadin or vitamin deficiency.

The remaining 1% of patients with hemophilia are deficient in FXI, classified as hemophilia C. Hemophilia C, or Rosenthal syndrome, is an extremely rare autosomal recessive disorder,

occurring almost solely in people of Ashkenazi Jewish descent. Hemophilia C is clinically distinguishable from A and B due to the absence of spontaneous bleeding into joints and muscles. In fact, bleeding in patients with hemophilia C is typically mild; however, it has been associated with trauma involving the oral and nasal cavities or the urinary tract. Perplexingly, there is a discrepancy in the literature suggesting that FXI activity levels and/or aPTT results are not predictive of bleeding in hemophilia C patients.

Deficiencies of other coagulation factors may occur, albeit, at a much lower frequency with an incidence in the general population of (1:20,000 to 1:1,000,000) as seen in **Table 31.4**.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:419–458.

Despotis G, Eby C, Lublin DM. A review of transfusion risks and optimal management of perioperative bleeding with cardiac surgery. *Transfusion*. 2008;48(suppl 1):2S–30S.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier Saunders; 2017:477–506.

Naseef M, Sheehan JP. New developments in the management of moderate-to-severe hemophilia B. *J Blood Med*. 2016;7:27–38.

Wheeler AP, Gailani D. Why factor XI deficiency is a clinical concern. *Expert Rev Hematol*. 2016;9(7):629–637.

A.9. What are the differences in factor replacement therapy between patients with hemophilia A and hemophilia B?

Patients with hemophilia A typically require repletion of FVIII prior to major surgery to normalize FVIII levels to approximately 100% of normal. The half-life of administered pooled or recombinant FVIII is about 12 hours but can vary based on the recombinant formulation. Further supplementation or redosing is typically performed every 12 hours for days to weeks depending on the severity of the bleeding episode and

baseline factor levels. Patients with hemophilia B typically require higher initial doses of FIX due to extensive redistribution of FIX to the extravascular compartment. However, FIX has a much longer half-life (18 to 30 hours), and thus, redosing is typically only preformed every 24 hours.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:419–458.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier Saunders; 2017:477–506.

Lee CA, Owens D, Bray G, et al. Pharmacokinetics of recombinant factor VIII (recombinate) using one-stage clotting and chromogenic factor VIII assay. *Thromb Haemost*. 1999;82(6):1644–1647.

A.10. What is acquired hemophilia?

Acquired hemophilia is caused by the formation of antibody targeting and neutralizing FVIII, or less commonly FIX. Antibody formation may be de novo (approximately 1:100,000 to 1:1,000,000), or it can be associated with hemophilia presumably as a result of therapeutic exposure animal sources of FVIII. Patients with de novo acquired hemophilia are typically >65 years of age (approximately 80%) and approximately 50% of cases are associated with an underlying medical condition (i.e., an autoimmune disorder, malignancy, or a drug/allergic reaction). Acquired hemophilia should be suspected when a prolonged aPTT fails to correct following a mixing study in a patient with previously normal results or when a patient with known hemophilia fails to adequately respond to appropriate doses of clotting factors. The recommend test for the detection/measurement of inhibitors is the Bethesda assay. The test measures the amount of factor that is inactivated by patient plasma. A Bethesda unit (BU) is the amount of inhibitor necessary to inactivate half of the factor present in normal human plasma. Patients with low titer inhibitors (<5%) may achieve hemostasis following treatment with slightly increased

doses of factor concentrates.

Interestingly, the formation of antibodies directed at FIX is far less common in patients with hemophilia B (1% to 5%) than the formation of anti-FVIII antibodies in hemophilia A (25% to 30%). It has been theorized that the genetic mutations most common in hemophilia B (point mutations) are more likely to result in non- or hypofunctional FIX, whereas the mutations more commonly associated hemophilia A (inversions) are more likely to result in absent protein expression.

Mintz P, ed. *Transfusion Therapy: Clinical Principles and Practice*. 3rd ed. Bethesda, MD: AABB Press; 2011:167–195.

A.11. Which plasma protein is important in maintaining normal levels of factor VIII (FVIII)?

FVIII is an X-linked gene product that functions to accelerate FIXa-mediated activation of FX by four orders of magnitude. However, FVIII is one of the largest and least stable coagulation factors with a half-life of about 2 hours when unbound. FVIII circulates in the plasma covalently bound to vWF, which serves to stabilize the protein by protecting it from inactivation by activated protein C and preventing its binding to phospholipids and activated platelets. vWF also facilitates optimal delivery of FVIII localizing it to sites of endothelial injury and enabling approximation with FIX (i.e., the FVIII and FIX complex leads to activation of FX on the platelet surface). Although vWF is important in maintaining adequate levels of FVIII, less than 10% of vWF multimers bind FVIII.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:419–458.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier Saunders; 2017:477–506.

A.12. How are patients with severe hemophilia managed in

the outpatient setting?

Episodic or as needed clotting factor replacement at the time of clinically significant bleeding was the standard of care for patients with hemophilia for many years. However, in the past 15 to 20 years, it has been conclusively shown that morbidity and mortality can be significantly reduced for patients with severe disease through the implementation prophylactic clotting factor therapy. Prophylactic treatment is initiated as early as 1 to 2 years of age with the goal of reducing chronic progressive joint disease or in older children/adults to prevent rebleeding into a target joint. There are now a variety of options available for factor replenishment for patients with severe hemophilia. Historically, factor repletion was performed using pooled plasma concentrates derived from thousands of volunteer donors. The use pooled concentrates was the source of transfusion-related transmission of human immunodeficiency virus (HIV) and hepatitis C virus (HCV) to hemophiliacs in the 1980s. Plasma-derived concentrates are still available, and donors are subjected to rigorous screening along with repetitive retesting to overcome with silent or window phase of testing insensitivity (e.g., 12 months after initial donation), and products additionally undergo viral inactivation processes. However, pooled concentrates may still carry a risk for transfusion-related transmission of infection, particularly from nonenveloped viruses. There is a lack of trust in the safety of plasma-derived products inherent in the hemophilia community.

The cloning of the FVIII gene in 1984 opened the door for the production of the recombinant factor products. Recombinant products are now in their third generation of production, with each successive generation being designed with the goal of reducing immunogenicity and increasing product half-life. The half-life of plasma-derived FVIII is 8 to 12 hours; thus, it is dosed frequently, typically 2 to 3 times weekly. FVIII undergoes

extensive posttranslational modification in the form of glycosylation and sulfonylation and is stabilized by its chaperone protein vWF. Strategies to prolong FVIII half-life in recombinant products involve conjugating with larger molecules such as polyethylene glycol (PEG), albumin, or human immunoglobulin Fc, and/or generating single chain or domain deleted products (**Table 31.5**). The products also differ with respect to the type of stabilizer used (albumin/sucrose) and viral inactivation method applied. Currently, products are available with reported half-lives of 14 to 19 hours. Interestingly, none of these products have yet conclusively demonstrated superiority with respect to reducing immunogenicity or rates of inhibitor formation. Similarly, there are recombinant forms of FIX available and considerable progress has been made in developing extended half-life forms of FIX allowing for less frequent dosing (7 to 14 days).

TABLE 31.5 Factor VIII Replacement Products

Product	FVIII	Technology	Half-life
Antihemophilic factor (Koate-DVI, Hemo ÀI M, Monarc-M, Monoclate-P)	Full length	Pooled human plasma	14.8–17.5
Antihemophilic factor/vWF complex (Alphantate, Humate-P, Wilate)	Full length	Pooled human plasma	12.2–17.9
Recombinant antihemophilic factor—first generation (Recombinate)	Full length	Culture—BSA/albumin stabilizer	14.6 (±4.9)
Recombinant antihemophilic factor—second generation (Helixate, Kogenate)	Full length	Culture—human plasma proteins	13.7
Recombinant antihemophilic factor—third generation (Advate, Kovaltry)	Full length	No human/animal protein	12–14.2
Recombinant—second generation (ReFacto)	BDD	Culture—human plasma proteins	14.5 (±5.3)
Recombinant—third generation (Xyntha, Novoeight)	BDD	No human/animal protein	10.8–12
Recombinant—fourth generation (Nuwiq)	BDD	Glycosylated in HEK cells	17.1 (±11.2)

Recombinant—third generation EHL (Adynovate)	BDD-Pegylated	Pegylated Advate (no human/animal protein)	14.7 (±3.7)
Recombinant—fourth generation EHL (Eloctate)	BDD-rFVIII-Fc	Glycosylated in HEK cells	19.7 (±2.3)
Recombinant—third generation EHL (Afstyla)	Single chain	No human/animal protein	14.2

BDD, B domain deleted; BSA, bovine serum albumin; EHL, extended half-life; HEK, human embryonic kidney; rFVIII, recombinant factor VIII; vWF, von Willebrand factor.
Adapted from Lieuw K. Many factor VIII products available in the treatment of hemophilia A: an embarrassment of riches? *J Blood Med*. 2017;8:67–73.

Recently, a novel bispecific antibody, emicizumab (ACE910; Hoffman-La Roche Pharmaceutical, Basel, Switzerland), which mimics the in vivo function of FVIII (by simultaneously binding activated FIX and FX, allowing for proteolysis and activation of FX) has been U.S. Food and Drug Administration (FDA) approved. Emicizumab has efficacy in preventing bleeding events in patients with both congenital and acquired hemophilia. However, many patients still require coagulation factor bypass agents in the setting of acute/active bleeding. Based primarily on results from preliminary ex vivo studies, it has been suggested that bypass agents containing FIX (i.e., prothrombin complex concentrates [PCC] or activated prothrombin complex concentrates [aPCC] or factor eight inhibitor bypassing activity [FEIBA]; Baxter Healthcare Corp, Deerfield, IL) may have an enhanced coagulant effect on patients receiving emicizumab potentially predisposing them to the formation of thrombus.

Additionally, early clinical trials are currently being conducted focusing on inhibitors of the anticoagulant cascade. Two such drugs, fitusiran (Alnylam Pharmaceuticals, Cambridge, MA) and concizumab (Novo Nordisk, Bagsværd, Denmark), targeting AT and TFPI, respectively, are in clinical trials.

Finally, there is ongoing work developing gene therapy for patients with hemophilia. Studies have used adeno-associated

viral vectors (AAVs), lentiviral vectors, and, more recently, gene-editing approaches based on designer nucleases or clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated protein 9 (Cas9) technologies. Early gene therapy trials have had variable success showing clinically transient or subtherapeutic clotting factor expression levels. Recently, therapeutic FVIII and FIX expression levels (e.g., mean of 30% to 40% activity) have been described after gene therapy in patients with severe hemophilia. However, complications related to transient liver toxicity and the use of immunosuppression have been reported. Patients who have undergone gene therapy will likely still benefit from preoperative FVIII assessment and may yet require additional repletion in the setting of bleeding events.

Arruda VR, Doshi BS, Samelson-Jones BJ. Novel approaches to hemophilia therapy: successes and challenges. *Blood*. 2017;130(21):2251–2256.

Collins PW, Liesner R, Makris M, et al. Treatment of bleeding episodes in haemophilia A complicated by a factor VIII inhibitor in patients receiving emicizumab. Interim guidance from UKHCDO Inhibitor Working Party and Executive Committee. *Haemophilia*. 2018;24:344–347.

Lieuw K. Many factor VIII products available in the treatment of hemophilia A: an embarrassment of riches? *J Blood Med*. 2017;8:67–73.

Makris M. Hemophilia gene therapy is effective and safe. *Blood*. 2018;131:952–953.

Mintz P, ed. *Transfusion Therapy: Clinical Principles and Practice*. 3rd ed. Bethesda, MD: AABB Press; 2011:167–195.

VandenDriessche T, Chuah MK. Hemophilia gene therapy: ready for prime time? *Hum Gene Ther*. 2017;28(11):1013–1023.

A.13. Describe the levels of FVIII necessary to maintain hemostasis in patients with spontaneous or surgical bleeding.

The levels of FVIII necessary for hemostasis vary given patient clinical condition/presentation (**Table 31.6**). When life-

threatening airway, neurologic bleeding, or major surgery is anticipated, correction to 100% FVIII levels is desired. In the setting of operative need, correction should be performed preoperatively and maintained for some interval postoperatively as defined by the bleeding risk and clinical circumstances. Patients receiving outpatient/home therapy using factor-derived, recombinant, and/or even porcine factor products can have testing performed with minimal difficulty to assess FVIII functional activity for repletion in the setting of a bleed or impending operative intervention. The new FVIII monoclonal reagent is more complicated from a monitoring standpoint. Emicizumab cofactor restores activity of missing activated FVIII and will overcorrect any laboratory tests that use total intrinsic clotting time, including the one-stage FVIII activity assay, which is based on the aPTT. However, assays utilizing chromogenic or immuno-based methods are unaffected. Of note, chromogenic assays containing human coagulation factors may overestimate hemostasis. Hemostatic assays utilizing bovine coagulation factors are insensitive and are optimal for monitoring endogenous or infused FVIII activity or to measure anti-FVIII inhibitors. Similarly, emicizumab remains active in the presence of inhibitors and can cause false-negative results in clot-based Bethesda assays; a bovine-based FVIII chromogenic assay should be used instead.

TABLE 31.6 Levels of Factor VIII Necessary for Hemostasis

Type of Bleeding	Desired Factor Level	Suggested Duration of Treatment
Dental procedures (including extractions)	30%–60%	1 hr prior to the procedure
Intramuscular hemorrhage	30%–50%	2–5 d
Iliopsoas or other retroperitoneal bleeding	30%–50%	3–10 d
Retropharyngeal bleeding	40%–50%	3–4 d

Gastrointestinal bleeding	30%–50%	2–3 d
Intracranial hemorrhage	80%–100%	10–14[a] d
Surgery	80%–100%	10–14[a] d

[a]Continuous infusion may be preferable in order to avoid dangerously low trough levels.
Adapted from Mintz P, ed. *Transfusion Therapy: Clinical Principles and Practice*. 3rd ed. Bethesda, MD: AABB Press; 2011:167–195. With permission.

Hemlibra® (emicizimab-kxwh) [package insert]. South San Francisco, CA: Genentech, Inc; 2018.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier Saunders; 2017:477–506.

Janco RL, Maclean WE, Perrin JM, et al. A prospective study of patterns of bleeding in boys with haemophilia. *Haemophilia*. 1996;2:202–206.

Mintz P, ed. *Transfusion Therapy: Clinical Principles and Practice*. 3rd ed. Bethesda, MD: AABB Press; 2011:167–195.

B. Preoperative Evaluation and Preparation

B.1. What steps would you take to normalize this patient's coagulation status before surgery?

Orthopedic surgical procedures in particular require maintenance of normal levels of FVIII in order to minimize bleeding into and/or around a prosthetic joint, which can lead to infection risk or destruction of the surrounding tissue or hematoma formation. FVIII levels of 30% of normal are usually considered adequate for baseline hemostasis; nevertheless, most clinicians will target normal FVIII levels prior to most surgical procedures (approximately 100%). These levels are necessary because factor levels typically decrease due to redistribution in addition to normal consumption and decay.

For major orthopedic procedures, FVIII levels should be corrected to 100% of normal 1 hour before the procedure. A repeat dose may be needed based on the duration of the procedure, amount of blood loss, and dose initially used. Repletion strategies are typically based on quantification of

peaks and troughs or factor levels.

Rodriguez-Merchan EC. Aspects of current management: orthopaedic surgery in haemophilia. *Haemophilia*. 2012;18(1):8–16.

B.2. What is meant by 1 unit of FVIII clotting activity, and how much does 1 unit of FVIII clotting activity per kilogram of body weight increase FVIII concentrations?

One unit of FVIII clotting activity is defined as the amount of factor present in 1 mL of fresh, normal plasma; however, normal factor levels typically range between 0.8 and 1.2 U per mL because there is substantial variability in factor levels in normal patients. On average, an individual with a plasma volume of 3,000 mL would have 3,000 IU of each clotting factor in their circulation (i.e., intravascular compartment). If an individual has less than 1% of normal FVIII activity, it would take 3,000 IU of FVIII to raise the plasma levels to normal (assuming the absence of an inhibitor), which is around 100%, assuming the source of the FVIII does not result in expansion of the patient plasma volume compartment beyond 3,000 mL (e.g., 3,000 U administered via a factor concentrate requiring reconstitution using only 50 to 100 mL) and the patient does not have a neutralizing antibody. In other words, 100% factor activity is equivalent to a concentration of 1 IU per mL of the factor of interest. Dosing a single unit of FVIII clotting activity per kilogram of body weight will increase plasma FVIII levels approximately 1 U per mL or 100% activity. Therefore, to prescribe the FVIII activity necessary to correct a 70-kg hemophilia patient with 5% FVIII activity to 95% of normal, one can calculate using 0.90 U per mL × plasma volume [blood volume × (1 − Hct)] or either of the following approaches:

Approach 1

Weight (kg) × (desired percent increase) × 0.5 = Dose of FVIII (IU)

70 kg × (95% – 5%) × 0.5 = 3,150 IU of FVIII

Approach 2

(Plasma volume [PV]) × (desired increase in factor level [U per mL]) = Dose of FVIII (IU)

Plasma Volume Calculation

PV = kg weight × (65 [female] or 75 [male] mL per kg) × (1 – Hematocrit [Hct])

For example, PV = 70 kg × 75 mL per kg × (1 – 0.4) = 3,150 mL

3,150 mL × (0.95 – 0.5 U per mL) = 2,835 U

Henrard S, Speybroeck N, Hermans C. Body weight and fat mass index as strong predictors of factor VIII in vivo recovery in adults with hemophilia A. *J Thromb Haemost*. 2011;9(9):1784–1790.

Jameson JL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:830–839.

B.3. Would you administer FVIII using a bolus or infusion technique?

Based on the relative stability of FVIII concentrates at room temperature after reconstitution, infusions can be used. By titrating the infusion, the desired FVIII level can be maintained, eliminating both the overshoot and the subtherapeutic levels seen with the bolus technique. A continuous infusion is typically initiated to maintain factor levels following administration of an initial loading dose of FVIII.

Batorova A, Martinowitz U. Intermittent injections vs. continuous infusion of factor VIII in haemophilia patients undergoing major surgery. *Br J Haematol*. 2000;110(3):715–720.

Jameson JL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York: McGraw-Hill; 2018:830–839.

B.4. Can hemophiliac patients fail to mount an appropriate coagulation response following FVIII infusion?

As described earlier, a substantial percentage of hemophiliacs (approximately 30% of patients with hemophilia A) develop a neutralizing antibody (inhibitor) against FVIII and thus the anticipated response following FVIII infusion will not be achieved. Inhibitor titers can vary between patients. The development of neutralizing inhibitors is important to recognize because it causes patients to be refractory to FVIII concentrates, which if undiagnosed can lead to excessive and perhaps life-threatening bleeding. Patients with high-titer inhibitors may require alternative acute management interventions (e.g., rFVIIa, PCC, or even recombinant porcine FVIII or intravenous immunoglobulin [IVIg]) or when time permits, more sustainable effects with other interventions (e.g., plasma exchange or rituximab).

Individuals with congenital factor deficiencies may develop alloantibody inhibitors targeting specific epitopes of the hemostatic factor. The mechanisms leading to functional factor inhibition by these inhibitors include steric hindrance of appropriate functional binding sites, hydrolysis of the factor, and more rapid clearance by the reticuloendothelial system. The antibodies may be directed against one of many different domains, some of which are pathologic and others are not. Pathogenicity is generally determined by which of the domains is targeted by the antibody.

Bayry JS, Lacroix-Desmazes A, Pashov D, et al. Autoantibodies to factor VIII with catalytic activity. *Autoimmun Rev*. 2003;2(1):30–35.

Bolton-Maggs PHB, Pasi KJ. Haemophilias A and B. *Lancet*. 2003;361(9371):1801–1809.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier Saunders; 2017:477–506.

B.5. If a patient with hemophilia does not respond to a bolus injection of FVIII, can an infusion technique be effective?

Some patients who do not respond well to bolus injections may in fact have low-titer FVIII inhibitors. A continuous infusion may prove effective in this situation to stop hemorrhage because appropriate levels of the missing factor can be achieved relatively easily by infusion. In fact, some patients with high antibody/inhibitor titers and no measurable factor level during the infusion may respond to an infusion technique. This is believed to be due to the kinetics of inhibitors; that is, complete inhibition of the factor may require 1 to 2 hours. In the setting of continuous FVIII infusion, there will always be some factor that is circulating in an unneutralized and hemostatically active state. Depending on the degree of the inhibitor, efforts at immune tolerance may be effective. An immune tolerance regimen consists of continuous infusions in conjunction with immunosuppression over an extended period of time to promote development of immune tolerance to the factor and thereby eradicate the inhibitor.

Bolton-Maggs PHB, Pasi KJ. Haemophilias A and B. *Lancet*. 2003;361(9371):1801–1809.

Gordon EM, Mungo R, Goldsmith JC. Lingual hemorrhage in a patient with hemophilia A complicated by a high titer inhibitor. Management by continuous infusion of monoclonal antibody-purified factor VIII. *Am J Pediatr Hematol Oncol*. 1993;15:107–110.

Schulman S, Martinowitz U. Continuous infusion instead of bolus injections of factor concentrate? *Haemophilia*. 1996;2:189–191.

B.6. How much FVIII activity is present in plasma? What are the risks associated with plasma administration?

Following whole blood donation and separation of RBCs and plasma by centrifugation, approximately 200 mL of plasma is

prepared from one unit of whole blood. Thus, plasma is prepared from a single donor and contains all coagulation factors and plasma proteins, including FVIII. When people refer to plasma in the United States, they typically mean fresh frozen plasma (FFP). However, the vast majority of what is dispensed from the blood bank is actually thawed plasma (TP) or plasma frozen within 24 hours of collection (FP24). FFP specifically refers to products that are processed and frozen within 8 hour of phlebotomy. FP24 is frozen within 24 hours of collection. When either of these products is thawed, but not transfused within 24 hours, it is relabeled as TP, which may be dispensed/transfused for up to 5 days if stored at 4°F. These products are considered hemostatically equivalent. The typical FVIII activity of plasma is 0.5 to 0.9 units of clotting activity per milliliter because the activity of FVIII and FV decays during storage.

The risks associated with transfusion of FFP are similar to those associated with any single-donor product. The most feared risk is potential exposure to infectious agents, particularly lipid-enveloped viruses that cause hepatitis B and C as well as HIV. The incidence of transfusion-related infections has decreased over the last several decades largely due to the implementation of rigorous screening and testing procedures (e.g., donor history questionnaires, serologic and nucleic acid amplification technology [NAT]/polymerase chain reaction [PCR]-based testing). Currently, the risk of transmitting hepatitis B infection following transfusion of FFP slightly exceeds that of HIV and hepatitis C. The decrease in transfusion-related hepatitis C is in part related to the implementation of NAT to reduce or minimize the window period. Hepatitis B occurs at approximately 1:300,000 (this may be an overestimate with the implementation of PCR testing for hepatitis B), and hepatitis C occurs at approximately 1:1,500,000. HIV infection currently occurs at approximately 1:2,000,000 donor exposures, although these

numbers can vary because they are mathematical estimates.

In contrast to plasma, nonrecombinant factor concentrates undergo several interventions to reduce infectious risk of pooled products. Techniques commonly used for factor concentrate preparation include donor retesting after 12 months, heat (pasteurization), nanofiltration, and solvent detergent treatments, which can minimize the risk of viral pathogen transmission.

There are additional risks associated with transfusion that are not associated with transmission of infectious organisms. These include allergic reactions, transfusion-associated circulatory overload (TACO), transfusion-related acute lung injury (TRALI), in addition to the common cytokine mediated occurrence of febrile nonhemolytic reactions. TRALI is the leading case of transfusion related mortality in the United States. It is more common following transfusion of plasma as opposed to other blood products. However, the incidence of TRALI following plasma transfusion has decreased since the early 2000s following the practice of limiting plasma collection to male donors. Female donors have been excluded from the donor pool because of the higher likelihood of antibodies associated with TRALI (i.e., antibodies targeting either human leukocyte antigens [HLA] and/or human neutrophil antigens [HNA]) acquired during/through pregnancy. It has been proposed these antibodies activate recipient neutrophils along the pulmonary endothelium resulting in degranulation and development of noncardiogenic pulmonary edema. TACO is a serious and underrecognized transfusion complication of plasma transfusion. The typically used doses of 2 or 4 units of plasma represent a volume of 400 to 800 mL. This volume, in addition to potentiating fluid overload, often represents an inadequate therapeutic dose of plasma (recommended dosing is 10 to 15 mL per kg body weight). Plasma exposure additionally carries the risk for allergic reactions to blood proteins in up to 1% to 2% of

recipients. Anaphylactic reactions are unusual and are sometimes associated with patients with immunoglobulin A (IgA) deficiency who through exposure have developed antibodies to IgA. Patients with this condition should only receive plasma from IgA-deficient donors and must only receive RBCs and/or platelets that have been washed to remove a high percentage of plasma proteins.

Chapman CE, Stainsby D, Jones H, et al. Ten years of hemovigilance reports of transfusion-related acute lung injury in the United Kingdom and the impact of preferential use of male donor plasma. *Transfusion*. 2009;49(3):440–452.

Kaufman RM, Djulbegovic B, Gernsheimer T, et al. Platelet transfusion: a clinical practice guideline from the AABB. *Ann Intern Med*. 2015;162(3):205–213.

Theusinger OM, Baulig W, Seifert B, et al. Relative concentrations of haemostatic factors and cytokines in solvent/detergent-treated and fresh-frozen plasma. *Br J Anaesth*. 2011;106(4):505–511.

Triulzi D, Gottschall J, Murphy E, et al. A multicenter study of plasma use in the United States. *Transfusion*. 2015;55(6):1313–1319.

Zou S, Stramer SL, Dodd RY. Donor testing and risk: current prevalence, incidence, and residual risk of transfusion-transmissible agents in US allogeneic donations. *Transfus Med Rev*. 2012;26(2):119–128.

B.7. What are the indications for the administration of plasma?

The National Institutes of Health multidisciplinary consensus development panel determined that plasma was the most overused blood product for transfusion. Although there are few if any large-scale randomized clinical trials regarding the optimal/appropriate use of plasma, there are consensus guidelines providing recommendations for plasma use. It is generally deemed appropriate to transfuse plasma to patients who are massively bleeding (as part of a massive transfusion protocol) or have deficits/consumption of multiple coagulation factors (DIC) or as replacement fluid for patients with thrombotic thrombocytopenic purpura. In all other scenarios,

plasma transfusion is sometimes recommended when better products are unavailable, that is, for the reversal of vitamin K antagonist (if factor concentrates are unavailable) or for the treatment of bleeding patients with an isolated congenital factor deficiency (when no factor concentrate is available), hereditary angioedema (if C1 esterase inhibitor is unavailable), or treatment of AT deficiency (if AT concentrate is unavailable). Despite this, plasma is often inappropriately used as a volume expander or as prophylaxis in stable, nonbleeding with mild elevation of their coagulation factor tests prior to minor procedures.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:419–458.

Bryan AW Jr, Staley EM, Kennell T Jr, et al. Plasma transfusion demystified: a review of the key factors influencing the response to plasma transfusion. *Lab Med*. 2017;48(2):108–112.

Dzik W, Rao A. Why do physicians request fresh frozen plasma? *Transfusion*. 2004;44:1393–1394.

B.8. What is cryoprecipitate, and how is it prepared? How much FVIII activity is present in cryoprecipitate? When is cryoprecipitate indicated?

Cryoprecipitate is the fraction of plasma that precipitates when FFP is thawed at 1°F to 6°F. After centrifugation, the precipitate is extracted and refrozen for use as cryoprecipitate. Each unit of cryoprecipitate consists of 10 to 15 mL and thaws rapidly. Cryoprecipitate must be used within 4 to 6 hours of thawing. In addition to FVIII, it contains significant levels of vWF, FXIII, fibronectin, and fibrinogen. The American Association of Blood Banks (AABB) Standards require that 1 unit of cryoprecipitate must contain a minimum 80 IU of FVIII as well at least 150 mg of fibrinogen.

Cryoprecipitate can be used to manage patients with

hemophilia A, vWD, hereditary or acquired hypofibrinogenemia (especially when concentrates are unavailable), hereditary FXIII deficiency (if concentrates are unavailable), uremia-induced platelet dysfunction along with DDAVP as well as thrombolysis-related bleeding with low fibrinogen levels. However, cryoprecipitate is most frequently used to replete fibrinogen in bleeding patients. Fibrinogen plays a critical role in hemostasis; it functions both as the precursor to fibrin and as a mediator of platelet aggregation. In bleeding patients, fibrinogen is sometimes the first coagulation factor to be depleted. It is recommended that fibrinogen levels be maintained at >100 mg per dL for bleeding patients or those undergoing surgery; however, more recent evidence indicates that even higher levels should be maintained during cardiac surgery. Fibrinogen factor concentrate is now available in the United States. Fibrinogen concentrate is only approved for use in the United States for patients with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia. Fibrinogen concentrate may represent an improvement over cryoprecipitate in that it undergoes a viral inactive step during manufacture, it can be rapidly reconstituted and can be infused immediately (no need to thaw), is stable at room temperature, and the dose can be easily titrated to clinical response; these advantages may offset its high cost in certain circumstances.

Of note, small amounts of red cell fragments may be present in cryoprecipitate; therefore, use of cryoprecipitate constitutes a potential sensitization risk for Rhesus (Rh)-negative individuals.

Callum JL, Karkouti K, Lin Y. Cryoprecipitate: the current state of knowledge. *Transfus Med Rev*. 2009;23(3):177–188.

Levy JH, Szlam F, Tanaka KA, et al. Fibrinogen and hemostasis: a primary hemostatic target for the management of acquired bleeding. *Anesth Analg*. 2012;114:261–274.

Okerberg CK, Williams LA III, Kilgore ML, et al. Cryoprecipitate AHF vs.

fibrinogen concentrates for fibrinogen replacement in acquired bleeding patients—an economic evaluation. *Vox Sang*. 2016;111(3):292–298.

Rahe-Meyer N, Solomon C, Hanke A, et al. Effects of fibrinogen concentrate as first-line therapy during major aortic replacement surgery: a randomized, placebo-controlled trial. *Anesthesiology*. 2013;118(1):40–50.

B.9. Describe the advantages and disadvantages of the products that are available for repletion of FVIII activity.

When cost is not an issue, recombinant or monoclonal purified FVIII is generally preferred. Alternatively, plasma-derived FVIII concentrates may be the optimal choice. Hospitals that stock both plasma-derived and recombinant FVIII may have a policy such that patients who have already been diagnosed with hepatitis C or HIV be supplied with plasma-derived factor concentrates. If FVIII concentrates are unavailable, cryoprecipitate, plasma, or PCC may be used to replete FVIII activity.

Franchini M. Plasma-derived versus recombinant factor VIII concentrates for the treatment of haemophilia A: recombinant is better. *Blood Transfus*. 2010;8(4):292–296.

Schulman S, Varon D, Keller N, et al. Monoclonal purified F VIII for continuous infusion: stability, microbiological safety and clinical experience. *Thromb Haemost*. 1994;72:403–407.

B.10. What is the role of desmopressin (D-amino D-arginine vasopressin [DDAVP]) for hemostatic management in this patient?

This synthetic analog of the antidiuretic hormone is FDA approved for use in patients with mild and moderate hemophilia for minor surgery to attenuate the incidence and severity of bleeding complications especially with high-risk operative procedures. Intravenous DDAVP induces rapid release of FVIII and vWF from storage sites, resulting in a twofold to threefold increase in circulating FVIII within 30 to 60 minutes of

administration. The recommended intravenous dose is 0.3 μg per kg body weight (max dose 20 μg over 30 minutes to minimize the incidence of hypotension related to the concomitant release of endothelial prostacyclin) and with repeat dosing every 12 to 24 hours. However, patients can have tachyphylaxis if repeat dosing is used at frequent intervals, likely as a result of depleted endothelial storage reservoirs. Given the substantial variability in response to therapy, a preprocedural DDAVP trial is often performed to assess the response to therapy. Postinfusion levels of 30% are considered adequate for minor bleeding, whereas levels of 50% or greater are adequate for surgical interventions. Of note, desmopressin is a potent antidiuretic, and thus, there is a slight but realistic risk of hyponatremia/water intoxication following repetitive use. It is recommended that patients receiving desmopressin not receive hypotonic fluids postoperatively and that electrolytes be monitored closely. DDAVP also induces the release of plasminogen activator (which can cause fibrinolysis); however, it is usually unnecessary to inhibit fibrinolysis when DDAVP is used clinically in operative scenarios other than cardiac surgery or liver transplantation.

DDAVP is also approved to manage some patients with type 1 vWD. DDAVP may also be useful for patients with hereditary or acquired platelet abnormalities (e.g., uremia-induced or CBP-induced platelet dysfunction).

Despotis GJ, Levine V, Saleem R, et al. Use of point-of-care test in identification of patients who can benefit from desmopressin during cardiac surgery: a randomised controlled trial. *Lancet*. 1999;354(9173):106–110.

Mannucci PM. Desmopressin (DDAVP) in the treatment of bleeding disorders: the first twenty years. *Haemophilia*. 2000;6(suppl 1):60–67.

Mintz P, ed. *Transfusion Therapy: Clinical Principles and Practice*. 3rd ed. Bethesda, MD: AABB Press; 2011:167–195.

B.11. What is the role of antifibrinolytic therapy in the

perioperative period for the patient with hemophilia? What are examples of antifibrinolytics used in the treatment of hemophilia?

Antifibrinolytics have been used successfully in patients with hemophilia to prevent or manage bleeding, following minor bleeding (e.g., menorrhagia and epistaxis) and in preparation for minor surgical procedures (e.g., dental extractions). Their use in major surgical procedures for patients with hemophilia has not been well documented. Tranexamic acid (TXA) and ε-aminocaproic acid (EACA) are both lysine analogue antifibrinolytic agents that have been used for prevention and treatment of bleeding. Use of these agents to minimize bleeding and transfusion has been extensively studied; these agents have been shown to be effective to a variable degree in several surgical populations such as patients undergoing liver transplantation (i.e., during anhepatic stage), trauma, and high-risk cardiac and orthopedic procedures.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:419–458.

Mannucci PM. Desmopressin (DDAVP) in the treatment of bleeding disorders: the first twenty years. *Haemophilia*. 2000;6(suppl 1):60–67.

B.12. What are the options for operative treatment of patients with acquired hemophilia? Describe the mechanism of action and dosing considerations for each of these therapies.

Hemophilia A represents the majority of patients afflicted with hemophilia. Risk factors for the development of inhibitors include race, severity of the disease (<1% FVIII levels), having a hemophiliac brother with inhibitors, certain genetic mutations involving the FVIII gene, and/or exposure to FVIII derived from animal sources as opposed recombinant techniques. Acquired

hemophilia can also occur in patients without congenital hemophilia; these patients are typically >65 years old and have additional underlying medical conditions.

In patients with inhibitors, alternative treatment is occasionally necessary to address surgical and nonsurgical hemorrhagic crises. Frequently, the strategy employed is a FVIII bypass agent. These agents circumvent the need for FVIII activity in the coagulation cascade. The FDA has approved use of either rFVIIa or PCC for actively bleeding patients with FVIII inhibitors.

FVIIa binds to TF exposed at the site of injury and leads to generation of enough local thrombin to activate FV, FVIII, and FXI as well as platelets via an alternate mechanism other than the FVIIIa/FIXa complex. Moreover, in high doses, rFVIIa binds to activated platelets and activates FX. The prohemostatic effect of rFVIIa is generally limited when there are one or a few sites of local injury (e.g., spontaneous or traumatic CNS bleeding) because the expression of TF is limited to these localized sites. The risk of thrombosis is increased when there is a systemic state of TF activation as occurs in many clinical conditions that result in DIC. For on-label use, the typical doing schedule for hemostatic prophylaxis in patients undergoing elective surgery is 90 to 120 μg per kg, with repeated doses every 2 to 3 hours.

Prothombin complex concentrates (PCC or Profilnine SD, Grifols Biologicals, Los Angeles, CA; KCentra, CSL Behring, King of Prussia, PA) and aPCC (FEIBA, Baxter, Vienna, Austria) are commercially available plasma-derived products containing FII, FVII, FIX, and FX. Activated PCC contains activated FVII and small amounts of activated FII, FIX, and FX. PCCs have been shown to have a higher rate of adverse reactions and be less effective than aPCCs in treating patients with FVIII inhibitors. In the 1990s, rFVIIa concentrate was

available for use for patient with FVIII inhibitors. In clinical trials, both aPCCs and rFVIIa were shown to be efficacious for the management of bleeding in inhibitor patients with FVIII inhibitors.

aPCC is dosed at 50 U per kg and can be redosed if needed depending on the extent of the bleeding/clinical situation. However, there is no laboratory testing available for monitoring any of the bypass reagents. Moreover, there are multiple published cases associating repeated large doses of PCCs with myocardial infarctions in young patients with FVIII inhibitors. Additionally, it has been reported that coadministration of large doses of aPCC and emicizumab (the novel bispecific antibody therapy for hemophilia A patients with an inhibitor) is associated with venous thrombus and skin necrosis, leading to the recent guidance that first-line treatment of bleeding patients on emicizumab should be rFVIIa.

Recently, there has been increased focus on the use of porcine FVIII for the treatment of bleeding in hemophilia A patients with inhibitors. The original product derived from pig plasma (pd-FVIII; Hyate:C, Ipsen Biopharmaceuticals, Cambridge, MA) was withdrawn from use in 2004 out of concern for parvovirus contamination. However, recombinant porcine FVIII (rpFVIII; OBIZUR, Baxalta Inc, Deerfield, IL) was made available in 2014, and it has been shown be hemostatically effective in patients with FVIII inhibitors. The dose used in the initial studies (200 U per kg) frequently results in FVIII activity higher than is desirable in some patients. Dose adjustment should be considered to titrate to clinical response and inhibitor titers. Porcine FVIII may be preferable to bypass agents because its effects are quantifiable using the FVIII activity assay.

One additional approach to patients with inhibitors involves immune tolerance induction (ITI). ITI regimens typically involve administration of large doses of FVIII (50 or 200 U per

kg) daily or twice weekly until the inhibitor titer becomes negative, FVIII levels recover, and/or sustained half-lives are normal.

Abshire T, Kenet G. Safety update on the use of recombinant factor VIIa and the treatment of congenital and acquired deficiency of factor VIII or IX with inhibitors. *Haemophilia*. 2008;14:898–902.

Fosbury E, Drebes A, Riddell A, et al. Review of recombinant anti-haemophilic porcine sequence factor VIII in adults with acquired haemophilia A. *Ther Adv Hematol*. 2017;8(9):263–272.

Hedner U. Mechanism of action, development and clinical experience of recombinant FVIIa. *J Biotechnol*. 2006;124:747–757.

Hedner U. Treatment of patients with factor VIII and factor IX inhibitors with special focus on the use of recombinant factor VIIa. *Thromb Haemost*. 1999;82:531–539.

Key NS, Christie B, Henderson N, et al. Possible synergy between recombinant factor VIIa and prothrombin complex concentrate in hemophilia therapy. *Thromb Haemost*. 2002;88:60–65.

Mintz P, ed. *Transfusion Therapy: Clinical Principles and Practice*. 3rd ed. Bethesda, MD: AABB Press; 2011:167–195.

Negrier C, Goudemand J, Sultan Y, et al. Multicenter retrospective study on the utilization of FEIBA in France in patients with factor VIII and factor IX inhibitors. French FEIBA Study Group. Factor Eight Bypassing Activity. *Thromb Haemost*. 1997;77:1113–1119.

C. Intraoperative Management

C.1. Is it safe to administer an intramuscular injection to this patient before surgery?

Intramuscular injections can be safely administered to any patient with an FVIII activity greater than 30%. Therefore, if appropriate FVIII correction has occurred, an intramuscular injection would be safe. It is unlikely, though, that an intramuscular injection would be necessary for this patient. If a sedative hypnotic or anticholinergic drug is indicated before the induction of anesthesia, it may be more appropriate to use an

intravenous route, if available. Intravenous administration also enables immediate bioavailability with higher peak levels.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:419–458.

C.2. Would an axillary block be appropriate for this patient?

Regional anesthesia has been considered contraindicated in patients with hemophilia because the concern of hematoma formation at the injection site. However, with proper management of coagulation status, regional techniques have been successfully performed in patients with hemophilia. As with any patient, the benefit of the regional technique must be weighed against the potential risks. In a patient with a full stomach, a regional technique may be more appropriate to reduce the potential risk of aspiration. For a completely elective procedure in the patient with hemophilia, a more prudent course might be general anesthesia. If a regional anesthetic technique were being considered, it would be advisable to verify appropriate levels of factor activity at the time of the intervention as well as prior to removal of an epidural catheter, especially in the setting of the presence of neutralizing antibodies.

Sampson JF, Hamstra R, Aldrete JA. Management of hemophiliac patients undergoing surgical procedures. *Anesth Analg*. 1979;58:133–135.

C.3. If general anesthesia is used, would it be safe to intubate the patient's trachea?

Airway management of the patient with hemophilia presents a unique challenge for the anesthesiologist due to the potential for hemorrhage in the tongue or neck, which could compromise (i.e., complete or near complete occlusion) the upper airway. Therefore, manipulation of the airway during elective intubation

ideally should not be performed until appropriate replacement factors have been administered. Care should be used when applying pressure during mask ventilation to avoid trauma to the lips, tongue, or face; elective laryngoscopy should be attempted only following appropriate factor correction. Careful examination for swelling of the upper airway should be pursued prior to extubation; if substantial swelling or a hematoma is observed, extubation should be postponed until resolution. Depending on the procedure and operative needs, a smaller than predicted well-lubricated tracheal tube should be considered for intubation. Nasal intubation, with its propensity for epistaxis, should be avoided if possible.

Bogdan CJ, Strauss M, Ratnoff OD. Airway obstruction in hemophilia (factor VIII deficiency): a 28-year institutional review. *Laryngoscope*. 1994;104:789–794.

C.4. Would you use any special precautions for this patient who is positive for HIV?

Standard precautions should be used for all patients regardless of their HIV status. Strict attention to aseptic technique throughout the surgical procedure should be emphasized. Postoperative infections may be more common in HIV-positive patients undergoing orthopedic procedures such as these due to their potentially immunocompromised state.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier Saunders; 2017:477–506.

Thomason HC III, Wilson FC, Lachiewicz PF, et al. Knee arthroplasty in hemophiliac arthropathy. *Clin Ortho*. 1999;360:169–173.

C.5. What special considerations should be taken in choosing anesthetic drugs for this patient?

Historically, coexisting liver disease was a frequent complication in patients with hemophilia, likely resulting from

transfusion-transmitted hepatitis, an unfortunate consequence of a history of multiple previous blood or factor transfusions. This has been dramatically reduced due to improvements in donor screening and allogeneic blood testing. It is thus reasonable to use caution with drugs that are metabolized by the liver in the setting of substantial liver dysfunction (i.e., reduced protein synthetic function).

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier Saunders; 2017:477–506.

C.6. During an operative procedure, if the surgeon indicates that significant blood loss is occurring, would you transfuse this patient with packed red blood cells (RBCs) or whole blood?

As general transfusion practice, blood banks fractionate donated blood into component parts, resulting in the production of RBCs, platelets, plasma, and/or cryoprecipitate components. Following blood loss and subsequent to substantial volume replacement with crystalloids and/or colloids, RBCs may be required when oxygen-carrying capacity and oxygen delivery reach critically low levels. The trigger for RBC transfusion can be variable between patients with various clinical scenarios. Important factors to be considered include hematocrit, rate of blood loss, age, and comorbidities, in addition to monitoring other indices that allow assessment of a critical imbalance in oxygen delivery/consumption systemically, or in critical organ systems (i.e., CNS or myocardial ischemia). In a patient with hemophilia, transfusion of packed RBCs will further dilute already depressed circulating FVIII levels; therefore, transfusion of whole blood in such a patient would be appropriate, if it can be obtained. With administration of whole blood, both oxygen-carrying capacity and all components of coagulation would be replenished. Given the general unavailability of whole blood

other than for use as part of massive transfusion protocols within the trauma setting, additional factor repletion is typically required depending on the amount, rate, and expected course of the bleeding. Replenishment may take the form of whole blood fractions (cryoprecipitate or plasma), additional recombinant factor replacements, or pooled factor concentrates.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1579–1603.

C.7. During the transfusion of the first unit of whole blood, the patient's temperature rose from 36.8°C to 37.9°C (98.2°F to 100.2°F). What immediate steps should be taken by the anesthesiologist at this time?

Ruling out an acute hemolytic transfusion reaction should always be considered when a patient becomes febrile during a blood transfusion. The anesthesiologist should immediately discontinue the transfusion, drain any remaining allogeneic blood from the intravenous blood administration set, and blood should be drawn from the patient and sent to the blood bank with the unit of blood in question to allow for the performance of a transfusion reaction workup. Although blood banks may vary slightly with regard to the extent/manner of reaction testing performed, most blood banks will repeat product crossmatching and will use the sample to assess the plasma for visual evidence of free hemoglobin or icterus as well perform a direct antiglobulin test (DAT) to assess for antibody bound to transfused RBCs (mixed field pattern). If there is concern for hemolysis, haptoglobin, bilirubin, and lactate dehydrogenase (LDH) would be helpful for the assessment of intravascular hemolysis. Urine may also be assessed for hematuria and urine free hemoglobin. In the presence of an acute hemolytic blood transfusion reaction, profound hypotension requiring use of vasopressors is believed to be related to release of a number of

vasoactive mediators (e.g., serotonin, bradykinin, cytokines, histamine). Fluid and diuretic therapy as well as alkalization of the urine should be considered to reduce renal injury and maintain function. A febrile reaction that is not due to an acute hemolytic transfusion reaction frequently occurs with blood transfusion (e.g., 1% to 2%); these reactions are usually self-limited or easily managed. They are believed to be related to cytokines that are released by apoptotic leukocytes during red cell processing and storage. Simultaneous to the transfusion reaction evaluation, further investigations into the temperature increase is warranted because there are other potential causes of fever. Additionally, the transfusion reaction evaluation may take a few hours. Of note, a negative DAT makes transfusion-related immune-mediated intravascular hemolysis unlikely.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1579–1603.

C.8. Does giving blood intraoperatively increase the potential for the development of FVIII inhibitors?

Although approximately 30% of all patients with hemophilia A will develop a circulating inhibitor of FVIII, there is no evidence to suggest that development of an inhibitor is related to the number of transfusions a patient receives. As a result, administration of blood products in this setting should not be withheld for fear of inducing inhibitor development.

Rodriguez-Merchan EC, Lee CA. *Inhibitors in Patients with Haemophilia*. Oxford: Wiley-Blackwell; 2002:17–19.

C.9. Can FVIII be safely administered to patients who have developed circulating inhibitors?

Occasionally, patients with the most severe phenotype of hemophilia (factor levels <1%) develop immunoglobulin antibodies (IgG) to the deficient factor. The inhibitors may be of

low titer (generally thought of as less than 5 BU) or of extremely higher titer. The “Bethesda unit” of inhibition is defined as the amount of inhibitory activity present in 1 mL of plasma that decreases the FVIII level in 1 mL of normal plasma by 50% (i.e., from 1 to 0.5 units). The more dilutions needed to produce 50% activity, the higher the titer of antibody and the greater the number of BU. It is almost impossible to overpower a high-titer inhibitor with large doses of FVIII, but when life-threatening hemorrhage occurs, massive doses of FVIII concentrates or plasmapheresis with concomitant administration of FVIII may be of temporary benefit. However, this approach requires a substantial amount of time because four to five plasma exchange procedures are typically required to reduce IgG levels by 90%. Replacement with large amounts of FVIII concentrate may provide temporary hemostasis but may stimulate an increase in the antibody titer. Porcine FVIII, when available, may provide hemostasis because of its distinct antigenicity, even in the presence of a circulating inhibitor. Immunosuppressive therapy is of no value in the acute setting.

Alternative approaches to therapy of the hemophiliac patient with inhibitors involve the use of other agents, such as aPCCs such as FEIBA that contain activated vitamin K–dependent coagulation factors as well as use of recombinant FVIIa. These activated factors affect the coagulation cascade downstream of FVIII and therefore bypass the FVIII mechanism for hemostatic system activation and negate the effects of the inhibitor. FEIBA, a PCC that is used in the United States to treat hemophilia patients with inhibitors, has been associated with thrombosis in several case reports; the propensity for thrombosis with this agent may be related to the fact that it contains four activated factors as well as other by-products that promote hemostatic system activation. Therefore, thrombosis is a possible complication when using aPCC.

Porcine FVIII is sometimes effective in patients with hemophilia with inhibitors. Porcine FVIII provides adequate FVIII activity in patients with less than 50 BU of inhibitor. The usual starting dose is 100 to 150 porcine units per kg.

Bui JD, Despotis GD, Trulock EP, et al. Fatal thrombosis after administration of activated prothrombin complex concentrates in a patient supported by extracorporeal membrane oxygenation who had received activated recombinant factor VII. *J Thorac Cardiovasc Surg*. 2002;124(4):852–854.

DiMichele D. Hemophilia 1996. New approach to an old disease. *Pediatr Clin North Am*. 1996;43:709–736.

Hines RL, Marschall KE. *Stoelting's Anesthesia and Co-existing Disease*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2012:407–436.

C.10. The surgeon has requested the use of a tourniquet to minimize surgical bleeding. What are the physiologic and hemodynamic responses to tourniquet use?

Although the tourniquet may optimize surgical conditions, the physiologic and hemodynamic consequences can be significant. Anaerobic metabolism distal to the tourniquet begins approximately 8 minutes after inflation; a decrease in nicotinamide adenine dinucleotide (NAD) and creatine phosphate stores in muscle beds will occur over the next 30 to 60 minutes. As a result, the anaerobic conditions lead to cellular acidosis, which will in turn cause the release of myoglobin, intracellular enzymes, and potassium. In addition, the limb loses heat and may approach room temperature.

Hemodynamic disturbances are seen when the tourniquet is deflated. Exsanguination of the limb and tourniquet inflation acutely expands central venous blood volume, which can have significant hemodynamic consequences in a patient with limited cardiac reserve (i.e., reduced myocardial function). Tourniquet deflation and reperfusion of the limb can be associated with profound decreases in central venous and arterial blood pressure, as a result in a decrease in vascular resistance, which is related

to vasodilation that occurs with the circulation of metabolites produced during the ischemic period. Prolonged inflation (>45 to 60 minutes) can result in systemic hypertension likely due to the presence of a critical level of ischemia in the muscle or nerve or to pain.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1579–1603.

C.11. Is it appropriate to suction the endotracheal tube and oropharynx of this patient before extubation?

Removal of secretions that might be aspirated is essential before the extubation of any patient; nevertheless, suctioning of the oropharynx of hemophiliac patient can irritate mucosa by the suction catheter and result in the formation of an oral hematoma. In a patient with hemophilia, gentle oral suctioning with reduced suction pressures under direct vision is appropriate to eliminate secretions.

Hyderally H, Stark DC. Hemophilia: anesthetic implications. *Mt Sinai J Med*. 1977;44:397–399.

D. Postoperative Management

D.1. What special consideration should be given to postoperative pain management for this patient?

It is important to avoid any postoperative pain supplements that may predispose hemophiliac patients to a bleeding diathesis. Analgesics containing aspirin or nonsteroidal anti-inflammatory drugs should be avoided based on their antiplatelet effects. Antihistamines and antitussives may also inhibit platelet aggregation. Opioid analgesics or acetaminophen-based products should be appropriately titrated for postoperative pain management. If regional blockade with a catheter technique was

used for anesthesia, postoperative analgesics should be administered through this route; because the patient has undergone the risk of placement, they should also receive the benefit. Care must be taken to ensure appropriate timing for removal of the catheter, preferably after confirmation of normal FVIII levels.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1579–1603.

D.2. What steps should be taken to enhance the coagulation status of this patient in the postoperative period while at home?

It is important that FVIII levels are supplemented following surgery. If FVIII levels are allowed to fall to the levels normally seen in these patients, it can result in postoperative hemorrhage. Postoperatively, many clinicians recommend maintaining levels at 80% of normal for the first 4 postoperative days, whereas others have opined that levels of at least 40% of normal are adequate. The consensus is that FVIII levels on postoperative days 5 to 8 should be maintained at least at 30% to 40% of normal, whereas levels of 10% to 20% of normal should be maintained for several weeks unless there is evidence of ongoing bleeding (see **Table 31.6**).

Löfqvist T, Nilsson IM, Petersson C. Orthopaedic surgery in hemophilia. 20 Years' experience in Sweden. *Clin Orthop Relat Res*. 1996;(332):232–241.

Mintz P, ed. *Transfusion Therapy: Clinical Principles and Practice*. 3rd ed. Bethesda, MD: AABB Press; 2011:167–195.

D.3. Can this patient be treated with FVIII supplements using home infusion?

Administration of FVIII concentrate by continuous infusion can be administered to patients with hemophilia at medical centers in the postoperative inpatient period. With transition of many

surgical procedures to the outpatient arena, home infusion of FVIII can provide the same level of hemostatic integrity. Home infusion of purified FVIII concentrate has been shown to be safe, efficacious, and convenient for postoperative patients and should be considered for patients with hemophilia.

Lee CA, Berntop EE, Hoots WK. *Textbook of Hemophilia*. 2nd ed. New York: Wiley; 2010:48–51.

Varon D, Schulman S, Bashari D, et al. Home therapy with continuous infusion of factor VIII after minor surgery or serious haemorrhage. *Haemophilia*. 1996;2:207–210.

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32 Sickle Cell Disease

Chris R. Edmonds and Vinod Malhotra

A 30-year-old African-American woman with avascular necrosis of her right hip was admitted for a total hip arthroplasty. Her hematocrit was 22%, blood pressure was 130/90 mmHg, and pulse was 107 beats per minute. Her medications included hydroxyurea and oxycodone. She has a past medical history of recurrent joint pain, bone pain, acute chest syndrome, dyspnea, multiple transfusions, jaundice, and abdominal pain requiring multiple hospitalizations for analgesia. Her past surgical history was remarkable for a cholecystectomy, and her postoperative course was remarkable for a prolonged hospitalization for respiratory complications.

A. Medical Disease and Differential Diagnosis

1. What was the most likely underlying medical condition in this patient? How would you confirm the diagnosis of sickle cell anemia (SCA)?
2. What is sickle cell disease (SCD)?
3. What is sickle cell trait (SCT)?
4. What are some of the other common hemoglobinopathies and what are their clinical features?
5. What are the clinical features of SCD?
6. Describe the different types of sickle cell crises.

7. Discuss the pathophysiologic effects of SCD.
8. What is acute chest syndrome?

B. Preoperative Evaluation and Preparation

1. What preoperative evaluation and testing would you perform on this patient prior to anesthesia? Would you ask for a hematology consult, and what question(s) would you ask?
2. What preoperative instructions would you give this patient prior to being admitted to the hospital? How would you prepare this patient for general anesthesia and regional anesthesia?
3. Discuss the indications for perioperative exchange transfusion in this patient.
4. What are the indications for blood transfusion in SCD?

C. Intraoperative Management

1. Discuss the anesthetic management for this patient. Discuss both regional and general anesthesia considerations.
2. Discuss how the comorbidities associated with SCD can affect your anesthetic management.
3. What precautions should one take to prevent sickling in this patient?
4. Discuss what issues or concerns should be brought up by the team during the debrief at the conclusion of the case. What would you sign-out to the postanesthesia care unit (PACU) staff?

D. Postoperative Management

1. Discuss the postoperative management of this patient. What opioid sparing techniques can you use and discuss a multimodal analgesic plan?
2. What complications might occur in this patient in the immediate postoperative period?
3. What is the treatment of sickle cell crisis?

4. What is the role of hyperbaric oxygen therapy in treatment of sickle cell crisis?

A. Medical Disease and Differential Diagnosis

A.1. What was the most likely underlying medical condition in this patient? How would you confirm the diagnosis of sickle cell anemia (SCA)?

For a young African-American patient presenting with a history of joint pain, bone pain, abdominal pain, and anemia, the most likely diagnosis is SCD. Other diagnoses to consider include other hemoglobinopathies, dermatomyositis, glucose-6-phosphate dehydrogenase (G6PD) deficiency, and porphyria. Nevertheless, given the constellation of symptoms and the laboratory findings, SCD is the most likely diagnosis. A hemoglobin (Hgb) electrophoresis will confirm the diagnosis and provide the percentage of abnormal hemoglobin S (HgbS).

Adjepong KO, Otegbeye F, Adjepong YA. Perioperative management of sickle cell disease. *Mediterr J Hematol Infect Dis*. 2018;10(1):e2018032.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:634–636.

Firth PG. Anaesthesia for peculiar cells—a century of sickle cell disease. *Br J Anaesth*. 2005;95:287–299.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321–336. doi:10.1016/j.anclin.2009.05.001.

Firth PG, Head A. Sickle cell disease and anesthesia. *Anesthesiology*. 2004;101:766–785.

Khurmi N, Gorlin A, Misra L. Perioperative considerations for patients with sickle cell disease: a narrative review. *Can J Anaesth*. 2017;64:860–869.

A.2. What is sickle cell disease (SCD)?

SCD is a hereditary hemoglobinopathy resulting from inheritance of a *β-globin* gene mutation located on chromosome 11. This mutation leads to a single-point mutation where adenine

is replaced with thymine. The mutant *β*-allele codes for production and assembly of a variant Hgb (*β*-S). The molecular basis of SCD has been demonstrated to be the substitution of valine for glutamic acid in the sixth position from the *N*-terminus of the *β*-chains of Hgb. This substitution replaces a hydrophilic negative-charged amino acid (glutamic acid) with a hydrophobic nonpolar amino acid (valine). This greatly destabilizes the structure of Hgb and exposes highly reactive hydroxyl groups on the protein surface. The mutation in *β*-S Hgb accelerates the denaturation of the Hgb molecule and significantly decreases its solubility. Decreased oxygen tension causes conformational changes in the Hgb molecule, allowing hydrophobic bonds to form between the BS-6 valine of one chain and the BS-85 phenylalanine and the BS-88 leucine of a second chain. This bond forms insoluble tetramers that bond with other tetramers to form long helical strands that subsequently polymerize, causing deformation of the red blood cell membrane into a sickle shape. The result is a red blood cell that is less able to transverse the capillaries of the microcirculation, disposing the end organ to hypoxia, and ischemic damage when sickle cells are present in sufficient quantity. In the United States, the estimated prevalence of Hgb SS disease is 1:625 (0.2%) in people of African descent. Patients with SCA have early mortality, with the median age of death in the late 40s to early 50s.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA; Wolters Kluwer; 2017:634–636.

Bunn HF. Pathogenesis and treatment of sickle cell disease. *N Engl J Med*. 1997;337:762–769.

Firth PG. Anaesthesia for peculiar cells—a century of sickle cell disease. *Br J Anaesth*. 2005;95:287–299.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321–336. doi:10.1016/j.anclin.2009.05.001.

Firth PG, Head A. Sickle cell disease and anesthesia. *Anesthesiology*. 2004;101:766–785.

Steinberg MH. Management of sickle cell disease. *N Engl J Med*. 1999;340:1021–1030.

A.3. What is sickle cell trait (SCT)?

SCT is the heterozygous or carrier state of SCD. Large-scale screening for SCD in American military recruits revealed an incidence of SCT (HbAS) of 8% to 10% in African Americans and 0.05% to 0.08% in others. HbAS cells begin to sickle only when oxygen saturation of Hgb is less than 20%. No difference has been found between normal persons (HbAA) and those with HbAS regarding survival rates or incidence of severe disease, with one exception: patients with HbAS have a 50% increased risk for pulmonary infarctions. Studies have suggested that SCT provides a survival advantage over hematologic normal individuals when infected by the malarial parasite *Plasmodium falciparum*.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:634–636.

Firth PG. Anaesthesia for peculiar cells—a century of sickle cell disease. *Br J Anaesth*. 2005;95:287–299.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321–336. doi:10.1016/j.anclin.2009.05.001.

Firth PG, Head A. Sickle cell disease and anesthesia. *Anesthesiology*. 2004;101:766–785.

Gong L, Parikh S, Rosenthal PJ, et al. Biochemical and immunological mechanisms by which sickle cell trait protects against malaria. *Malar J*. 2013;12:317.

A.4. What are some of the other common hemoglobinopathies and what are their clinical features?

The most common hemoglobinopathies include the thalassemias, Hgb C disease, and SCA. Thalassemia arises from

alterations in one or more of the four genes that code for the α-chain. The mildest form of thalassemia (loss of one α-gene) presents as a mild form of anemia, whereas the most severe form (loss of all four genes) is incompatible with life. Hgb C results from a mutation in the *β-globin* gene. Hgb C disease is a relatively benign disease producing a mild hemolytic anemia and splenomegaly. However, when it is paired with a β-S mutation, the disease is more severe. Other rare hemoglobinopathies will not be discussed further.

Each Hgb gene mutation of the heterozygous form causes little or no clinical consequence, but when both genes of a heterozygote are abnormal, a disease state is evident. Heterozygous combinations such as HbS and HbC (HbSC disease), and β-thalassemia mutation (HbS-β-thalassemia) usually cause a milder clinical course than that of SCD.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:634–636.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321–336. doi:10.1016/j.anclin.2009.05.001.

Park KW. Sickle cell disease and other hemoglobinopathies. *Int Anesthesiol Clin*. 2004;42:77–93.

A.5. What are the clinical features of SCD?

The clinical features of SCD are manifested through indolent end-organ damage with intermittent acute episodes of severe pain and pulmonary complications. Although SCD is a disease of Hgb, it ultimately affects all organ systems. It is usually the acute problems that bring these individuals to the attention of a physician. The clinical manifestations by organ systems are presented in **Table 32.1**.

TABLE 32.1 Clinical Manifestations of Sickle Cell Disease

System	Symptoms
Central nervous system/neurologic	• Stroke (cerebrovascular accident) in children as well

	as adults (50%−70% recurrence within 3 years) • Proliferative retinopathy/blindness • Painful crisis (>70%) • Chronic pain (not common) • Peripheral neuropathy (not common) • Poor school performance
Cardiovascular	• Conduction abnormalities secondary to iron overload • Hypertension • Cor pulmonale • Left and right ventricular dysfunction • Chronic ulcers
Pulmonary	• Infarction, pulmonary fibrosis • Infection • Restrictive/obstructive lung disease (10%−15%) • Acute chest syndrome (40%) • Pulmonary hypertension (30%−40%) • Airway hyperactivity
Genitourinary	• Hyposthenuria, hematuria, proteinuria • Chronic renal insufficiency (5%−20%) • Renal failure • Priapism (10%−40% of men) • Urinary tract infection
Gastrointestinal	• Cholelithiasis (70%) • Acute hepatic syndrome • Elevated liver function tests, hyperbilirubinemia • Hepatopathy • Cirrhosis (16%−29%) • Dyspepsia secondary to mucosal ischemia • Sickle girdle syndrome (mesenteric ischemia)
Musculoskeletal	• Osteomyelitis (*Staphylococcus/Salmonella*) • Dactylitis • Avascular necrosis (50%) • Infarction
Heme/immunologic	• Chronic anemia • Autosplenism • Susceptibility to infections with encapsulated organisms • Erythrocyte alloimmunization from blood transfusions • Sequestration crisis • Hemolytic crisis • Aplastic crisis • Immune dysfunction • Hypercoagulability

The progression and severity of SCD is variable. Many of the patients have an indolent course, whereas a smaller subset suffer from an early end-organ failure and an early death. Pulmonary, neurologic, and renal disease are the leading causes of morbidity and mortality. Hydroxyurea is a medication that increases the percentage of fetal Hgb, thereby decreasing the severity of the disease. However, it does not seem to decrease the perioperative complications of the disease.

Adjepong KO, Otegbeye F, Adjepong YA. Perioperative management of sickle cell disease. *Mediterr J Hematol Infect Dis*. 2018;10(1):e2018032.

Ataga KI, Derebail VK, Archer DR. The glomerulopathy of sickle cell disease. *Am J Hematol*. 2014;89(9):907–914.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:634–636.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiology Clin*. 2009;27:321–336. doi:10.1016/j.anclin.2009.05.001.

A.6. Describe the different types of sickle cell crises.

Sickle cell crisis refers to the acute clinical picture generally caused by sickling of red blood cells in the *microcirculation*. Four main clinical types of crises have been described as follows in **Table 32.2**.

TABLE 32.2 Types of Sickle Cell Crises

Type	Pathophysiology	Treatment
Vaso-occlusive	Pain secondary to obstruction of flow in the microvascular beds leading to localized ischemia	• Hydration • Analgesia • Incentive spirometry
Splenic sequestration	Acute painful enlargement of the spleen Acute hypovolemia	• Restore circulatory volume, possible splenectomy
Aplastic	Sudden cessation of bone marrow activity Acute worsening of anemia usually associated with viral	• Supportive therapy • Blood transfusion

	infection (parvovirus B19) Recovery in 7–10 days	
Hemolytic crisis	Acute accentuated decrease in hemoglobin level Secondary to red cell destruction Usually associated with coexisting G6PD deficiency	• Supportive therapy • Blood transfusion

G6PD, glucose-6-phosphate dehydrogenase.

The most common crises in SCD is vaso-occlusive crisis, which is characterized with intermittent, recurrent acute episodes of severe pain. It is generally felt that the central cause of pain is ongoing acute ischemia, vaso-occlusion, and infarction. The precise pathophysiology and nociceptive pathways have not been elucidated. Patients in vaso-occlusive crisis present with fever, anemia, spine pain, limb pain, and abdominal pain. They are tachypneic and may have an enlarged liver and spleen in addition to abdominal tenderness. Serjeant et al. reported that in 118 patients having 183 painful crises, the location was noted to be in the lumbar spine (49%), abdomen (32%), femoral shaft (30%), and the knee (21%). There is usually no identifying triggering agent for most vaso-occlusive crises. The average rate of painful crises per patient year is 0.8%. There is a subset of patients (5.2%) who average 8 to 10 crises a year, which accounts for 33% of all hospitalizations. Mortality positively correlates with increased pain rate in adults.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321–336. doi:10.1016/j.anclin.2009.05.001.

Serjeant GR, Ceulaer CD, Lethbridge R, et al. The painful crisis of homozygous sickle cell disease: clinical features. *Br J Haematol*. 1994;87:586–591.

Vijay V, Cavenagh JD, Yate P. The anaesthetist's role in acute sickle cell crisis. *Br J Anaesth*. 1998;80:820–828.

A.7. Discuss the pathophysiologic effects of SCD.

The pathophysiologic effects of SCD is not limited to the structure or deformation of the erythrocyte. The interaction and

balance between the Hgb molecule, cytoplasm, and cell wall and the vascular endothelium is drastically altered to create chronic systemic biochemical alterations that produce the clinical features of SCD. As in vaso-occlusive crisis, there is a triggering insult, such as infection, surgical stress, or ischemia-reperfusion injury, that catalyzes a complex interaction among sickled cells, endothelial regulation of flow, inflammatory cytokines, platelet aggregation factors, and vasoconstriction, leading eventually to ischemia, infarction, and cell death. This cascade leads to a vicious cycle that eventually causes end-organ damage and dysfunction. End-organ damage that occurs in sickle cell states is attributable to three pathways. In the erythrocyte cytoplasm, the loss of Hgb structural stability leads to increased oxidation of heme with subsequent denaturation, deterioration, and polymerization. Iron oxidation produces superoxides (O_2^-) and hydrogen peroxides ($H_2O_2^-$), which increases the formation of highly reactive hydroxyl radicals (−OH). In the cell membrane, free iron and iron-containing compounds accumulate, leading to clustering of membrane surface membranes, abnormal cation permeability, and cellular dehydration. This complex series of events within the erythrocyte increases adherence to the vascular endothelium, exposing it to shear and oxidative stress. The interaction between the abnormal erythrocytes and the vascular endothelium produces chronic inflammation, upregulation of endothelial cell adhesion molecules, and altered expression of endothelial nitric oxide synthetase. Systemically, there is an increase in leukocyte counts, activation of the coagulation pathways, increase in inflammatory compounds, and increase in circulating endothelial cells in the plasma. The complex pathologic interaction between sickling of cells in blood vessels and the vascular endothelium leads to infarcts, tissue destruction, and consequent end-organ failure. The pathogenesis

is shown in **Figure 32.1**.

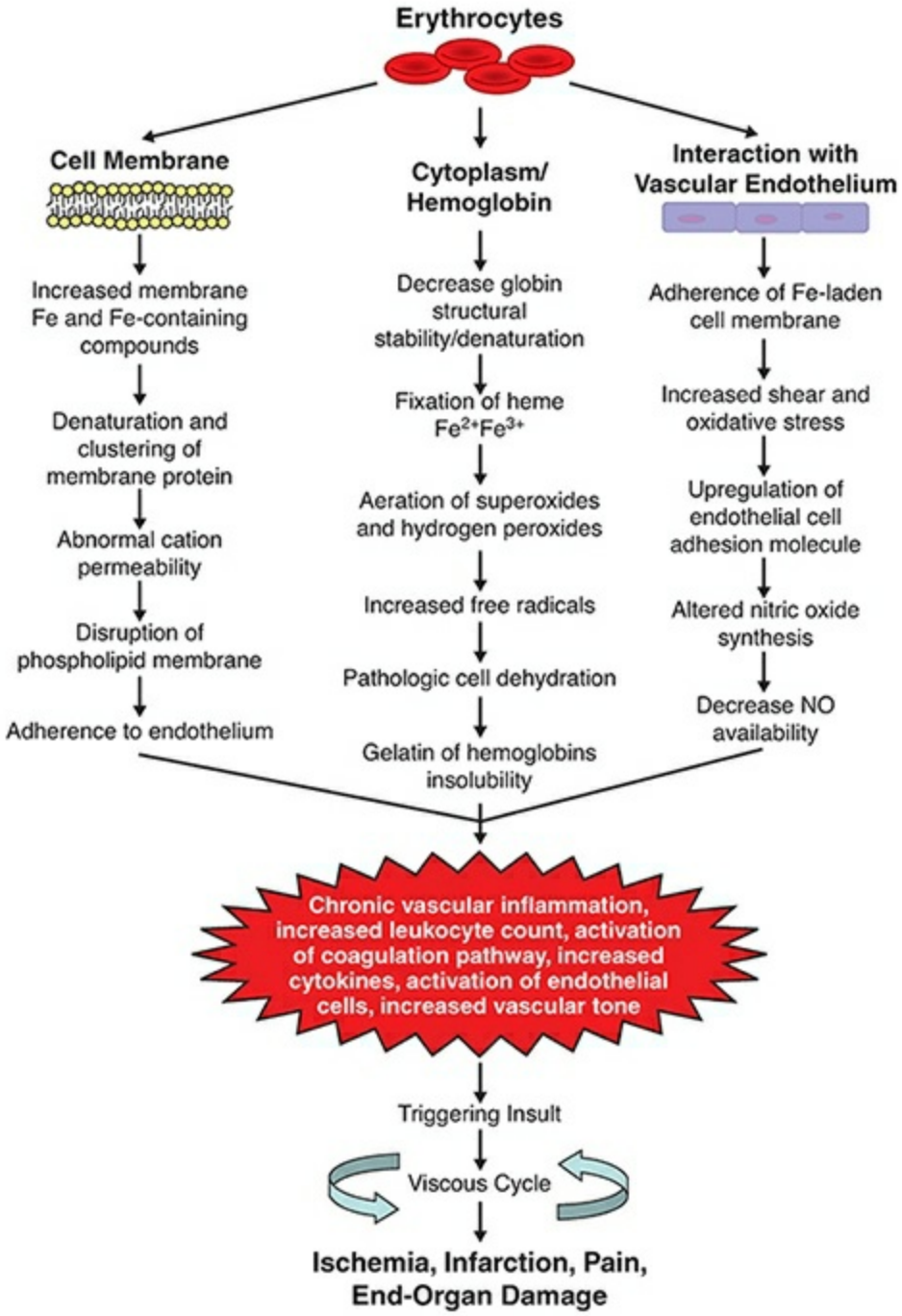

FIGURE 32.1. Pathogenesis of sickle cell damage. Fe, iron; NO, nitric oxide.

Adjepong KO, Otegbeye F, Adjepong YA. Perioperative management of sickle cell disease. *Mediterr J Hematol Infect Dis*. 2018;10(1):e2018032.

Conran N, Franco-Penteado CF, Costa FF. Newer aspects of the

pathophysiology of sickle cell disease vaso-occlusion. *Hemoglobin*. 2009;33(1):1–16.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiology Clin*. 2009;27:321–336.

Strijbos MH, Landburg PP, Nur E, et al. Circulating endothelial cells: a potential parameter of organ damage in sickle cell anemia? *Blood Cells Mol Dis*. 2009;43:63–67.

A.8. What is acute chest syndrome?

Acute chest syndrome is a term used to describe an acute pulmonary complication of SCD. It is defined by the finding of a new pulmonary infiltrate involving at least one complete lung segment on chest radiograph that is not due to atelectasis. It presents with a constellation of pulmonary symptoms and signs in a patient with SCD. These include fever (temperature 38.5°C [101.3°F]), wheezing, coughing, tachypnea, chest pain, and hypoxemia (less than 92% on room air). Pleural effusions (55%) are commonly seen on chest radiographs. Acute chest syndrome frequently follows vaso-occlusive crises; therefore, vaso-occlusive pulmonary infarction may be a precipitating factor. Other causes include infection (viral, chlamydia, mycoplasma, and bacterial) and pulmonary fat embolism resulting from bone marrow necrosis. Acute chest syndrome is a common postoperative complication in patients with SCD who have a history of pulmonary disease following general anesthesia. It is one of the most common causes of death in adults with SCD. Acute chest syndrome can be prevented by judicious hydration, incentive spirometry, effective analgesia, and avoidance of even mild hypothermia during the crises. Acute chest syndrome should be treated with bronchodilators, antibiotics, and exchange transfusion, when necessary. Exchange transfusion is recommended if the patient is clinically deteriorating.

Adjepong KO, Otegbeye F, Adjepong YA. Perioperative management of sickle cell disease. *Mediterr J Hematol Infect Dis*. 2018;10(1):e2018032.

Emre U, Miller ST, Gutierez M, et al. Effect of transfusion in acute chest syndrome of sickle cell disease. *J Pediatr*. 1995;127:901–904.

Stuart MJ, Yamaja S. Sickle cell acute chest syndrome: pathogenesis and rationale for treatment. *Blood*. 1999;94:1555–1560.

Vichinsky EP, Haberkern CM, Neumayr L, et al. A comparison of conservative and aggressive transfusion regimens in the perioperative management of sickle cell disease. The Preoperative Transfusion in Sickle Cell Disease Study Group. *N Engl J Med*. 1995;333:206–213.

Vichinsky EP, Neumayr LD, Earles AN, et al. Causes and outcomes of the acute chest syndrome in sickle cell disease. National Acute Chest Syndrome Study Group. *N Engl J Med*. 2010;342:1855–1865.

B. Preoperative Evaluation and Preparation

B.1. What preoperative evaluation and testing would you perform on this patient prior to anesthesia? Would you ask for a hematology consult, and what question(s) would you ask?

The aim of the preoperative assessment in a patient with SCD is to determine the preoperative risk of this multisystemic disease and how the end-organ damage will affect the anesthetic management (see **Table 32.1**). A careful history should be obtained with a complete physical examination. The cardiopulmonary status should be thoroughly investigated, in view of the increased incidence of cardiac and pulmonary morbidity in these patients especially in a patient with a history of acute chest syndrome and dyspnea. A history of frequent hospitalizations in the year before surgery significantly increases the likelihood of a vaso-occlusive crisis in the perioperative period. Immunization status for Pneumovax and *Haemophilus influenzae* vaccine should be checked. Other characteristics that increase the perioperative risk are age, pregnancy, smoking, and infection. If possible, cessation of smoking prior to elective surgery should be strongly encouraged because smoking

increases the risk of acute chest syndrome and pain in the preoperative period. One should correct hypovolemia and treat infection appropriately preoperatively. Laboratory investigation should include a complete blood count, blood urea nitrogen, serum creatinine, urinalysis, electrocardiogram, chest radiograph, pulse oximetry, and liver function tests. In addition, the following tests may be helpful:

- Arterial blood gas, if indicated
- Sickle cell preparation (if diagnosis is unclear)
- Hgb electrophoresis to determine HbS, quantitatively
- Reticulocyte count
- Type and cross (Alloimmunization may make this difficult.)
- Pulmonary function test (if severe pathology, paroxysmal dyspnea, or history of acute chest syndrome)
- Echocardiogram in patients with history of pulmonary hypertension or cardiomegaly
- Neurologic imaging (if there are psychological or behavioral changes)

A hematology consult should be asked for if the diagnosis of SCD is unclear and/or to obtain an Hgb electrophoresis to determine the percentage of sickle Hgb. They can also help in patients that are difficult to crossmatch.

Adjepong KO, Otegbeye F, Adjepong YA. Perioperative management of sickle cell disease. *Mediterr J Hematol Infect Dis*. 2018;10(1):e2018032.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:634–636.

Cohen RT, DeBaun MR, Blinder MA, et al. Smoking is associated with an increased risk of acute syndrome and pain among adults with sickle cell disease. *Blood*. 2010;115(18):3852–3854.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321–336. doi:10.1016/j.anclin.2009.05.001.

Firth PG, Head A. Sickle cell disease and anesthesia. *Anesthesiology*. 2004;101:766–785.

Knight-Madden JM, Barton-Gooden A, Weaver SR, et al. Mortality, asthma,

smoking and acute chest syndrome in young adults with sickle cell disease. *Lung*. 2013;191(1):95–100.

B.2. What preoperative instructions would you give this patient prior to being admitted to the hospital? How would you prepare this patient for general anesthesia and regional anesthesia?

Prior to being admitted to the hospital for elective surgery, this patient should be given nothing by mouth instructions, which include clear fluids up until 2 hours prior to surgery and carbohydrate loading to maintain a baseline metabolic state.

- Informed consent should be obtained to explain the options, risk, and benefits of the different types of anesthetics used.
- Preoperative hydration should be initiated to treat baseline volume deficit.
- Euvolemia should be maintained preoperatively (remembering that the patient is on nothing by mouth status and may have a urine concentration defect requiring volume replacement).
- Any infections should be treated preoperatively, if possible.
- End-organ dysfunction should be identified and treated appropriately.
- Type and crossmatching may be difficult in these patient's because of alloimmunization.
- Consider transfusion of red blood cells to maintain oxygen-carrying capacity. Transfusion guidelines should be based on comorbidities, surgical risk, and degree of anemia. Transfusions should be individualized and based on the patient's risk/benefit. Efforts should be made for leukocyte reduction techniques, as with buffy coat–poor red cells, to reduce the incidence of leukocyte antigen alloimmunization. The goals of transfusion are to achieve an Hgb concentration of greater than 8 g per dL and to ensure that Hgb A represents

more than 40% of the total Hgb present. Past practices of reducing HgbS levels to less than 30% do not seem to improve outcome and increase transfusion-related complications.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:634–636.

Fawcett WJ, Thomas M. Preoperative fasting in adults and children: clinical practice and guidelines. *Anaesthesia*. 2019;74(1):83–88.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321–336. doi:10.1016/j.anclin.2009.05.001.

Khurmi N, Gorlin A, Misra L. Perioperative considerations for patients with sickle cell disease: a narrative review. *Can J Anaesth*. 2017;64:860–869.

Soffin EM, Gibbons MM, Ko CY, et al. Evidence review conducted for the Agency for Healthcare Research and Quality Safety Program for Improving Surgical Care and Recovery: focus on anesthesiology for total hip arthroplasty. *Anesth Analg*. 2019;128(3):454–465.

B.3. Discuss the indications for perioperative exchange transfusion in this patient.

Controversy exists as to whether these patients benefit from preoperative exchange transfusion. For high-risk surgical procedures such as cardiopulmonary bypass an exchange transfusion may be recommended. Nevertheless, a series of reports of cardiopulmonary bypass cases in which exchange transfusions were not performed or only a partial exchange was performed. If an exchange transfusion is required, the exchange transfusion should be performed with buffy coat–free packed red blood cells to reduce the HbS fraction to less than 40%. Nevertheless, growing evidence indicates that most surgical procedures can be safely performed in patients with SCD without aggressively transfusing. For example, for certain surgical procedures, it has been shown that a packed red blood cell transfusion done simply to increase the Hgb level to 10 g per dL is as effective in decreasing perioperative morbidity, as is

exchange transfusions to reduce the HbS(S) levels to less than 40%. Exchange transfusion is a therapy often used in patients with SCD complicated by acute chest syndrome. It is beneficial to keep the hematocrit lower than 35% with an exchange transfusion because an increased hematocrit will increase blood viscosity and stasis in the circulation.

Adhikari RK, Maddali MM, Zacharias S. Preoperative exchange transfusion for sickle cell disease patients undergoing open-heart surgery: exception to the rule. *J Card Surg*. 2010;25(6):691–693.

Adjepong KO, Otegbeye F, Adjepong YA. Perioperative management of sickle cell disease. *Mediterr J Hematol Infect Dis*. 2018;10(1):e2018032.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:634–636.

Vichinsky EP, Haberkern CM, Neumayr L, et al. A comparison of conservative and aggressive transfusion regimens in the perioperative management of sickle cell disease. The Preoperative Transfusion in Sickle Cell Disease Study Group. *N Engl J Med*. 1995;333:206–213.

B.4. What are the indications for blood transfusion in SCD?

Blood transfusions should be guided by the clinical picture and the potential for blood loss. Prophylactic transfusion remains controversial and is of questionable benefit in mild-to-moderate risk cases. Some of the clinical indications for blood transfusion in SCD include the following:

Acute conditions

- Vaso-occlusive crises with organ infarction and dysfunction
- Sequestration syndrome
- Acute hemolysis with exacerbation of anemia
- Aplastic crisis
- Acute chest syndrome
- Acute multiorgan failure
- Severe unresponsive priapism
- Protracted painful crisis

- High-risk surgery (e.g., cardiovascular, thoracic)

Chronic conditions

- Intractable leg ulcers
- Complicated pregnancy
- Stroke
- Recurrent painful syndrome
- Recurrent acute chest syndrome

Howard J, Malfroy M, Llewelyn C, et al. The Transfusion Alternatives Preoperatively in Sickle Cell Disease (TAPS) study: a randomized, controlled, multicentre clinical trial. *Lancet*. 2013;381(9870):930–938.

Wun T, Hassell K. Best practices for transfusion for patients with sickle cell disease. *Hematol Rev*. 2009;1(2):e22.

C. Intraoperative Management

C.1. Discuss the anesthetic management for this patient. Discuss both regional and general anesthesia considerations.

The definitive anesthetic technique has not been established secondary to the wide clinical spectrum of SCD and the different severities in the surgical procedures. Koshy et al. retrospectively reviewed 1,079 anesthetics and noted an apparent association between postoperative complications and the use of regional anesthesia. Nevertheless, this study did not control for obstetric procedures and the tendency that clinicians often use regional anesthesia for sicker patients. Other studies did not find an adverse effect of regional anesthesia. Theoretically, regional anesthesia, especially when used with epinephrine, may produce a compensatory vasoconstriction in the nonblocked area, but this has not been supported in the literature. Yaster et al. found that epidural analgesia markedly improved oxygenation in children in vaso-occlusive crises, either through superior pain control or

opioid sparing effects. Therefore, almost any anesthetic technique can be used, provided the following principles are considered:

- Good intravenous access for maintenance of intravascular volume
- Adequate oxygenation
- Denitrogenation before induction of general anesthesia
- Endotracheal intubation for general anesthesia to ensure a controlled airway and adequate ventilation
- Maintenance of adequate oxygen-carrying capacity through judicious use of red cell transfusions
- Maintenance of normothermia
- Opioids for analgesia carefully titrated for perioperative and postoperative analgesia
- Avoidance of tourniquet use
- Considering regional analgesia for both intraoperative and postoperative courses
- Avoidance of hypotension and venous stasis to prevent sickling of red blood cells
- Considering invasive monitoring (arterial line, central venous pressure line) for beat-to-beat blood pressure monitoring, volume monitoring, and frequent laboratory test
- Avoidance of hypoventilation of lungs to prevent acidosis
- Possible increased inspired oxygen concentration to ensure maintenance of normal to increased Pa_{O_2}

Adjepong KO, Otegbeye F, Adjepong YA. Perioperative management of sickle cell disease. *Mediterr J Hematol Infect Dis*. 2018;10(1):e2018032.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:634–636.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321–336. doi:10.1016/j.anclin.2009.05.001.

Khurmi N, Gorlin A, Misra L. Perioperative considerations for patients with sickle cell disease: a narrative review. *Can J Anaesth*. 2017;64:860–869.

Koshy M, Weiner SJ, Miller ST, et al. Surgery and anesthesia in sickle cell disease. Cooperative study of sickle cell diseases. *Blood*. 1995;86(10):3676–3684.

Yaster M, Tobin JR, Billet C, et al. Epidural analgesia in the management of severe vaso-occlusive sickle cell crises. *Pediatrics*. 1994;93(2):310–315.

C.2. Discuss how the comorbidities associated with SCD can affect your anesthetic management.

SCA is a disease that can affect every end organ. Therefore, evaluating the patient for end-organ dysfunction is paramount. This patient is anemic, tachycardic, and hypertensive. She may have dyspepsia, a hyperreactive airway, chronic renal insufficiency, and liver disease and might be debilitated with cardiopulmonary complications. Patients with SCD often present with cardiomegaly, pulmonary hypertension, and heart failure. For this surgery, she will probably require transfusions and may be difficult to crossmatch. In the postoperative period, pulmonary infarcts and infection are common, which can lead to acute chest syndrome. These problems, in addition to the potential for sickling crisis or sequestration syndrome, pose a greater risk than normal for perioperative morbidity and mortality. The patients at greater risk include those with a homozygous state SCD, sickle C disease (HbSC), and sickle thalassemia. In contrast, patients with SCT do not present an increased risk for intraoperative morbidity. As a perioperative specialist, one can have a profound effect on outcome in these patients by attention to detail, with a multisystem approach to address all end-organ dysfunction to reduce morbidity by maintaining oxygen delivery and preventing ongoing sickling.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321–336.

Khurmi N, Gorlin A, Misra L. Perioperative considerations for patients with sickle cell disease: a narrative review. *Can J Anaesth*. 2017;64:860–869.

C.3. What precautions should one take to prevent sickling

in this patient?

Sickling of red blood cells is triggered by a variety of factors. One should avoid or correct factors that can precipitate sickling. Special precautions include the following:

- Avoid hypoxia by preoxygenating the patient and employing higher than usual concentrations of inspired oxygen.
- Prevent acidosis by maintaining adequate oxygenation, normovolemia, and cardiac output.
- Prevent respiratory acidosis by avoiding hypoventilation.
- Prevent stasis. This requires proper hydration and good regional blood flow. Blood viscosity should be maintained at a low level by limiting a rise in hematocrit to 35% and avoiding over transfusion.
- Avoid hypovolemia.
- Avoid hypothermia by using body warming and intravenous fluid warming devices perioperatively.
- Replace blood loss to prevent anemia.
- The use of tourniquets is controversial. Some advise against the use of tourniquets, although they have been used without ill effects by others. If a tourniquet is to be used, it should only be used when absolutely necessary and for a short period as possible. Special attention should be paid to maintain adequate oxygenation and to prevent respiratory or metabolic acidosis at the time of tourniquet release.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:634–636.

Firth PG. Anesthesia and hemoglobinopathies. *Anesthesiol Clin*. 2009;27:321–336.

Khurmi N, Gorlin A, Misra L. Perioperative considerations for patients with sickle cell disease: a narrative review. *Can J Anaesth*. 2017;64:860–869.

C.4. Discuss what issues or concerns should be brought up by the team during the debrief at the conclusion of

the case. What would you sign-out to the postanesthesia care unit (PACU) staff?

Checklist, surgical time outs, and a postoperative debrief are all ways to improve patient safety by creating an environment where there is team involvement and communication is enhanced not diminished. They promote collaborative information sharing by pausing to allow the team as a whole to address both positive aspects of the case and to address deficiencies and areas for improvement in a nonpunitive way. Operating room efficiency, patient safety, and the opportunity to learn from each case is improved. For a patient with SCD who underwent a total hip arthroplasty (THA), the postoperative concerns include pain control, adequate hydration, cardiopulmonary monitoring, and hematologic monitoring. Early ambulation, incentive spirometry, supplemental oxygen, multimodal analgesia, and laboratory evaluation of hematocrit and renal function is paramount until the patient is stable from a multiorgan stand point. The sign-out to the PACU should include all of these concerns and any issues that have happened preoperatively, intraoperatively, or may occur postoperatively.

Magill ST, Wang DD, Rutledge WC, et al. Changing operating room culture: implementation of a postoperative debrief and improved safety culture. *World Neurosurg*. 2017;107:597–603.

Rose MR, Rose KM. Use of a surgical debriefing checklist to achieve higher value health care. *AM J Med Qual*. 2018;33:514–522.

Sew Lan Leong KBM, Hanskamp-Sebregts M, van der Wal RA, et al. Effects of perioperative briefing and debriefing on patient safety: a prospective intervention study. *BMJ Open*. 2017;7(12):e018367.

D. Postoperative Management

D.1. Discuss the postoperative management of this patient. What opioid sparing techniques can you use

and discuss a multimodal analgesic plan?

The postoperative period is a crucial time with SCD. Surgical pain, hypoventilation, a high incidence of pulmonary infarction, and an expected decrease in Pa_{O_2} will predispose these patients to the formation of sickle cells, leading to the possibility of developing vaso-occlusive crisis or acute chest syndrome. The mainstay of postoperative management is supportive and preventive care. Supplemental oxygen, maintenance of intravascular fluid volume, maintenance of normothermia, glycemic control, blood transfusion management, and adequate analgesia are important considerations. There is evidence suggesting that patients with SCD have an altered pain response and both intravenous patient-controlled analgesia and epidural patient-controlled analgesia has been shown to improve postoperative pain control. However, regional analgesia has been shown to decrease pain scores while improving oxygenation. A multimodal analgesia approach to pain control is paramount, which improves patient recovery and reduces reliance on opioids. Supportive and preventive care should be continued in the extended postoperative period. The basic outline of routine postoperative care includes the following:

- Early mobilization
- Maintenance of normothermia
- Supplemental oxygenation
- Early effective multimodal analgesia or adjunctive analgesic should be continued in the extended postoperative period, pregabalin.
- Maintain euvolemia.
- Conservative transfusion therapy and Hgb management
- Incentive spirometry
- Pulse oximetry
- Pulmonary monitoring
- Psychological support

- Considering extended postoperative cardiovascular monitoring
- Considering regional analgesia for postoperative pain management

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:634–636.

Khurmi N, Gorlin A, Misra L. Perioperative considerations for patients with sickle cell disease: a narrative review. *Can J Anaesth*. 2017;64:860–869.

Soffin EM, Gibbons MM, Ko CY, et al. Evidence review conducted for the Agency for Healthcare Research and Quality Safety Program for Improving Surgical Care and Recovery: focus on anesthesiology for total hip arthroplasty. *Anesth Analg*. 2019;128(3):454–465.

D.2. What complications might occur in this patient in the immediate postoperative period?

The postoperative complications most likely to occur in the patient with SCD include deep vein thrombosis, vaso-occlusive crisis, pulmonary infarction, acute chest syndrome, and infection. Hypoxemic episodes are always a threat in the postoperative period secondary to pain, splinting, or oversedation and can precipitate a sickling crisis. The incidence of postoperative respiratory infection is high and is a leading cause of morbidity and mortality. Acute chest syndrome is one of the most common causes of death in adult patients and is a potentially lethal postoperative complication in patients with SCD who undergo major or high-risk surgery. Sequestration syndrome with shock is another potentially lethal complication, especially in the obstetric patient immediately postpartum. Patients with cardiomegaly and pulmonary hypertension are susceptible to heart failure. Renal and hepatic dysfunction may result in prolongation of the effects of certain medications. Orthopedic patients with SCD are at risk for deep vein thrombosis, acute thrombosis, and pulmonary embolism. Antithrombotic therapy has to be geared toward decreasing this

common complication.

Adjepong KO, Otegbeye F, Adjepong YA. Perioperative management of sickle cell disease. *Mediterr J Hematol Infect Dis*. 2018;10(1):e2018032.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:634–636.

Khurmi N, Gorlin A, Misra L. Perioperative considerations for patients with sickle cell disease: a narrative review. *Can J Anaesth*. 2017;64:860–869.

D.3. What is the treatment of sickle cell crisis?

The treatment of sickle cell crisis is to break the vicious cycle of sickling, ischemia, infarction, pain, and end-organ failure. An aggressive multimodal approach can reduce the clinical symptoms of the crises. The principles of treatment of painful sickle cell crisis include the following:

- Rest
- Hydration
- Oxygen therapy
- Treatment of infection
- Analgesics (consider patient-controlled analgesia)
- Considering regional analgesia
- Transfusion to reduce the Hgb SS disease concentration
- Incentive spirometry
- Maintenance of normothermia

Adjepong KO, Otegbeye F, Adjepong YA. Perioperative management of sickle cell disease. *Mediterr J Hematol Infect Dis*. 2018;10(1):e2018032.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:634–636.

Khurmi N, Gorlin A, Misra L. Perioperative considerations for patients with sickle cell disease: a narrative review. *Can J Anaesth*. 2017;64:860–869.

D.4. What is the role of hyperbaric oxygen therapy in treatment of sickle cell crisis?

Hyperbaric oxygen has been used empirically in some institutions for treatment of acute sickle cell crisis, although it is

not widely available. Although some published reports claim instant improvement of symptoms, others have failed to show beneficial effects. There is better evidence that therapy is useful in management of ischemic disorders of the anterior segment of the eye or in chronic leg ulcers. Studies have shown no apparent effects of hyperbaric oxygen on sickle cell morphology in vitro. It appears, then, that its reported benefit in vivo may be due to a decrease in the rate of sickling or improved tissue oxygenation by direct diffusion. Although case series have supported its use, there is not enough evidence to recommend its routine use over conventional therapy.

Butler FK Jr, Hagan C, Murphy-Lavoie H. Hyperbaric oxygen therapy and the eye. *Undersea Hyperb Med*. 2008;35:333–387.

Mychaskiw G II, Woodyard SA, Brunson CD, et al. In vitro effects of hyperbaric oxygen on sickle cell morphology. *J Clin Anesth*. 2001;13:255–258.

Reynolds JD. Painful sickle cell crisis. Successful treatment with hyperbaric oxygen therapy. *JAMA*. 1971;216:1977–1978.

Stirnemann J, Letellier E, Aras N, et al. Hyperbaric oxygen therapy for vaso-occlusive crises in nine patients with sickle-cell disease. *Diving Hyperb Med*. 2012;42(2):82–84.

Wallyn CR, Jampol LM, Goldberg MF, et al. The use of hyperbaric oxygen in treatment of sickle cell hyphema. *Invest Ophthalmol Vis Sci*. 1985;26:1155–1158.

SECTION 9 Eye, Ear, Nose, and Throat

33 Airway Trauma

Richard P. Dutton and LaRita Yvette Fouchè-Weber

A 46-year-old man was thrown from his motorcycle at a high rate of speed and impaled in the base of the neck by a tree branch. At presentation to the trauma center, he is awake and alert with a heart rate (HR) of 122 beats per minute, blood pressure of 143/85 mmHg, respiratory rate of 20 breaths per minute, and oxygen saturation of 98% on 100% nonrebreathing mask. There is a 5-cm-wide piece of wood protruding from his anterior lower neck at the sternal notch, without visible bleeding. The patient is neurologically intact but admits to consuming six beers in the hours before injury. His medical history is unremarkable.

A. Medical Disease and Differential Diagnosis

1. What variables mitigate injury from motorcycle collisions?
2. What other significant trauma may be present?
3. How is the initial assessment of a trauma patient organized?

4. How would you evaluate airway and breathing?
5. How would you evaluate the circulation?
6. How would you evaluate mental status and neurologic condition?
7. What diagnostic tests are indicated for this patient based on the mechanism of injury?
8. What are the zones of the neck, and what is their clinical significance?
9. What immediate treatment is necessary before diagnostic studies?
10. When and where should the impaling object be removed?

B. Preoperative Evaluation and Preparation

1. What laboratory tests would you want?
2. What x-ray studies are most important to the anesthesiologist?
3. Is an electrocardiogram (ECG) necessary?
4. Should this patient be intubated before going for computed tomography (CT) scanning?
5. When and where should this patient's airway be managed?
6. Are any prophylactic medications indicated?

C. Intraoperative Management

1. What monitors would you use? Is invasive monitoring necessary before definitive airway control?
2. What is the surgical approach to a zone I neck injury?
3. Is the patient likely to require tube thoracostomy? Should this be placed before managing the airway?
4. What are the options for managing this patient's airway?
5. What are the risks of rapid sequence induction in this patient?
6. What anesthetic agents would you use for a rapid sequence induction?
7. How can you minimize the risk of exacerbating cervical spine trauma?
8. How can you minimize the risks of aspiration?

9. How would you anesthetize the airway for an awake intubation?
10. What are the risks of awake fiberoptic intubation?
11. If the patient cannot be ventilated, what options are available?
12. Would a laryngeal mask airway (LMA) or other pharyngeal airway be of assistance?
13. What surgical airway options are available in this case?
14. What maintenance anesthetics are indicated or contraindicated in this patient?
15. What complications will the surgical plan introduce?

D. Postoperative Management

1. What are the criteria for extubation?
2. What techniques may be used during extubation?
3. How does alcohol abuse affect postoperative management?
4. What pain medication should be used?

A. Medical Disease and Differential Diagnosis

A.1. What variables mitigate injury from motorcycle collisions?

Trauma involving motorcycles accounts for 2% to 5% of all motor vehicle trauma, but there is a higher proportion of death and serious injury because of the relative exposure of the motorcycle rider to the environment. Factors such as youth, high speed, and intoxication contribute to motorcycle collisions just as they do for automobiles. Motorcycle riders also are much more susceptible to factors beyond their own control, such as lack of vigilance on the part of automobile and truck drivers, road conditions (oil or debris), and the weather.

Factors that can reduce the seriousness of motorcycle collisions when they do occur include helmets and protective clothing. Reenactment of a mandatory helmet law in the state of

Washington in 1990 resulted in a decline in serious brain injury in motorcycle trauma victims from 20% to 9% and a reduction in mortality from 10% to 6%. Full leather or synthetic "armor" reduces the risk of massive skin and soft-tissue injuries in the event of a high-speed collision.

Liu BC, Ivers R, Norton R, et al. Helmets for preventing injury in motorcycle riders. *Cochrane Database Syst Rev*. 2008;(1):CD004333.

Meredith L, Brown J, Ivers R, et al. Distribution and type of crash damage to motorcyclists' clothing: validation of the zone approach in the European Standard for motorcycle protective clothing, EN13595. *Traffic Inj Prev*. 2014;15(5):501–507.

A.2. What other significant trauma may be present?

Motorcycle collisions are high-energy trauma that can result in injury to any organ system or region of the body. This patient will need a complete head-to-toe assessment and a number of diagnostic studies to establish the full extent of injury. Common injuries in motorcyclists include brain trauma from direct impact with the road and with other vehicles, pelvic fractures from impact with the frame of the motorcycle, abdominal trauma from impact with the handlebars, and lower extremity orthopedic and soft tissue trauma from impact with the road.

A.3. How is the initial assessment of a trauma patient organized?

The initial management of trauma patients is best described by the tenets of the Advanced Trauma Life Support (ATLS) course, written by the American College of Surgeons Committee on Trauma. This course provides a unified philosophy and common language to organize practitioners from different specialties in the care of complex patients with the potential for multiple injuries. Assessment of the seriously injured patient begins with the ABCs: *A*irway, *B*reathing, and *C*irculation; followed by a brief neurologic examination and a catalogue of visible injuries.

This "primary survey" is followed by diagnostic testing and a more detailed secondary survey to discover all of the patient's injuries. Despite the revision of this assessment in the combat and disaster setting, ATLS continues to support prioritizing the rapid assessment and treatment of life-threatening airway and breathing problems ahead of circulation problems. No evidence-based data were identified that justified a modification to this approach in the care of civilian patients. One important principle of ATLS is interruption of the diagnostic sequence as necessary to provide lifesaving resuscitative care, up to and including surgery for airway management or hemorrhage control prior to completion of diagnostic studies.

American College of Surgeons. *Advanced Trauma Life Support*. 10th ed. Chicago: American College of Surgeons; 2018:2–21.

A.4. How would you evaluate airway and breathing?

On first contact with the patient, the provider should attempt verbal communication: "How are you?" A patient who answers coherently in a normal voice has no immediate airway issue, adequate circulatory function, and minimal traumatic brain injury. In an unconscious patient, initial assessment is by looking, listening, and feeling for airflow. If airflow is absent, the airway should be opened by jaw thrust (*not* head tilt because this may exacerbate a cervical spinal column injury), cleared of any visible foreign bodies or secretions, and should have the placement of an oral or nasopharyngeal airway.

Breathing is assessed by observation of the chest wall and diaphragm once the airway is open and by immediate placement of a pulse oximeter probe. Patients who are not breathing adequately should be assisted with bag-valve-mask ventilation while preparations are made for securing a definitive airway and instituting mechanical ventilation.

A.5. How would you evaluate the circulation?

Initial assessment for shock is by vital signs (HR, blood pressure, pulse oximetry) and physical examination (pallor, diaphoresis, peripheral circulation, visible or suspected hemorrhage). Mental status is also a useful sign; the patient in hemorrhagic shock will be first agitated and then lethargic. Young patients have significant compensatory reserves and will maintain a normal systolic blood pressure even in the face of hemorrhage as great as 40% of their blood volume. This state of compensated shock can be diagnosed by a narrowed pulse pressure (especially on automated sphygmomanometers), elevated HR, pallor, abnormal lactate, and a base deficit. Shock in this patient could be the result of hemorrhage from chest or abdominal trauma (including a great vessel injury associated with the impalement) or tension pneumothorax in either side of the chest.

American College of Surgeons. *Advanced Trauma Life Support*. 10th ed. Chicago: American College of Surgeons; 2018:2–21.

Bouglé A, Harrois A, Duranteau J. Resuscitative strategies in traumatic hemorrhagic shock. *Ann Intensive Care*. 2013;3(1):1.

Dutton RP. Initial resuscitation of the hemorrhaging patient. In: Spiess B, Spence R, Shander A, eds. *Perioperative Transfusion Medicine*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:289–300.

Glorsky SL, Wonderlich DA, Goei AD. Evaluation and management of the trauma patient for the interventional radiologist. *Semin Intervent Radiol*. 2010;27(1):29–37.

A.6. How would you evaluate mental status and neurologic condition?

The quick neurologic examination consists of questions to determine alertness and orientation (assuming the patient is responsive) followed by gross assessment of voluntary motion in all extremities. In the less responsive patient, the Glasgow Coma Score (GCS) (**Table 33.1**) is used to stratify the degree of

impairment: GCS 3 to 8 is a severe injury, GCS 9 to 13 is moderate traumatic brain injury, and GCS 14 to 15 is mild injury. Cranial nerve, spinal cord, and peripheral nervous system function is assessed by specific motor and sensory testing of each extremity during the secondary survey.

TABLE 33.1 Glasgow Coma Scores[a]

Eye-Opening Response	Verbal Response	Motor Response
4 = Spontaneous	5 = Oriented to name	6 = Follows commands
3 = To speech	4 = Confused	5 = Localizes to painful stimuli
2 = To pain	3 = Inappropriate speech	4 = Withdraws from painful stimuli
1 = None	2 = Incomprehensible sounds	3 = Abnormal flexion (decorticate posturing)
	1 = None	2 = Abnormal extension (decerebrate posturing)
		1 = None

[a]The Glasgow Coma Score is the sum of the best scores in each of three categories.

Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. *Lancet*. 1974;2:81–84.

A.7. What diagnostic tests are indicated for this patient based on the mechanism of injury?

Because of the high-energy mechanism of injury, this patient must be assessed from head to toe. Ultrasonography examination of the abdomen and chest is used to diagnose free peritoneal fluid, pneumothorax (in the hands of a skilled operator), and pericardial tamponade. Chest and pelvis plain-film radiography will reveal fractures, pneumothoraces, and hemothorax. CT scanning should include the head, neck, chest, abdomen, and pelvis; newer technology will allow for three-dimensional (3D) reconstructions of organs and vasculature with sensitivity and specificity equivalent to more traditional angiographic imaging.

This patient's obvious injury—to zone I of the neck—will

necessitate a focused assessment of the trachea, great vessels, esophagus, and bilateral pleural cavities. Traditionally, this has been accomplished by a combination of plain-film radiography, angiography, bronchoscopy, and esophagoscopy. Increasing CT speed and resolution as well as point-of-care ultrasonography is leading to the increased use of these tests at centers with experienced radiographers and traumatologists. The sequencing of diagnostic studies will depend on the patient's stability. In this case, he is likely to require intubation and perhaps exploratory surgery first. A noninvasive study such as contrast-enhanced CT (with angiographic reconstructions) may help to guide the surgical approach to removal of the impaling object if the patient is calm and stable enough to tolerate the test.

Wilson CT, Clebone A. Initial assessment and management of the trauma patient. In: Scher CS, ed. *Anesthesia for Trauma: New Evidence and New Challenges*. New York: Springer; 2014:1–15.

A.8. What are the zones of the neck, and what is their clinical significance?

Zone I of the neck includes the area from the inferior aspect of the cricoid cartilage down to the thoracic outlet. Zone I injuries require the complex diagnostic workup described in the previous section, followed by a surgical approach that allows access to both the neck and chest. Partial or complete median sternotomy is often necessary to access an injured great vessel or to repair the trachea or esophagus.

Zone II of the neck includes the area from the angle of the mandible down to the cricoid cartilage. Injuries in zone II are addressed through a lateral or transverse cervical incision, with the surgeon able to achieve both proximal and distal control of the carotid or jugular vessels before exploring the wound itself.

Zone III of the neck includes the area from the angle of the mandible upward to the base of the skull. Zone III vascular

injuries pose a significant operative risk because distal control of an injured vessel cannot be achieved. Injuries in zone III are therefore approached angiographically or as part of a more complex neurosurgical operation.

Britt LD, Weireter LJ, Cole FJ. Management of acute neck injuries. In: Feliciano DV, Mattox KL, Moore EE, eds. *Trauma*. 6th ed. New York: McGraw-Hill; 2008:467–478.

A.9. What immediate treatment is necessary before diagnostic studies?

The key to this case will be control of the patient's airway. Once hemodynamic stability is confirmed, the timing and sequence of diagnostic studies will be determined by the patient's degree of cooperation and ability to spontaneously ventilate. Although a CT scan before a controlled intubation in the operating room (OR) would be ideal, it is possible that the patient will decompensate before this can be accomplished. Preemptive airway control will allow for a more secure and safer diagnostic workup before the operation.

A.10. When and where should the impaling object be removed?

All things being equal, the impaling tree branch is best removed in the OR in an anesthetized patient. All of the personnel and equipment should be present to perform an emergent median sternotomy and major vascular and/or tracheal surgery if necessary.

B. Preoperative Evaluation and Preparation

B.1. What laboratory tests would you want?

The patient should have a full set of laboratory studies, both to identify abnormalities and to establish a baseline for future

changes. Hemoglobin and hematocrit will not indicate hemorrhage on the initial draw—the bleeding trauma patient is losing whole blood—but will drop with subsequent fluid resuscitation. Arterial blood gas and arterial or venous lactate measurement will be the most sensitive indicators of hypoperfusion and shock. Serum electrolytes will reveal baseline abnormalities, if any, and the effects of alcohol consumption and dehydration. Clotting studies are important to rule out congenital abnormalities or the effects of liver disease before what could be a major surgical procedure; coagulopathy at the time of trauma center admission is an indicator of substantial blood loss and severe hemorrhagic shock. Toxicology screening is indicated in every trauma patient and is important to rule out the use of drugs of abuse, such as heroin or cocaine, that have implications for the anesthesiologist.

Initial laboratory studies also should include a sample for the blood bank with the request for an urgent crossmatch of red blood cells and plasma. If there has been a major vascular injury, substantial blood loss is a possibility and should be treated with immediate transfusion of blood and coagulation factors.

American College of Surgeons. *Advanced Trauma Life Support*. 10th ed. Chicago: American College of Surgeons; 2018:2–21.

Hess JR, Lindell AL, Stansbury LG, et al. The prevalence of abnormal results of conventional coagulation tests on admission to a trauma center. *Transfusion*. 2009;49(1):34–39.

B.2. What x-ray studies are most important to the anesthesiologist?

Although all of the studies described in the preceding text will have some relevance, there are a few that have particular implications for the anesthesiologist. The chest radiograph and/or CT scan will suggest the degree of tracheal involvement

of the impaling object, the risk that there is of a major vascular injury, or the presence of a pneumothorax. Plain radiographs or a CT scan of the cervical spine will be useful in ruling out bony or ligamentous injury that might be exacerbated by manipulation of the neck during airway management.

B.3. Is an electrocardiogram (ECG) necessary?

In the absence of dysrhythmias on the cardiac monitor, the criteria for ordering a preoperative ECG are the same as in any other surgical candidate, that is, patients presenting with symptoms or with a history suggestive of coronary artery disease. Dysrhythmias or visible injury to the precordium would be an indication for a baseline ECG and cardiac enzyme assay.

B.4. Should this patient be intubated before going for computed tomography (CT) scanning?

The answer to this question involves an assessment of risks and benefits. If the patient is cooperative, vital signs are stable, CT scanner is close at hand, and anesthesia personnel are available to accompany the patient, then an immediate CT scan would be indicated. If the patient is deteriorating in any way, his degree of cooperation is in doubt, or a CT scan would place the patient far from expert resources for an extended period, then it would be wise to secure the airway first. In this case, there is a possibility that successful airway management will precipitate patient deterioration (e.g., hemorrhage, conversion from simple to tension pneumothorax), which suggests that if airway management is attempted before CT, it should probably be done in the OR with the surgical team on hand.

One approach to this kind of complex decision is to define an ideal course of care that provides the best information for each of the experts involved while minimizing risk to the patient and maximizing flexibility in dealing with changing circumstances. In this case, the surgeon and anesthesiologist might define a plan

that includes transport to the OR; induction, intubation, and mechanical ventilation in this (safest possible) environment; transport to CT or angiography with the anesthesiologist in attendance for diagnostic studies; and then return to the OR for definitive surgery.

B.5. When and where should this patient's airway be managed?

Because of the potential for rapid deterioration and the desire to examine the airway closely before and during the intubation process, the patient should be moved as rapidly as possible to the OR before airway management is attempted. The surgical team should be on hand from the start, and instruments should be available for video laryngoscopy and bronchoscopy, emergent tracheostomy, control of large vessel bleeding, and median sternotomy.

B.6. Are any prophylactic medications indicated?

Tetanus toxoid treatment is indicated for any trauma patient with an open wound who is more than 5 years removed from his or her last booster. Any patient with a significant open wound should receive prophylactic antibiotic therapy that covers gram-positive organisms for at least the first 24 hours following injury.

Prophylactic treatment to reduce the consequences of aspiration would be considered but probably rejected in this case. Promotility agents such as metoclopramide and histamine H_2-receptor antagonists such as ranitidine will not have time to work before definitive airway control is achieved and the more immediate approach of administering oral sodium citrate/citric acid (e.g. Bicitra) would be contraindicated because of the possibility of esophageal injury.

Because of the patient's history of intoxication, prophylactic

intravenous administration of vitamins and thiamine is indicated. Prophylaxis against alcohol withdrawal and deep venous thrombosis are indicated in the immediate postoperative period.

C. Intraoperative Management

C.1. What monitors would you use? Is invasive monitoring necessary before definitive airway control?

Blood pressure, electrocardiography, capnography, and pulse oximetry should be employed as with any patient. A Foley catheter should be inserted once the patient is anesthetized, although urine output is not an accurate measure of intravascular volume status in a recently intoxicated patient. An arterial line is useful for moment-to-moment measurement of blood pressure and for easy access to blood for laboratory assay including arterial blood gases. A central venous catheter should be placed if there is need to monitor central venous intravascular volume, in anticipation of the need for rapid intravascular expansion (using a large-bore catheter such as a pulmonary artery introducer), and for the administration of vasoactive drugs. A pulmonary artery catheter is rarely indicated and seldom used acutely for resuscitation, although it *may* be helpful in selected patients with known coronary artery or valvular disease. Because of the potential for great vessel injury in this case, initial central access should be through the femoral vein.

Invasive monitoring lines usually are best placed after induction and intubation, when the patient is anesthetized and both surgeons and anesthesiologists can be working at the same time. Delaying surgical hemostasis in an unstable patient is unwise. In the case under discussion, it would be appropriate to place an arterial line in the OR before airway management, as

long as the patient remains cooperative and stable, and in this case to place a femoral central line thereafter. Placing the arterial line on the right side also will allow for assessment of blood flow in the innominate artery during surgical exploration.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2115–2155.

C.2. What is the surgical approach to a zone I neck injury?

In the present case, the surgery is likely to start with a collar incision through the impalement wound to allow for better visualization of the path of injury. If injury to the trachea or a great vessel is discovered, a partial or complete median sternotomy would be the next step. It is the uncertain nature of this patient's injuries that makes preoperative diagnostic information so valuable, which is why a CT scan before definitive surgery (but after airway management) is a strong consideration.

C.3. Is the patient likely to require tube thoracostomy? Should this be placed before managing the airway?

Pneumothorax and hemothorax are common in trauma patients and should be suspected and definitively ruled out following any high-energy blunt trauma (e.g., motor vehicle collision, pedestrian struck, fall from a height) or any penetrating trauma to the neck, thorax, or upper abdomen. Immediate temporizing needle decompression and/or tube thoracostomy are indicated in any hemodynamically unstable patient with a suspicious injury, even before chest radiograph. Intubation and the change to positive pressure ventilation may precipitate decompensation in a patient with chest injury, due to either decreased preload in the setting of hemorrhage or increased intrathoracic pressure caused by conversion from a simple to tension pneumothorax.

In this case, there is the possibility of pathology in either or both hemithoraces. A portable anterior-posterior chest radiograph should be obtained at the earliest moment, followed by CT of the chest as outlined previously. If a simple pneumothorax is present, it is most prudent to prepare for chest tube placement (personnel, equipment) before airway management but to wait until the airway is secure before actually placing the chest tube.

C.4. What are the options for managing this patient's airway?

Choices for induction of anesthesia should be considered in concert with choices for securing the airway and transitioning to positive pressure ventilation. Airway management can occur with the patient awake under topical anesthesia or asleep, with either a continued spontaneous ventilation (a "breathe down" induction with a volatile anesthetic) or an immediate transition to positive pressure, as in a rapid sequence induction.

C.5. What are the risks of rapid sequence induction in this patient?

Although most trauma patients are best managed with rapid sequence induction and intubation, this case may represent an exception. Swelling or bleeding in the airway may make intubation physically difficult and the impaling object itself may prevent distal passage of an endotracheal tube. Furthermore, dislodgment due to patient agitation or intubation attempts could precipitate hemorrhage or airway disruption. Finally, the transition from spontaneous to positive pressure ventilation could precipitate a tension pneumothorax.

Stephens CT, Kahntroff S, Dutton RP. The success of emergency endotracheal intubation in trauma patients: a 10-year experience at a major adult trauma referral center. *Anesth Analg*. 2009;109:866–872.

C.6. What anesthetic agents would you use for a rapid sequence induction?

Succinylcholine is the key component of a rapid sequence intubation (RSI). No other relaxant provides as consistently good intubating conditions as quickly and as reversibly as succinylcholine. The usual dose for a trauma patient is 1.5 mg per kg—somewhat greater than normal to compensate for a potentially lower cardiac output due to hemorrhage.

Because succinylcholine has no amnestic or analgesic properties, an induction sedative is also indicated in most patients. Any induction agent, including ketamine or etomidate, will precipitate hypotension in the hypovolemic patient with a high endogenous catecholamine level; so care with dosing is required. In young and previously healthy patients, sodium thiopental in a titrated dose from 1 to 5 mg per kg or propofol 0.5 to 2 mg per kg is effective and inexpensive. Etomidate (0.1 to 0.4 mg per kg) is a reasonable choice in elderly patients or in those with known cardiovascular disease.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2115–2155.

C.7. How can you minimize the risk of exacerbating cervical spine trauma?

Appropriate precautions must be taken to avoid worsening an occult spinal cord injury. In the worst case, fractures or ligamentous injury can leave the cervical spine so unstable that the normal manipulation of a direct laryngoscopy will injure the spinal cord. This is a low probability event but is of concern to the health care team because quadriplegia is a catastrophic complication.

Manual in-line cervical stabilization has been shown to be safe and effective in protecting the cervical spine over tens of thousands of direct laryngoscopies and is the common approach

to urgent intubations in the trauma population. Another option commonly used only in patients with known cervical instability is an awake intubation over a fiberoptic bronchoscope. This approach allows for the least manipulation of the neck but requires a cooperative patient who can tolerate the time required for topical anesthesia of the airway and a slower intubation. Awake fiberoptic intubation also may increase the risk of aspiration in patients with a full stomach, especially if topical anesthesia of the pharynx and vocal cords is provided.

Other intubation devices may also decrease the need for manipulation of the neck. Good results have been achieved with the newer generation of video laryngoscopes, lighted stylet intubations, and use of an intubating stylet with a less forceful laryngoscopy. Manual cervical stabilization is recommended with each of these approaches. In a difficult case such as the present one, the intubation technique chosen should be one that the anesthesiologist is experienced and comfortable with; this factor may be more relevant than the specific technology used.

Cranshaw J, Nolan J. Airway management after major trauma. *Contin Educ Anaesth Crit Care Pain*. 2006;6(3):124–127.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2115–2155.

Pierre EJ, McNeer RR, Shamir MY. Early management of the traumatized airway. *Anesthesiol Clin*. 2007;25(1):1–11.

C.8. How can you minimize the risks of aspiration?

Because any significant injury is associated with decreased gastrointestinal motility, all trauma patients are considered to have full stomachs. The risk of aspiration is further increased by intoxication with drugs or alcohol; obesity; the use of analgesics; and injuries to the face, neck, or abdomen that may lead to bleeding within the gastrointestinal tract.

Minimization of risk is a function of how quickly the

intubation must be accomplished. One component of prophylaxis is the normal use of rapid sequence induction to minimize the time during which the airway is at risk. Another is the use of cricoid pressure (the Sellick maneuver) to obstruct the upper esophagus against passive reflux, although recent magnetic resonance imaging research has shown significant variability in the relative anatomy of the cricoid ring and the esophagus, casting doubt on the efficacy of cricoid pressure. Application of cricoid pressure for patients undergoing RSI is controversial. Not only might cricoid pressure not be effective in preventing aspiration but also it may worsen laryngoscopic view and impair bag-valve-mask ventilation. Some experts think that cricoid pressure should be applied in trauma patients and patients at risk for aspiration; however, cricoid pressure, if necessary, should be altered or removed to facilitate intubation. In the case under consideration, there would be a risk of dislodging the impaling object, making cricoid pressure inadvisable. It would be reasonable to administer an H_2 antagonist such as cimetidine and a promotility agent such as metoclopramide if time allowed, but these agents would require 1 to 2 hours to have any substantial effect. An oral antacid is contraindicated because of the potential injury to the esophagus.

Smith KJ, Dobranowski J, Yip G, et al. Cricoid pressure displaces the esophagus: an observational study using magnetic resonance imaging. *Anesthesiology*. 2003;99(1):60–64.

Stewart JC, Bhananker S, Ramaiah R. Rapid-sequence intubation and cricoid pressure. *Int J Crit Illn Inj Sci*. 2014;4(1):42–49.

C.9. How would you anesthetize the airway for an awake intubation?

Innervation of the airway can be separated into three neural pathways. If nasal intubation is planned, some method of anesthetizing maxillary branches from the trigeminal nerve is

required. Involvement of the posterior tongue will require blockade of the glossopharyngeal nerve. Structures more distal in the airway to the epiglottis will require blockade of vagal branches, with the superior laryngeal nerve supplying the pharyngeal apparatus and the recurrent laryngeal nerve supplying the vocal cord and the tracheal mucosa.

The trigeminal nerve, which supplies sensory innervation to the nasal mucosa, can be anesthetized by inserting a nasal airway lubricated with lidocaine jelly into the patent naris. Mixing the lidocaine jelly with oxymetazoline 0.05%, phenylephrine 10 mg, or 4% cocaine may help vasoconstrict the nasal blood vessels and diminish bleeding from the nasal mucosa. The liquid local anesthetic and vasoconstrictor may also be applied in droplet form from a syringe.

The glossopharyngeal nerves of interest are the tonsillar nerves, which provide sensation to the mucosa overlying the palatine tonsil and continuous parts of the soft palate, and the sensory branches to the posterior one-third of the tongue. First, one must provide topical intraoral anesthesia with local anesthetic spray or nebulized lidocaine. Following topical anesthesia of the tongue, the mouth is opened wide and the posterior tonsillar pillar (palatopharyngeal fold) is identified. Then, a 22-gauge needle can be inserted at the caudad portion of the tonsillar pillar. The needle tip is inserted submucosally and following careful aspiration for blood, 5 mL of 0.5% lidocaine is injected. The block is then repeated on the contralateral side. A similar block can be performed with direct application of anesthetic soaked cotton to the bilateral tonsillar fossae.

The vagus nerve supplies innervation to the mucosa of the airway from the level of the epiglottis to the distal airways through both the superior and recurrent laryngeal nerves. A superior laryngeal nerve block and a translaryngeal block can be useful in anesthetizing these pathways. With the patient lying

supine, the superior laryngeal block is done with a 22-gauge needle attached to a syringe, which is directed at the most posterior palpable part of the hyoid bone, near the greater cornu, and anterior to the carotid sheath. The needle must be parallel to the table and never directed posteriorly for fear of penetrating the carotid sheath. When the needle strikes the hyoid, it is carefully walked caudad until it just slips off the hyoid and then advanced a short distance through the hyothyroid membrane. Aspiration should produce nothing. Then, 2 mL of 2% lidocaine is injected and the block repeated on the opposite side.

The translaryngeal block is performed with a 20- or 22-gauge needle attached to a syringe. The needle is inserted through the cricothyroid membrane in the midline and air is aspirated. The patient is asked to inhale deeply and then to exhale fully. At the end of expiration, 4 mL of 2% to 4% lidocaine is injected rapidly and the needle is quickly removed. The resultant coughing will ensure a wide distribution of local anesthetic droplets throughout the airway. If stability of the cervical spine is in doubt, then in-line stabilization should be held while the block is performed and coughing occurs. In the present case, both superior laryngeal and transtracheal blocks would be difficult to perform, and induced coughing might exacerbate the injury. Administration of nebulized lidocaine might be a safer choice.

Brown DL. Cervical plexus block. In: Farag E, Mounir-Soliman L, eds. *Brown's Atlas of Regional Anesthesia*. 5th ed. Philadelphia, PA: Elsevier; 2017:189–194.

Gotta AW, Sullivan CA. Anaesthesia of the upper airway using topical anaesthetic and superior laryngeal nerve block. *Br J Anaesth*. 1981;53:1055–1058.

C.10. What are the risks of awake fiberoptic intubation?

The greatest risk of awake fiberoptic intubation is deterioration of the patient's airway and/or mental status during the

procedure. Ineffective topical anesthesia can lead to agitation and combativeness, which in turn leads to increased use of intravenous sedatives. Blood and secretions in the airway can cause coughing, laryngospasm, or aspiration. Oversedation causes respiratory depression and desaturation, which can pressure the anesthesia providers and lead to hasty decisions. More uncommon complications include injury to nerves or vessels during local nerve blocks, toxicity from local anesthesia ingestion, and direct injury to the laryngeal or pharyngeal mucosa.

This particular case also includes the possibility of inadvertent dislodgment of the impaling tree branch during sedation and topicalization or during the intubation effort itself. Bleeding from a loss of tamponade or open disruption of the airway could necessitate a sudden change in anesthetic and surgical plans. Although awake fiberoptic intubation in the OR is a reasonable starting point for this case, the anesthesiologists and surgeons involved must be prepared for other eventualities. These would include both RSI and emergency surgical airway access.

C.11. If the patient cannot be ventilated, what options are available?

Failure of awake fiberoptic intubation in this case should be followed by an immediate attempt at RSI. If RSI is not possible and the patient cannot be ventilated by mask or LMA, then a surgical airway may be required. An alternate technique involves placing a 14-gauge catheter over a needle through the cricothyroid membrane, removing the needle and using the catheter for jet ventilation. This technique provides a temporary route for oxygenation, as a bridge to a surgical airway, but is highly tenuous. Kinking or dislodgment of the jet catheter is common complications, with tension pneumothorax a possibility

if the catheter tip is displaced into the paratracheal tissues. In this case, accessibility to the trachea or cricoid cartilage may be difficult or impossible due to the impaling object.

Benumof JL, Scheller MS. The importance of transtracheal jet ventilation in the management of the difficult airway. *Anesthesiology*. 1989;71:769–778.

C.12. Would a laryngeal mask airway (LMA) or other pharyngeal airway be of assistance?

Although an LMA or other supraglottic airway support device is often a great help in the difficult airway algorithm, this case may represent an exception. Establishing an efficient mask airway is beneficial if the cause of patient distress is neurologic (diminished respiratory drive due to anesthesia or traumatic brain injury) or related to pharyngeal anatomy (obstruction after muscle relaxation). Supraglottic ventilation will not help with more distal causes of airway obstruction, such as laryngospasm, tracheal disruption, or massive aspiration. Although an LMA or equivalent device should be on hand when this patient is brought to the OR, it is less likely to be of use.

C.13. What surgical airway options are available in this case?

As with the LMA, surgical airway access is beneficial when the cause of airway obstruction is proximal to the intervention. Cricothyroidotomy—the fastest and most readily performed surgical airway procedure—is therefore of benefit in patients who cannot be intubated and have airway obstruction involving the pharynx or larynx. This procedure may be accomplished by surgical opening of the cricothyroid membrane and placing an endotracheal tube into the trachea. Operative cricothyrotomy can be performed more rapidly than conventional tracheostomy; however, it is more traumatic to the larynx, and the cricothyrotomy tube should be removed after 24 hours. If the

patient cannot be decannulated at this time, a conventional tracheostomy should replace the cricothyrotomy.

Tracheostomy, performed lower in the airway, requires more extensive surgical dissection, takes longer, and carries a greater risk of hemorrhage secondary to thyroid tissue trauma. Surgical access to the lower trachea might be necessary in the present case if the impaling object has transected or significantly disrupted the airway. This would be accomplished essentially through the wound itself but would require a partial or complete median sternotomy and the full resources of the OR.

Britt LD, Weireter LJ, Cole FJ. Management of acute neck injuries. In: Feliciano DV, Mattox KL, Moore EE, eds. *Trauma*. 6th ed. New York: McGraw-Hill; 2008:467–478.

C.14. What maintenance anesthetics are indicated or contraindicated in this patient?

If the initial awake fiberoptic examination of the trachea (at the time of intubation) rules out an airway injury, then muscle relaxation to facilitate surgical exploration would be appropriate for the duration of the case. Any of the commonly used intermediate-acting nondepolarizing relaxants could be used. If an airway injury is present, then management of the patient using inhalational anesthesia alone, with continued spontaneous ventilation, offers additional security in the event of airway discontinuity during the course of surgical repair. Sevoflurane, because of its greater palatability, is the easiest volatile anesthetic to administer without interrupting the patient's ventilation. Care must be taken to ensure adequate fluid volume replacement during a pure inhalational anesthetic because hemodynamic instability is possible. Nitrous oxide is contraindicated when the potential for pneumothorax exists or when airway continuity is in doubt.

Narcotics certainly will be required for postoperative

analgesia and may offer some intraoperative advantages as well. Once airway patency is assured, a narcotic-based anesthetic provides for the lowest level of circulating catecholamines, making it easier to assess and manage fluid resuscitation. The usual concern with delayed emergence in a patient receiving a large dose of narcotics is not relevant in this case because the patient will most likely require postoperative mechanical ventilation. The only caveat to intraoperative narcotics is the potential need to sustain spontaneous ventilation while the airway is assessed; narcotic administration should, therefore, be delayed until the anesthetic and surgical plans have become clear.

C.15. What complications will the surgical plan introduce?

Maintenance of homeostasis in the face of surgical provocations is the theme of many anesthetics, and the present case is no exception. At some point—ideally after anesthetic induction, successful airway management, and placement of lines and monitors—the impaling object is going to be removed from the patient's neck. Blunt object impalements in patients seen alive in the trauma center may produce less organ-specific damage than predicted from the location and course of the injury due to the ability of mobile anatomic structures to deform away from low-speed penetrations. Even so, it is entirely possible that this object has injured one of the great vessels or the trachea and that removing it might lead to torrential bleeding or significant disruption of the airway. The anesthesia team must be prepared to change course rapidly from a spontaneous breathing inhalational approach (assuming that airway continuity is the initial concern) to a hemodynamically friendly narcotic-based approach if blood loss and hemorrhagic shock become the major issue. An open team discussion of both surgical and anesthetic plans, including likely contingencies, is highly recommended

before beginning definitive treatment.

Dutton RP. Shock management. In: Smith CE, ed. *Trauma Anesthesia*. 2nd ed. Cambridge, United Kingdom: Cambridge University Press; 2015:65–78.

D. Postoperative Management

D.1. What are the criteria for extubation?

Assuming that the case goes well and the patient's anatomic injuries are successfully repaired, it is appropriate to consider emergence and extubation when the following criteria are satisfied:

- Hemodynamic stability with complete cessation of bleeding and normal systemic coagulation
- Adequate respiratory drive and reserve including complete return of neuromuscular function and minimal requirement for ventilator support
- Acceptable mental status. The patient should be calm, cooperative, comfortable, not overly sedated, and recovered from acute intoxication. The patient should be able to follow commands.
- Evidence of airway patency. Edema at the site of injury will not be an issue with an endotracheal tube in place but might obstruct the airway quickly following extubation. Although not 100% predictive, the presence of an air leak around the endotracheal tube when the cuff is deflated is very reassuring.
- Completion of the diagnostic workup for high-energy trauma, including indicated CT scans, laboratory studies, and completion of all procedures that are likely to require general anesthesia. It would be poor judgment to extubate the patient after tracheal repair only to have the orthopedic surgeons schedule him for urgent pelvic surgery.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed.

Philadelphia, PA: Elsevier; 2020:2115–2155.

D.2. What techniques may be used during extubation?

The best results from extubation will be achieved when the patient is most calm and comfortable and when the extubation itself is as nonstimulating as possible. The appropriate level of sedation and analgesia is a complicated, controversial, and very important question. Sedative agents, such as benzodiazepines and propofol, will diminish the patient's respiratory drive, cooperation, and ability to protect the airway and should be minimized. The right level of narcotics, on the other hand, will allow for a comfortable patient with diminished airway reactivity who can open his or her eyes and follow commands but is not otherwise distressed by the endotracheal tube or ventilator. The endotracheal tube should be suctioned ahead of time, and extubation deferred if there are copious secretions. Enough time should be allowed after suctioning for the stimulation to pass and the patient to relax. The posterior pharynx is then suctioned, the patient is asked to inhale deeply, the cuff is deflated, and the endotracheal tube is removed in one swift motion as the patient exhales.

The airway is in jeopardy immediately after extubation because edema and secretions may compromise respiratory function. Continuous pulse oximetry in a monitored setting is required, and humidified oxygen should be administered for 24 hours postextubation.

D.3. How does alcohol abuse affect postoperative management?

Symptomatic withdrawal from alcohol usually occurs within 24 hours and manifests as agitation, tachycardia, and hypertension. Delirium tremens can occur thereafter if prophylactic therapy is not initiated. Prophylaxis should consist of a small basal dose of benzodiazepines or a low-dose intravenous alcohol infusion,

with frequent assessment of mental status and the willingness to provide supplemental short-acting benzodiazepines if symptoms develop. The plan for delirium tremens prophylaxis should be coordinated with the pain management plan, ideally under the direction of a single individual, to provide for overall consistency and to avoid oversedation and respiratory arrest secondary to polypharmaceutical administration.

D.4. What pain medication should be used?

Postoperative analgesia in this case will depend on the extent of the surgical procedure and on the individual tolerance of the patient. Soft-tissue exploration of the neck, including surgery on the trachea or major vessels, requires relatively little postoperative analgesia. Titrated intravenous narcotics can be used in the first 24 hours with a rapid transition to an oral narcotic/acetaminophen preparation thereafter. Median sternotomy or other significant extension of the surgery into the chest will necessitate more intensive postoperative analgesia, including a continuous narcotic infusion while the patient remains intubated, followed by intravenous patient-controlled analgesia after emergence and extubation. Nonsteroidal anti-inflammatory drugs are an appropriate adjuvant therapy once the risk of traumatic hemorrhage is past.

34 Open-Eye Injury and Cataract Surgery

Alaeldin A. Darwich

A 28-year-old, otherwise, healthy man presented to the emergency room with a fishhook embedded in his eye. He ate a full meal just before the fishing accident.

A. Medical Disease and Differential Diagnosis

1. Why is this patient a particular challenge to the anesthesiologist?
2. What are the determinants of intraocular pressure (IOP) under normal circumstances? What is the normal range? What was the expected IOP in this patient's injured eye?
3. How is aqueous humor formed and eliminated?
4. How is IOP affected by arterial P_{CO_2}, systemic blood pressure, coughing and vomiting, deep inspiration, and hypoxemia?
5. What is the role of the central nervous system (CNS) on IOP?
6. What is glaucoma?
7. Is atropine contraindicated in patients with glaucoma?
8. How do carbonic anhydrase inhibitors work to decrease IOP? By what mechanism may osmotic agents decrease IOP?
9. Are carbonic anhydrase inhibitors or osmotic diuretics indicated in open-globe injuries?

10. Are topically applied ophthalmic medications absorbed systemically? How can this absorption be reduced? Which eyedrops may have effects that are of concern to the anesthesiologist?

B. Preoperative Evaluation and Preparation

1. Is an open-globe injury always a surgical emergency?
2. What preoperative evaluation would you require?
3. The patient ate shortly before the accident. Would you attempt to pass a nasogastric tube or to administer emetics to empty the stomach?
4. Could this case be done with topical anesthesia or a retrobulbar block?
5. How would you premedicate this patient?

C. Intraoperative Management

1. What are some factors that may increase the risk of vitreous herniation during induction and maintenance of anesthesia?
2. Will you intubate this patient? Would you consider a laryngeal mask airway? How does intubation affect IOP? How can this effect be minimized?
3. Would you consider an awake intubation?
4. Is succinylcholine contraindicated in open-globe injuries? How does succinylcholine affect IOP?
5. Does pretreatment with nondepolarizing muscle relaxants prevent the succinylcholine-induced elevation in IOP?
6. How do nondepolarizing muscle relaxants affect IOP?
7. How will you perform a rapid sequence induction and intubation without using succinylcholine?
8. What are the effects of ketamine on the eye?
9. Would you consider the use of etomidate as an induction agent? What about propofol?
10. How do inhalation agents affect IOP and by what mechanism?
11. During the procedure, the patient's pulse suddenly dropped to

40 beats per minute. What do you think was happening? What is the oculocardiac reflex (OCR)?

12. What are the afferent and efferent pathways of the OCR?
13. What factors contribute to the incidence of the OCR?
14. How do you diagnose and treat the OCR?
15. Is atropine useful for the OCR?
16. Can a retrobulbar block prevent the OCR? Is it appropriate in this patient?

D. Postoperative Management

1. Would you reverse the neuromuscular blockade in this patient?
2. Do reversal doses of atropine affect IOP?
3. What would you do before extubating this patient?
4. When would you extubate this patient?
5. The patient awakened in the recovery room and complained of pain and tearing in the opposite eye. The conjunctiva was inflamed. What was the likely cause?
6. Will taping the eyes shut or applying ointment prevent corneal abrasions? Are there any contributing factors?
7. What should you do when you suspect your patient might have a corneal abrasion?
8. A month after the surgical repair, the patient complained of impaired vision in the operative eye. He was examined and found to have a detached retina. As part of the surgical treatment, the ophthalmologist injected a gas bubble into the patient's posterior chamber. Why is this important to an anesthesiologist?

A 77-year-old male is scheduled for cataract surgery. His medical history is significant for hypertension, diabetes mellitus type 2, chronic atrial fibrillation, coronary artery disease, and three coronary drug-eluding stents placed 5 years ago. He is on multiple medications related to his conditions.

E. Anesthesia for Cataract Surgery

1. What is a cataract?
2. What are the causes and risk factors of cataract formation?
3. How would you conduct the preoperative medical evaluation for a patient having cataract surgery?
4. What is the cardiac risk for this patient? If this patient is on anticoagulation and/or antiplatelet medications, should he stop or continue these medications?
5. What are the anesthetic options for cataract surgery?
6. What is the postoperative course after cataract surgery?

A. Medical Disease and Differential Diagnosis

A.1. Why is this patient a particular challenge to the anesthesiologist?

The combination of a full stomach and an open-globe injury presents a unique challenge to the anesthesiologist. In addition to the increased risk of aspiration of gastric contents, any drug or maneuver that raises IOP in the injured, open eye may cause extrusion of the vitreous humor and loss of vision when the globe is opened.

Cunningham AJ, Barry P. Intraocular pressure—physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195–208.

Kelly DJ, Farrell SM. Physiology and role of intraocular pressure in contemporary anesthesia. *Anesth Analg*. 2018;126:1551–1562.

A.2. What are the determinants of intraocular pressure (IOP) under normal circumstances? What is the normal range? What was the expected IOP in this patient's injured eye?

IOP is determined by the balance between production and

drainage of aqueous humor, by changes in choroidal blood volume, and by vitreous volume and extraocular muscle tone. Resistance to outflow of aqueous humor in the trabecular tissue is probably the factor that maintains IOP within physiologic range, but the mechanism of homeostasis is unknown.

Normal IOP is 12 to 16 torr in the upright posture and increases by 2 to 4 torr in the supine position. IOP has been observed to nearly double in steep head-down position in the operating room.

When the globe is open, the IOP is lowered and may be as low as ambient pressure. The concern in this case is for the relative volume of choroid and vitreous humor within the eye. If this volume increases while the eye is open, the vitreous humor may be lost. Any deformation of the eye by external pressure in the globe may cause an increase in IOP.

Jay JL. Functional organization of the human eye. *Br J Anaesth*. 1980;52:649–654.

Kelly DJ, Farrell SM. Physiology and role of intraocular pressure in contemporary anesthesia. *Anesth Analg*. 2018;126:1551–1562.

Kohli R, Ramsingh H, Makkad B. The anesthetic management of ocular trauma. *Int Anesthesiol Clin*. 2007;45:83–98.

A.3. How is aqueous humor formed and eliminated?

Aqueous humor is a clear fluid that occupies the anterior and posterior chambers of the eye. Its total volume is 0.3 mL. Aqueous humor is produced primarily by an active secretory process from the ciliary body in the posterior chambers at an equilibrium rate of 2 μL per minute. The aqueous humor then circulates through the pupil to the anterior chamber, passes through the trabeculated Fontana spaces, and enters the Schlemm canal. From here, the fluid drains into the episcleral veins and finally into the cavernous sinus or jugular venous systems (**Fig. 34.1**).

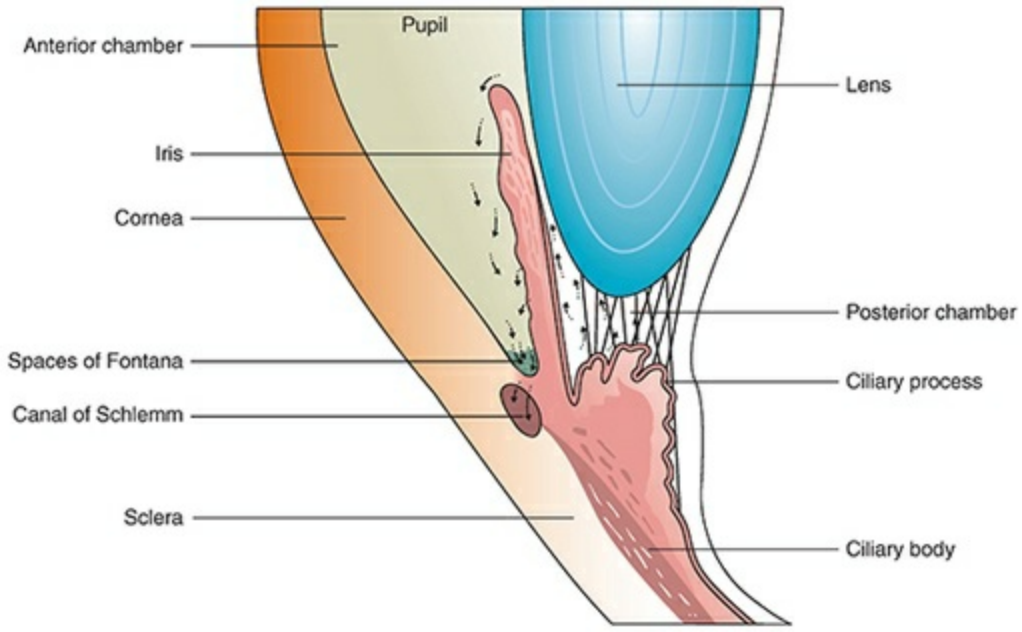

FIGURE 34.1. Sites of formation, circulation, and drainage of aqueous humor. (*Modified by permission from Springer: Cunningham AJ, Barry P. Intraocular pressure—physiology and implications for anaesthetic management*. Can Anaesth Soc J. *1986;33[2]:195–208. Copyright © 1986 Canadian Anesthesiologists.*)

Kelly DJ, Farrell SM. Physiology and role of intraocular pressure in contemporary anesthesia. *Anesth Analg*. 2018;126:1551–1562.

A.4. How is IOP affected by arterial P_{CO_2}, systemic blood pressure, coughing and vomiting, deep inspiration, and hypoxemia?

The choroidal arterioles vasodilate in response to hypercapnia and constrict during hypocapnia, thereby changing intraocular volume and pressure. However, the effect is minimal within the normal physiologic range of P_{CO_2}.

Minor fluctuations in arterial blood pressure also have minimal effects on IOP, although IOP may be seen to increase when hypertension is sustained and can fall significantly with induced hypotension. Changes in venous pressure, on the other hand, have a major impact on IOP. Vomiting, coughing, and bucking on the endotracheal tube cause a dramatic increase in IOP of 30 to 40 torr. These actions, and also a Valsalva

maneuver, cause congestion in the venous system, which impedes the outflow of aqueous humor and increases the volume of choroidal blood. A deep inspiration may reduce IOP by 5 torr. Hypoxemia may increase IOP through choroidal vasodilatation.

Beulen P, Rotteveel J, de Haan A, et al. Ultrasonographic assessment of congestion of the choroid plexus in relation to carbon dioxide pressure. *Eur J Ultrasound*. 2000;11:25–29.

Calobrisi BL, Lebowitz P. Muscle relaxants and the open globe. *Int Anesthesiol Clin*. 1990;28(2):83–88.

Cunningham AJ, Barry P. Intraocular pressure—physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195–208.

Kelly DJ, Farrell SM. Physiology and role of intraocular pressure in contemporary anesthesia. *Anesth Analg*. 2018;126:1551–1562.

A.5. What is the role of the central nervous system (CNS) on IOP?

The CNS influences IOP through alterations in extraocular muscle tone or, indirectly, by hormonal or hemodynamic changes.

Cunningham AJ, Barry P. Intraocular pressure—physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195–208.

Kelly DJ, Farrell SM. Physiology and role of intraocular pressure in contemporary anesthesia. *Anesth Analg*. 2018;126:1551–1562.

A.6. What is glaucoma?

Glaucoma is a pathologic elevation of IOP caused by an increased resistance to outflow of aqueous humor from the anterior chamber of the eye. It is classified as either open- or closed-angle glaucoma, depending on the anatomy and pathophysiology. Chronic elevation of IOP interferes with the intraocular blood supply and normal metabolism of the cornea. It can result in corneal opacities or decreased retinal blood flow.

The pathophysiology in open-angle glaucoma involves increased resistance to the flow of aqueous humor through the

Fontana spaces as a result of scarring of the trabecular network or thickening of the endothelial covering of these channels. In closed-angle glaucoma, the iris bulges forward blocking the access of aqueous humor to the trabecular network. This may occur with pupillary dilation or an acutely swollen lens.

Johnson DH, Brubaker RF. Glaucoma: an overview. *Mayo Clin Proc*. 1986;61:59–67.

Kelly DJ, Farrell SM. Physiology and role of intraocular pressure in contemporary anesthesia. *Anesth Analg*. 2018;126:1551–1562.

LeMay M. Aspects of measurement in ophthalmology. *Br J Anaesth*. 1980;52:655–662.

A.7. Is atropine contraindicated in patients with glaucoma?

Topical atropine in the eye is generally contraindicated in patients with glaucoma, especially in those with closed-angle glaucoma. Atropine, studied in a single dose of 0.01 mg per kg intramuscularly (IM) or given orally as 0.6 mg in two doses 4 hours apart, caused no increase in IOP in either open- or closed-angle glaucoma because by calculation, only approximately 0.0001 mg reaches the eye, which is far less than a topical dose. Intravenous (IV) atropine is associated with mydriasis and might be contraindicated in patients with glaucoma; however, preemptive topical use of pupillary constrictors such as pilocarpine and timolol avoid this problem.

Greenstein SH, Abramson DH, Pitts WR III. Systemic atropine and glaucoma. *Bull N Y Acad Med*. 1984;60:961–968.

Kelly DJ, Farrell SM. Physiology and role of intraocular pressure in contemporary anesthesia. *Anesth Analg*. 2018;126:1551–1562.

Schwartz B. Current concepts in ophthalmology: the glaucomas. *N Engl J Med*. 1978;299:182–184.

A.8. How do carbonic anhydrase inhibitors work to decrease IOP? By what mechanism may osmotic

agents decrease IOP?

Carbonic anhydrase inhibitors, such as acetazolamide, interfere with the sodium-pump mechanism necessary for secretion of aqueous humor. An IV dose acts in 5 minutes, with maximal effect in 20 to 30 minutes. Chronic acetazolamide therapy may result in potassium depletion.

Osmotic agents, such as mannitol, increase plasma oncotic pressure relative to that of aqueous humor and produce an acute, transient drop in IOP. The maximum reduction in IOP occurs after 30 to 45 minutes, and the effect lasts 5 to 6 hours.

Kelly DJ, Farrell SM. Physiology and role of intraocular pressure in contemporary anesthesia. *Anesth Analg*. 2018;126:1551–1562.

McGoldrick KE. Ocular drugs and anesthesia. *Int Anesthesiol Clin*. 1990;28(2):72–77.

A.9. Are carbonic anhydrase inhibitors or osmotic diuretics indicated in open-globe injuries?

No. If the globe is open, the IOP is low, and these agents are not useful. In addition, they may cause transient choroidal congestion, which could lead to loss of ocular contents.

Smith GB. *Ophthalmic Anaesthesia*. Baltimore: University Park Press; 1983.

A.10. Are topically applied ophthalmic medications absorbed systemically? How can this absorption be reduced? Which eyedrops may have effects that are of concern to the anesthesiologist?

Topical ophthalmic drugs may be absorbed through the conjunctiva or may drain through the nasolacrimal duct and be absorbed through the nasal mucosa. Absorption is increased when the eye is instrumented, diseased, or traumatized. Finger pressure on the inner canthus for a few minutes after instillation of eyedrops will impede absorption by occluding the nasolacrimal duct.

Usage of the following topical medications may have implications for the anesthesiologist:

Atropine

Atropine is used to produce mydriasis and cycloplegia. The 1% solution contains 0.2 to 0.5 mg of atropine per drop. Systemic reactions, seen primarily in children and older adults, include tachycardia, flushing, thirst, dry skin, and agitation. Atropine is contraindicated in closed-angle glaucoma.

Scopolamine

One drop of the 0.5% solution has 0.2 mg of scopolamine. CNS excitement can be treated with physostigmine, 0.015 mg per kg IV, repeated one or two times in a 15-minute period. Scopolamine is contraindicated in closed-angle glaucoma.

Cyclopentolate (Cyclogyl)

Cyclopentolate, a short-acting mydriatic and cycloplegic, may cause transient neurotoxic effects such as incoherence, visual hallucinations, slurred speech, ataxia, and seizures. It is contraindicated in closed-angle glaucoma.

Tropicamide (Mydriacyl)

Tropicamide is used to produce mydriasis for refraction or funduscopic examination. It may have CNS effects and can elevate IOP in closed-angle glaucoma.

Phenylephrine Hydrochloride (Neo-Synephrine)

Phenylephrine hydrochloride is used to produce capillary decongestion and pupillary dilatation. Applied to the cornea, phenylephrine hydrochloride can cause palpitations, nervousness, tachycardia, headache, nausea and vomiting, severe hypertension, reflex bradycardia, and subarachnoid hemorrhage. Solutions of 2.5%, 5%, and 10% (25 mg per mL, 50 mg per mL, and 100 mg per mL, respectively) are available.

There are 20 drops per mL. The dose is 1 drop per eye per hour of the 2.5% solution (children) or the 5% solution (adults).

Epinephrine

Topical 2% epinephrine will decrease aqueous secretion, improve outflow, and lower IOP in open-angle glaucoma. Side effects include hypertension, palpitations, fainting, pallor, and tachycardia. The effects last approximately 15 minutes. One drop of 2% solution contains 0.5 to 1 mg of epinephrine. Epinephrine 1:200,000 in a balanced salt solution is sometimes continuously infused into the anterior chamber during cataract surgery. Systemic effects may occur.

Timolol Maleate (Timoptic)

Timolol maleate is a β-blocker used in the treatment of chronic glaucoma. Side effects include light-headedness, fatigue, disorientation, depressed CNS function, and exacerbation of asthma. Bradycardia and bronchospasm may occur as well as potentiation of systemic β-blockers.

Betaxolol Hydrochloride (Betoptic)

Betaxolol HCl is a cardioselective (β_1) blocking agent used to treat glaucoma. It may be hazardous in patients with sinus bradycardia, heart block, or heart failure.

Acetylcholine

Acetylcholine may be injected intraoperatively into the anterior chamber to produce miosis. Side effects are due to its parasympathetic action and include hypotension, bradycardia, and bronchospasm. IV atropine is an effective treatment.

Echothiophate Iodide (Phospholine Iodide)

Echothiophate iodide, a cholinesterase inhibitor, is used as a miotic agent. It may prolong the effect of both succinylcholine and ester-type local anesthetics. Levels of pseudocholinesterase

decrease by 80% after 2 weeks on the drug. It takes 3 to 6 weeks to return to normal pseudocholinesterase activity after stopping the drug (4 weeks for return to 75% activity). Succinylcholine and ester-type local anesthetics should be avoided. Demecarium is another such cholinesterase inhibitor.

Cocaine

Cocaine is used to produce vasoconstriction and to shrink mucous membranes during dacryocystorhinostomy. One drop of 4% solution contains approximately 1.5 mg of cocaine, and the maximum dose is approximately 3 mg per kg. Systemic effects may be seen with a dose as low as 20 mg and involve the CNS, respiratory system, and cardiovascular system.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1380–1381.

Fraunfelder FW, Fraunfelder FT, Jensvold B. Adverse systemic effects from pledgets of topical ocular phenylephrine 10%. *Am J Ophthalmol*. 2002;134:624–625.

Johnson DH, Brubaker RF. Glaucoma: an overview. *Mayo Clin Proc*. 1986;61:59–67.

Kelly DJ, Farrell SM. Physiology and role of intraocular pressure in contemporary anesthesia. *Anesth Analg*. 2018;126:1551–1562.

McGoldrick KE. Ocular drugs and anesthesia. *Int Anesthesiol Clin*. 1990;28(2):72–77.

B. Preoperative Evaluation and Preparation

B.1. Is an open-globe injury always a surgical emergency?

No. In most cases, surgery is not required immediately and some time may be spent in adequately preparing the patient for anesthesia and surgery. However, the surgery should probably be performed within 12 hours to minimize the possibility of infection and other complications. Delaying surgery for gastric emptying to occur is not reliable because gastric emptying may

be prolonged in this stressful situation.

Arthur DS, Dewar KM. Anaesthesia for eye surgery in children. *Br J Anaesth*. 1980;52:681–688.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2206.

Kohli R, Ramsingh H, Makkad B. The anesthetic management of ocular trauma. *Int Anesthesiol Clin*. 2007;45:83–98.

B.2. What preoperative evaluation would you require?

An accurate, thorough history and physical examination are the best means of evaluating this patient preoperatively and should reveal any existing medical problems that will guide your selection of preoperative laboratory tests.

In this otherwise healthy young patient, no routine laboratory tests are indicated, unless required by the institution in which you are practicing. In cases where more extensive trauma is suspected, other injuries must also be addressed such as fractures to the skull and orbit, intracranial hemorrhage, and any other injuries suggested by the history and physical examination.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1381–1383.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2199.

B.3. The patient ate shortly before the accident. Would you attempt to pass a nasogastric tube or to administer emetics to empty the stomach?

Absolutely not. These procedures are contraindicated when there has been a perforation of the eye. Gagging, vomiting, and straining could cause a potentially disastrous increase in IOP and extrusion of intraocular contents. A cough can increase central venous pressure and choroidal blood volume and may raise IOP by 34 to 40 torr.

Kelly DJ, Farrell SM. Physiology and role of intraocular pressure in contemporary anesthesia. *Anesth Analg*. 2018;126:1551–1562.

Kohli R, Ramsingh H, Makkad B. The anesthetic management of ocular trauma. *Int Anesthesiol Clin*. 2007;45:83–98.

B.4. Could this case be done with topical anesthesia or a retrobulbar block?

General anesthesia is the preferred technique for open-globe injuries. The patient is completely immobilized, and there is no time limit for the procedure. In this case, because the patient is not fasting, an endotracheal tube will guard against aspiration.

A retrobulbar or peribulbar injection has the potential to increase IOP because of the volume of local anesthetic used and the likelihood of the patient squeezing his eyes during the injection. However, there have been reports of blocks being used successfully for the repair of open-globe injuries. Topical anesthesia with IV sedation also has been used to repair the globe in select patients with limited injury when general anesthesia is contraindicated.

Boscia F, La Tegola MG, Columbo G, et al. Combined topical anesthesia and sedation for open-globe injuries in selected patients. *Ophthalmology*. 2003;110:1555–1559.

Lo MW, Chalfin S. Retrobulbar anesthesia for repair of ruptured globes. *Am J Ophthalmol*. 1997;123:833–835.

Scott IU, Mccabe CM, Flynn HW, et al. Local anesthesia with intravenous sedation for surgical repair of selected open globe injuries. *Am J Ophthalmol*. 2002;134:707–711.

B.5. How would you premedicate this patient?

Premedications should be given parenterally because gastrointestinal absorption is unreliable. Sedatives and anxiolytics may be given as necessary. Metoclopramide (0.15 mg per kg IM or IV) may be used to facilitate gastric emptying and to increase the tone of the cardiac, lower esophageal, sphincter. Narcotics should be used cautiously because they may

cause nausea and vomiting. Nonparticulate antacids and H_2 receptor antagonists (cimetidine 2 mg per kg IM) should be considered to reduce the risk of aspiration pneumonitis. IV ondansetron (0.1 mg per kg) can be given for antiemesis. Atropine or glycopyrrolate will be useful to reduce secretions and gastric acidity, and they may also inhibit the OCR.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1383.

Cunningham AJ, Barry P. Intraocular pressure—physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195–208.

C. Intraoperative Management

C.1. What are some factors that may increase the risk of vitreous herniation during induction and maintenance of anesthesia?

Factors that may increase the risk of vitreous herniation during induction and maintenance of anesthesia include the following:

- Face mask pressing on the eyeball
- Increased pressure from coughing, straining, bucking, and head-down position
- Extraocular muscle spasm induced by depolarizing muscle relaxants or surgical stimulation during light anesthesia
- Poorly applied cricoid pressure that blocks venous drainage from the eye
- Choroidal congestion from hypercarbia, hypoxia, osmotic diuretics, intubation, or increases in blood pressure

Kelly DJ, Farrell SM. Physiology and role of intraocular pressure in contemporary anesthesia. *Anesth Analg*. 2018;126:1551–1562.

Kohli R, Ramsingh H, Makkad B. The anesthetic management of ocular trauma. *Int Anesthesiol Clin*. 2007;45:83–98.

C.2. Will you intubate this patient? Would you consider a

laryngeal mask airway? How does intubation affect IOP? How can this effect be minimized?

It is imperative that this patient be intubated not only to maintain the airway, which is close to the surgical field, but also to avoid pressure by a face mask on the eyeball and to minimize the risk of aspiration. Although the laryngeal mask airway has been used successfully in ophthalmologic anesthesia, it is not appropriate in this case because it does not protect the airway from aspiration. Many studies have demonstrated a significant increase in IOP caused by laryngoscopy and intubation under varying states of anesthetic depth and muscle relaxation. IOP may be increased even when there is no visible reaction to intubation. This increase in IOP can be attenuated by topical laryngeal anesthesia and by increased depth of anesthesia to reduce coughing, straining, and increases in blood pressure. The cardiovascular response to intubation can also be reduced by IV lidocaine (1.5 mg per kg), β-blockers, α_2-agonists, or calcium channel blockers. Topical anesthesia of the larynx is not recommended in a full-stomach situation because of the increased risk of aspiration.

Akhtar TM, McMurray P, Kerr WJ, et al. A comparison of laryngeal mask airway with tracheal tube for intra-ocular ophthalmic surgery. *Anaesthesia*. 1992;47:668–671.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1383–1387.

Kelly DJ, Farrell SM. Physiology and role of intraocular pressure in contemporary anesthesia. *Anesth Analg*. 2018;126:1551–1562.

C.3. Would you consider an awake intubation?

Awake intubation is frequently accompanied by coughing and bucking and is risky in an open-globe injury when other safe methods of intubation are available. However, when dealing with a possible compromised airway or difficult intubation, an

awake fiberoptic intubation expertly done under careful sedation may be indicated to safely secure the airway.

Calobrisi BL, Lebowitz P. Muscle relaxants and the open globe. *Int Anesthesiol Clin*. 1990;28(2):83–88.

Kelly DJ, Farrell SM. Physiology and role of intraocular pressure in contemporary anesthesia. *Anesth Analg*. 2018;126:1551–1562.

Kohli R, Ramsingh H, Makkad B. The anesthetic management of ocular trauma. *Int Anesthesiol Clin*. 2007;45:83–98.

C.4. Is succinylcholine contraindicated in open-globe injuries? How does succinylcholine affect IOP?

The use of succinylcholine in open-globe injuries is controversial. In the intact eye, following thiopental induction, succinylcholine has been shown to increase IOP by 6 to 8 torr between 1 and 4 minutes after administration. Tracheal intubation further increases IOP. IOP returns to baseline in 5 to 7 minutes. In open-globe injuries, succinylcholine use has been associated with loss of ocular contents. The increase in IOP may be mediated by prolonged tonic contraction of the extraocular muscles, although IOP has been shown to rise after succinylcholine even when the extraocular muscles have been severed. Other factors that may be contributory include choroidal blood flow, increased central venous pressure, and increased resistance to outflow of aqueous humor resulting from the cycloplegic effects of succinylcholine.

The hemodynamic response to laryngoscopy or intubation may have a much more significant effect on IOP than succinylcholine alone. Simply blinking will raise the IOP in a normal eye by 10 to 15 torr, similar to the effect of succinylcholine. Pretreatment with nifedipine or lidocaine may attenuate the increase in IOP following succinylcholine and intubation.

Kelly DJ, Farrell SM. Physiology and role of intraocular pressure in

contemporary anesthesia. *Anesth Analg*. 2018;126:1551–1562.

C.5. Does pretreatment with nondepolarizing muscle relaxants prevent the succinylcholine-induced elevation in IOP?

Available data are contradictory on this question, probably reflecting different methods of IOP measurement under varying depths of anesthesia with a variety of anesthetic adjuvant agents. Many techniques have been tried to prevent succinylcholine-induced elevation of IOP, and none has been consistently effective. However, there are no published reports of the loss of ocular contents when succinylcholine use has been preceded by pretreatment with a nondepolarizing relaxant and barbiturate for induction, and many anesthesiologists feel this is a safe combination for rapid sequence induction in the open-eye, full-stomach situation.

Bourke DL. Open eye injuries. *Anesthesiology*. 1985;63:727.

Calobrisi BL, Lebowitz P. Muscle relaxants and the open globe. *Int Anesthesiol Clin*. 1990;28(2):83–88.

Kelly DJ, Farrell SM. Physiology and role of intraocular pressure in contemporary anesthesia. *Anesth Analg*. 2018;126:1551–1562.

C.6. How do nondepolarizing muscle relaxants affect IOP?

Nondepolarizing muscle relaxants either decrease or have no effect on IOP.

Calobrisi BL, Lebowitz P. Muscle relaxants and the open globe. *Int Anesthesiol Clin*. 1990;28(2):83–88.

Kelly DJ, Farrell SM. Physiology and role of intraocular pressure in contemporary anesthesia. *Anesth Analg*. 2018;126:1551–1562.

C.7. How will you perform a rapid sequence induction and intubation without using succinylcholine?

The safety of the patient always must be the primary concern;

the preservation of the injured eye is secondary. Measures must be taken to guarantee adequate anesthetic depth and to blunt the hemodynamic responses to laryngoscopy and endotracheal intubation. Pretreatment measures such as narcotics, β-blockers, calcium channel blockers, lidocaine, or midazolam should be considered. Before induction, the patient should breathe 100% oxygen for several minutes, administered by a gently applied face mask. Anesthesia can then be induced using carefully applied cricoid pressure with IV methohexital (1 to 2 mg per kg) or propofol (2 to 3 mg per kg) and a nondepolarizing muscle relaxant. Several options exist:

- Atracurium (0.5 mg per kg) will allow safe intubation in 3 minutes. A larger bolus (1.5 mg per kg) will allow intubation in 60 to 90 seconds but may cause hypotension, tachycardia, and histamine release.
- Cisatracurium—because of its intermediate onset of action, cisatracurium (0.10 to 0.15 mg per kg) is not recommended for rapid sequence endotracheal intubations. Cisatracurium (0.4 mg per kg) 8 × effective dose (ED95) will allow intubation in 90 seconds without histamine release, but duration of action may exceed for 60 minutes. The ED95 is the amount of neuromuscular blocking agent (NMBA) required to reduce twitch height by 95%.
- Rocuronium in large dose (1.2 mg per kg) has been shown to create adequate intubating condition in 60 seconds. Sugammadex, in appropriate doses, can be used to effectively and quickly reverse the profound rocuronium blockade in case of difficult airway or short surgical time.
- Vecuronium (0.2 mg per kg) should provide adequate intubating conditions after 90 seconds.
- An alternative is to pretreat the patient with a small dose of the nondepolarizing relaxant several minutes before induction, which may shorten the onset of action and lessen

the dose required of subsequently administered relaxant. This has been referred to as a priming dose. Its use is controversial in that it may lead to diplopia, muscle weakness, respiratory distress, and aspiration while offering no definite advantage over the use of larger initial doses of nondepolarizing muscle relaxants. Whatever technique is selected, it is essential to monitor the degree of muscle relaxation with a neuromuscular blockade monitor. It is also possible to intubate the patient without any muscle relaxant at all after a deep level of anesthesia has been reached, but this is not a recommended technique. Not only is the airway unprotected for a long period but also prevention of bucking cannot be guaranteed, and positive pressure ventilation by face mask may exert pressure on the eye.

Disadvantages of use of a nondepolarizing NMBA include the risk of pulmonary aspiration of gastric contents during the longer period (compared to succinylcholine) when the airway is unprotected. Also, attempts to perform laryngoscopy and intubation prematurely, before full onset of neuromuscular blockade, may result in coughing and straining with a dramatic rise in IOP. For this reason, a peripheral nerve stimulator should be used to confirm muscle relaxation prior to laryngoscopy and endotracheal intubation when a nondepolarizing NMBA is used.

Abbott MA, Samuel JR. The control of intra-ocular pressure during the induction of anaesthesia for emergency eye surgery. A high-dose vecuronium technique. *Anaesthesia*. 1987;42:1008–1012.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:536, 1389–1390.

Kelly DJ, Farrell SM. Physiology and role of intraocular pressure in contemporary anesthesia. *Anesth Analg*. 2018;126:1551–1562.

Lennon RL, Olson RA, Gronert GA. Atracurium or vecuronium for rapid sequence endotracheal intubation. *Anesthesiology*. 1986;64:510–513.

Mehta MP, Choi WW, Gergis SD, et al. Facilitation of rapid endotracheal intubations with divided doses of nondepolarizing neuromuscular blocking

drugs. *Anesthesiology*. 1985;62:392–395.

Musich J, Walts LF. Pulmonary aspiration after a priming dose of vecuronium. *Anesthesiology*. 1986;64:517–519.

Rich AL, Witherspoon CD, Morris RE, et al. Use of nondepolarizing anesthetic agents in penetrating ocular injuries. *Anesthesiology*. 1986;65:108–109.

Sosis MB. On use of priming with vecuronium in a patient with an open globe and a full stomach. *Anesth Analg*. 1990;70:336–337.

C.8. What are the effects of ketamine on the eye?

Ketamine may cause nystagmus and blepharospasm and is therefore not suitable for ophthalmic surgery. Studies with respect to the effect of ketamine on IOP have shown both increased and decreased IOP in children and no change in IOP in adults premedicated with diazepam and meperidine. This may depend on whether ketamine is administered through the IM or IV route.

Antal M, Mucsi G, Faludi A. Ketamine anesthesia and intraocular pressure. *Ann Ophthalmol*. 1978;10:1281–1289.

Ausinsch B, Rayburn RL, Munson ES, et al. Ketamine and intraocular pressure in children. *Anesth Analg*. 1976;55:773–775.

Kelly DJ, Farrell SM. Physiology and role of intraocular pressure in contemporary anesthesia. *Anesth Analg*. 2018;126:1551–1562.

Peuler M, Glass DD, Arens JF. Ketamine and intraocular pressure. *Anesthesiology*. 1975;43(5):575–578.

C.9. Would you consider the use of etomidate as an induction agent? What about propofol?

Although etomidate has been associated with a decrease in IOP when used as an induction agent, the unpredictable incidence of generalized myoclonus seen with etomidate use and resultant elevation of IOP may preclude its use in open-globe injuries, unless rapid and complete prior muscle relaxation can be guaranteed. Propofol, with its antiemetic properties and ability to decrease IOP, would be an excellent choice for induction.

Berry JM, Merin RG. Etomidate myoclonus and the open globe. *Anesth Analg*. 1989;69:256–259.

Calla S, Gupta A, Sen N, et al. Comparison of the effects of etomidate and thiopentone on intraocular pressure. *Br J Anaesth*. 1987;59:437–439.

Ferrari LR, Donlon JV. A comparison of propofol, midazolam, and methohexital for sedation during retrobulbar and peribulbar block. *J Clin Anesth*. 1992;4:93–96.

Kelly DJ, Farrell SM. Physiology and role of intraocular pressure in contemporary anesthesia. *Anesth Analg*. 2018;126:1551–1562.

Kohli R, Ramsingh H, Makkad B. The anesthetic management of ocular trauma. *Int Anesthesiol Clin*. 2007;45:83–98.

C.10. How do inhalation agents affect IOP and by what mechanism?

Inhalation agents cause dose-related decreases in IOP as a consequence of the following:

- Reduced aqueous humor production
- Depression of the CNS control center
- Facilitation of aqueous humor outflow
- Decreased extraocular muscle tension
- Lowered arterial blood pressure

The degree of IOP reduction is proportional to the depth of anesthesia.

Cunningham AJ, Barry P. Intraocular pressure—physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195–208.

Kelly DJ, Farrell SM. Physiology and role of intraocular pressure in contemporary anesthesia. *Anesth Analg*. 2018;126:1551–1562.

C.11. During the procedure, the patient's pulse suddenly dropped to 40 beats per minute. What do you think was happening? What is the oculocardiac reflex (OCR)?

The OCR may be manifested by bradycardia, bigeminy, ectopy, nodal rhythms, atrioventricular block, and cardiac arrest. It is caused by traction on the extraocular muscles (especially medial

rectus), ocular manipulation, or manual pressure on the globe. The OCR is commonly seen during eye muscle surgery, detached retina repair, enucleation, or whenever there is extensive traction or rotation of the eyeball.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1379.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2196.

C.12. What are the afferent and efferent pathways of the OCR?

The OCR is trigeminovagal. The afferent pathway is by way of the ciliary ganglion to the ophthalmic division of the trigeminal nerve and through the gasserian ganglion to the main sensory nucleus in the fourth ventricle. The efferent pathway is the vagus nerve.

Adams AK, Jones RM. Anaesthesia for eye surgery: general considerations. *Br J Anaesth*. 1980;52:663–669.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1379.

C.13. What factors contribute to the incidence of the OCR?

Preoperative anxiety, light general anesthesia, hypoxia, hypercarbia, and increased vagal tone because of age or drugs are associated with an increased incidence of the OCR. The reported incidence of cardiac rhythm changes during eye muscle surgery is 32% to 82%. The incidence is higher in children.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2196.

C.14. How do you diagnose and treat the OCR?

- Monitor the electrocardiogram intraoperatively and during any eye manipulation.
- Stop the surgical stimulus immediately.

- Ensure that ventilation is adequate.
- Ensure sufficient anesthetic depth.

The OCR may fatigue with repeated stimulation.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2196.

C.15. Is atropine useful for the OCR?

Atropine use is controversial. Atropine, 0.4 mg IM, as a premedicant has no vagolytic effect after 60 minutes and is of no value in preventing or treating the OCR. Atropine, 0.4 mg IV, is effective for 30 minutes in preventing bradycardia associated with the OCR. Doses greater than 0.5 mg IV can cause tachycardia that may be detrimental in certain patients with heart disease. At least 2 to 3 mg is required to ensure a total vagal block.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2196.

C.16. Can a retrobulbar block prevent the OCR? Is it appropriate in this patient?

Retrobulbar block injection is not only unreliable in preventing the OCR but also may, during the injection, cause the OCR, a cardiac arrest, or a retrobulbar hemorrhage.

Local infiltration of the recti muscles and a delicate operating technique may decrease the incidence of the OCR. In this patient, a retrobulbar block is relatively contraindicated because it may increase IOP.

Allen ED, Elkington AR. Local anaesthesia and the eye. *Br J Anaesth*. 1980;52:689–694.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2196.

McGoldrick KE. Complications of regional anesthesia for ophthalmic surgery. *Yale J Biol Med*. 1993;66:443–445.

D. Postoperative Management

D.1. Would you reverse the neuromuscular blockade in this patient?

There is no contraindication to reversal provided that efforts are made to minimize coughing or bucking on the endotracheal tube.

D.2. Do reversal doses of atropine affect IOP?

Reversal doses of atropine, when given in conjunction with neostigmine, do not significantly alter IOP. This combination may be safely used even in patients with glaucoma.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1376–1377.

Cunningham AJ, Barry P. Intraocular pressure—physiology and implications for anaesthetic management. *Can Anaesth Soc J*. 1986;33:195–208.

D.3. What would you do before extubating this patient?

- Empty the stomach with an orogastric tube while the patient is still paralyzed.
- Suction the pharynx with the patient still paralyzed or deeply anesthetized.
- Give an antiemetic, such as ondansetron 0.1 mg per kg IV, 20 to 30 minutes before the end of surgery.
- Give lidocaine 1.5 mg per kg IV or remifentanil 0.5 to 0.8 μg per kg IV to prevent coughing during emergence.

Gefke K, Andersen LW, Friesel E. Lidocaine given intravenously as a suppressant of cough and laryngospasm in connection with extubation after tonsillectomy. *Acta Anaesthesiol Scand*. 1983;27:111–112.

D.4. When would you extubate this patient?

There may be a conflict between the desire to extubate awake because of the full stomach and the desire to extubate deep to prevent coughing and bucking. Because modern techniques of

eye repair involve minimal risk of suture disruption with coughing, one may extubate the patient awake, thereby protecting the airway.

D.5. The patient awakened in the recovery room and complained of pain and tearing in the opposite eye. The conjunctiva was inflamed. What was the likely cause?

General anesthesia decreases tear production and reduces normal mechanical eyelid closure. Corneal abrasions are the most common perioperative ocular injury, and this patient's complaints are consistent with that diagnosis.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1393.

Grixti A, Sadri M, Watts MT. Corneal protection during general anesthesia for nonocular surgery. *Ocul Surf*. 2013;11(2):109–118.

D.6. Will taping the eyes shut or applying ointment prevent corneal abrasions? Are there any contributing factors?

There is no guarantee that an eye that has been taped shut or lubricated will not sustain a corneal abrasion. Most anesthesiologists protect the eyes in some way; abrasions, however, still occur. Corneal abrasions represent the most common ophthalmic complication associated with general anesthesia. The incidence may be as high as 44% when no preventative measures have been taken and the cornea is exposed. The mechanism is thought to be drying of or direct trauma to exposed cornea. Possible contributing factors may be mask anesthesia; the prone, lateral, or Trendelenburg position; or having the patient's face in the surgical field.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1393.

Bronheim D, Abel M, Neustein S. Corneal abrasions following non-ophthalmic surgery: a retrospective view of 35,253 general anesthetics. *Anesthesiology*. 1995;83:A1071.

Gild WM, Posner KL, Caplan RA, et al. Eye injuries associated with anesthesia. A closed claims analysis. *Anesthesiology*. 1992;76:204–208.

Nair PN, White E. Care of the eye during anaesthesia and intensive care. *Anaesth Intensive Care Med*. 2014;15(1):40–43.

D.7. What should you do when you suspect your patient might have a corneal abrasion?

Prompt consultation with an ophthalmologist should be solicited for precise diagnosis and treatment. The patient should be reassured that corneal abrasions usually heal and that relief of pain occurs within 24 to 48 hours. Possible treatments include eye patching and topical administration of antibiotics, short-acting cycloplegics, or anti-inflammatory agents. The use of eye patches is controversial.

A topical anesthetic for the cornea should never be given to a patient for self-administration. Misuse may cause delayed wound healing and keratopathy.

Hulbert MF. Efficacy of eyepad in corneal healing after corneal foreign body removal. *Lancet*. 1991;337:643.

Kaiser PK. A comparison of pressure patching versus no patching for corneal abrasions due to trauma or foreign body removal. Corneal Abrasion Patching Study Group. *Ophthalmology*. 1995;102:1936–1942.

Turner A, Rabiu M. Patching for corneal abrasion. *Cochrane Database Syst Rev*. 2006;(2):CD004764.

D.7. A month after the surgical repair, the patient complained of impaired vision in the operative eye. He was examined and found to have a detached retina. As part of the surgical treatment, the ophthalmologist injected a gas bubble into the patient's posterior chamber. Why is this important to an anesthesiologist?

If a patient with intraocular gas needs to undergo general anesthesia before the gas bubble resorbs, nitrous oxide must be avoided because the gas will expand thereby increasing IOP. The effects on the eye may be disastrous. Various types of gases may be injected, with different durations. Patients are usually given bracelets to inform anesthesiologists that they have gas in their eye and nitrous oxide must be avoided.

Fu AD, McDonald HR, Eliott D, et al. Complications of general anesthesia using nitrous oxide in eyes with preexisting gas bubbles. *Retina*. 2002;22(5):569–574.

Hart RH, Vote BJ, Borthwick JH, et al. Loss of vision caused by expansion of intraocular perfluoropropane (C_3F_8) gas during nitrous oxide anesthesia. *Am J Ophthalmol*. 2002;134(5):761–763.

E. Anesthesia for Cataract Surgery

E.1. What is a cataract?

A cataract is an opacity of the lens of the eye, which interferes with clear vision.

E.2. What are the causes and risk factors of cataract formation?

Aging is the most common cause of cataracts. Other risks factors that may be linked to cataract development are diabetes, hypertension, long-term steroid use (topical, systemic, oral, or inhaled), obesity, intraocular surgeries, smoking, exposure to ionizing radiation, and ultraviolet light.

Jacobs DS. Cataract in adults. https://www.uptodate.com/contents/cataract-in-adults. Accessed December 5, 2019.

E.3. How would you conduct the preoperative medical evaluation for a patient having cataract surgery?

The majority of cataract patients are elderly with chronic

multiple coexisting diseases. Cataract patients can proceed with their scheduled cataract surgery as long as their comorbidities are controlled. Routine preoperative testing before cataract surgery does not improve the outcome or patient safety and is not indicated. Medical history and physical examination should direct the need to order any test.

The evaluation should be focused on the patient's ability to understand and communicate because cataract surgery is done mostly under topical or regional anesthesia, and the patient needs to be still and cooperative. Any condition that interferes with maintaining supine position should be evaluated, for example, chronic obstructive pulmonary disease, congestive heart failure, or claustrophobia.

Mafi JN, Godoy-Travieso P, Wei E, et al. Evaluation of an intervention to reduce low-value preoperative care for patients undergoing cataract surgery at a safety-net health system. *JAMA Intern Med*. 2019;179:648–657.

E.4. What is the cardiac risk for this patient? If this patient is on anticoagulation and/or antiplatelet medications, should he stop or continue these medications?

Cataract surgery is a low-risk procedure. The risk of major adverse cardiac events or death is less than 1%.

Cataract surgery has a low risk of bleeding. Anticoagulants or aspirin may be continued in the perioperative period as their benefits outweigh the bleeding risks in most cases.

Chen CL, Lin GA, Bardach NS, et al. Preoperative medical testing in medicare patients undergoing cataract surgery. *N Engl J Med*. 2015;372:1530–1538.

Cheung JJC, Liu S, Li KKW. Phacoemulsification cataract surgery in patients receiving novel oral anticoagulant medications. *Int Ophthalmol*. 2019;39:623–630.

Kumar CM, Seet E. Stopping antithrombotics during regional anaesthesia and eye surgery: crying wolf? *Br J Anaesth*. 2017;118:154–158.

E.5. What are the anesthetic options for cataract surgery?

The majority of cataract surgery is performed with local anesthesia or topical anesthetics with or without sedation. Some patients require general anesthesia if they cannot maintain supine position or remain still and cooperative during surgery (e.g., children, severe dementia patients).

Topical anesthesia is the most common technique used in United States followed by peribulbar and retrobulbar blocks.

The goal of sedation is to minimize anxiety and maintain a cooperative patient during the procedure. Short-acting agents are used, for example, midazolam, remifentanil, or small dosed of propofol.

To prevent rebreathing of CO_2, medical air is flushed under the surgical drapes at 10 L per minute.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1373–1399.

E.6. What is the postoperative course after cataract surgery?

Hospitalization on the same day after cataract surgery is very rare (0.3%). The majority of patients are discharged from the recovery room once the discharge criteria are met. Complications require admission may include uncontrolled elevation in the intraocular pressure, retrobulbar hemorrhage, and suprachoroidal hemorrhage. Other indications for admission may be related to a patient's coexisting diseases (e.g., uncontrolled hypertension, diabetes mellitus, unstable respiratory, or cardiovascular conditions).

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1373–1399.

Shoss BL, Tsai LM. Postoperative care in cataract surgery. *Curr Opin Ophthalmol*. 2013;24:66–73.

35 Laser Treatment for Laryngeal Lesions

Stephanie Marie Vecino and
Hugh C. Hemmings Jr.

A 7-year-old girl with a past history of recurrent respiratory papillomatosis (RRP) is scheduled for direct laryngoscopy and possible reexcision. The patient has had 10 papilloma reexcisions in the past 2 years. Currently, she is undergoing adjuvant treatment with α-interferon but now presents with slowly progressive hoarseness.

A. Medical Disease and Differential Diagnosis

1. What is the cause of RRP?
2. What is the usual presentation of RRP?
3. How do you diagnose RRP?
4. What are the available treatment options for RRP?
5. What are common adverse effects of α-interferon therapy?
6. What is the differential diagnosis of hoarseness in this child?

B. Preoperative Evaluation and Preparation

1. What are the key points of the preanesthetic history and physical examination in this patient?
2. What preoperative laboratory tests are necessary?
3. How should this child be premedicated before coming to the operating room?

4. What are the special anesthetic considerations prior to inducing anesthesia in this patient?

C. Intraoperative Management

1. What is a laser, and how does it work?
2. What are the characteristics of laser radiation?
3. Discuss some advantages associated with the use of lasers for laryngeal surgery.
4. What are some disadvantages of lasers compared with microdebriders?
5. How would you protect the external surface of a conventional endotracheal tube (ETT) for use during laser microlaryngoscopy?
6. What special ETTs are available for laser surgery?
7. How would you manage an airway fire?
8. What is the Venturi effect?
9. What is Venturi jet ventilation?
10. How would you institute and maintain manual jet ventilation?
11. How is anesthesia maintained during jet ventilation?
12. What are the complications of jet ventilation?
13. Are there contraindications for the use of jet ventilation?
14. Discuss airway management options during laryngeal papilloma resection.
15. How would you plan to monitor this patient?
16. How would you induce anesthesia for an intermittent apnea technique?

D. Postoperative Management

1. What are the common postoperative complications?

A. Medical Disease and Differential Diagnosis

A.1. What is the cause of RRP?

RRP is a disease of the respiratory mucosa characterized by

benign nonkeratinizing squamous papillomata caused by the human papilloma virus (HPV). Although there are approximately 100 genetically different HPV types identified to date, with respect to RRP, two types are important: HPV 6 and 11. They are not only the causative agents for RRP but are also responsible for 90% of genital warts (condylomata acuminata). Recently, there has been evidence implicating infections with non-HPV agents in the pathogenesis of RRP.

Donne AJ, Hampson L, Homer JJ, et al. The role of HPV type in recurrent respiratory papillomatosis. *Int J Pediatr Otorhinolaryngol*. 2010;74(1):7–14.

Flint PW, Haughey BH, Lund VJ, et al, eds. *Cummings Otolaryngology: Head and Neck Surgery*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2015:3142–3157.

Venkatesan NN, Pine HS, Underbrink MP. Recurrent respiratory papillomatosis. *Otolaryngol Clin North Am*. 2012;45(3):671–694.

A.2. What is the usual presentation of RRP?

The most common presenting symptom of RRP is persistent hoarseness, usually seen in patients between 2 and 4 years of age. The other more frequent diagnosis for hoarseness at this age is laryngitis, secondary to vocal cord nodules from the overuse of voice.

Flint PW, Haughey BH, Lund VJ, et al, eds. *Cummings Otolaryngology: Head and Neck Surgery*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2015:3142–3157.

Zacharisen MC, Conley SF. Recurrent respiratory papillomatosis in children: masquerader of common respiratory diseases. *Pediatrics*. 2006;118(5):1925–1931.

A.3. How do you diagnose RRP?

Any pediatric patient presenting with a change in voice, whether or not stridor is also present, should have a diagnostic flexible fiberoptic laryngoscopy. Definitive diagnosis usually involves a direct laryngoscopy and biopsy by a pediatric otolaryngologist for tissue diagnosis and viral typing. There are several types of

papilloma virus, with type 11 having a worse prognosis. If the diagnosis is delayed, it could potentially lead to respiratory distress due to upper airway obstruction (**Fig. 35.1**).

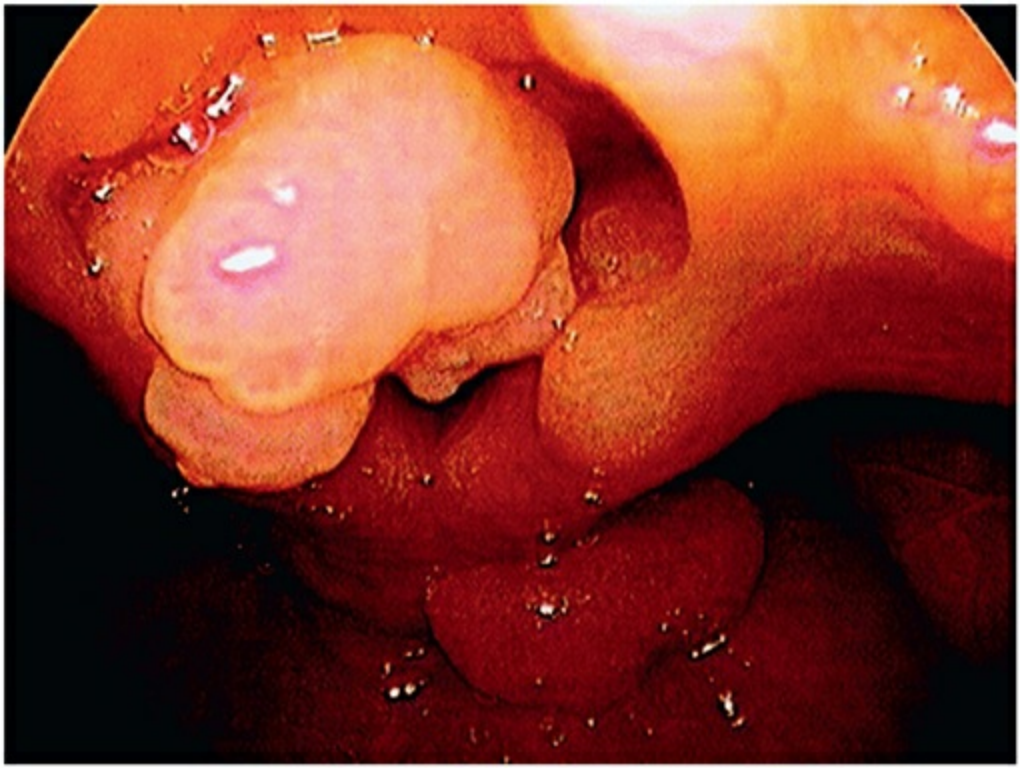

FIGURE 35.1. Laryngoscopic view of multiple papillomata surrounding the vocal cords and obstructing the airway. (*Reprinted with permission from Zacharisen MC, Conley SF. Recurrent respiratory papillomatosis in children: masquerader of common respiratory diseases.* Pediatrics. *2006;118[5]:1925–1931. Copyright © 2006 by the American Academy of Pediatrics*.)

A.4. What are the available treatment options for RRP?

There is no cure for RRP, but standard treatment involves carbon dioxide (CO_2) laser excision or microdebrider excision via direct laryngoscopy with adjuvant therapy as needed. The goal of treatment is to improve airway patency and also preserve voice quality. Because scarring from overaggressive laryngeal resections may lead to adverse clinical outcomes, most surgeons will accept incomplete papilloma resections, especially when near delicate structures such as the anterior laryngeal commissure. Even with removal of all clinically evident

papilloma, not all latent virus particles will have been eradicated.

Microdebriders have been used more frequently due to potential risks involved with the use of lasers. They are precise for surgical debulking and may also be used in combination with lasers. The advantage of using the microdebrider includes a shorter operating time and no risk of thermal injury to airway structures.

There continues to be an application for laser-based resections. Certain lesions, such as sessile lesions, those with ventricular involvement, or those in the area of significant scarring, are still best dealt with by CO_2, potassium titanyl phosphate (KTP), or pulsed-dye laser (PDL).

There is an increasing role for adjuvant medical therapy: α-interferon and various antiviral agents, of which the most commonly used is intralesional cidofovir.

Flint PW, Haughey BH, Lund VJ, et al, eds. *Cummings Otolaryngology: Head and Neck Surgery*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2015:3142–3157.

Gallagher TQ, Derkay CS. Recurrent respiratory papillomatosis: update 2008. *Curr Opin Otolaryngol Head Neck Surg*. 2008;16:536–542.

Ivancic R, Iqbal H, deSilva B, et al. Current and future management of recurrent respiratory papillomatosis. *Laryngoscope Investig Otolaryngol*. 2018;3(1):22–24.

Schraff S, Derkay CS, Burke B, et al. American Society of Pediatric Otolaryngology members' experience with recurrent respiratory papillomatosis and the use of adjuvant therapy. *Arch Otolaryngol Head Neck Surg*. 2004;130:1039–1042.

A.5. What are common adverse effects of α-interferon therapy?

Interferons (IFNs) are potent cytokines that possess antiviral, immunomodulating, and antiproliferative activities. They are part of adjuvant therapy for the treatment of RRP; only α-interferon is clinically used in RRP. A common therapeutic

regimen entails daily subcutaneous applications for a month, followed by a 6-month period of injections three times a week, and then further slow weaning as tolerated. Known adverse effects associated with systemic application are an acute, relatively benign influenza-like syndrome, characterized by fever, chills, headache, myalgia, arthralgia, nausea, vomiting, and diarrhea as well as more serious dose-limiting comorbidities, including myelosuppression and neurotoxicity. Neurotoxicity is characterized by somnolence, confusion, behavioral disturbance, and, rarely, seizures, debilitating neurasthenia, and depression. Alopecia and personality change are common in IFN-treated children. Cardiovascular toxicity (hypotension and tachycardia) and hepatotoxicity are rare.

Brunton LL, Hilal-Dandan R, Knollmann BC, eds. *Goodman & Gilman's the Pharmacological Basis of Therapeutics*. 13th ed. New York: McGraw-Hill; 2018:637–654.

Flint PW, Haughey BH, Lund VJ, et al, eds. *Cummings Otolaryngology: Head and Neck Surgery*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2015:3142–3157.

A.6. What is the differential diagnosis of hoarseness in this child?

Hoarseness always indicates an abnormality of laryngeal structure or function. Given the patient's previous history, local papilloma recurrence and/or postoperative scarring of laryngeal structures seems likely in this patient. A broader differential diagnosis for hoarseness in children would include:

- Anatomic and congenital causes
  - Cystic lesions (laryngocele, thyroglossal cyst)
  - Vocal fold nodules
  - Glottic webs
- Neoplastic causes
  - Squamous cell carcinoma
  - RRP

- Neurologic causes
  - Central (e.g., intracerebral hemorrhage, hydrocephalus)
  - Peripheral neuropathies
- Inflammatory
  - Gastroesophageal reflux
  - Rheumatoid arthritis
  - Angioneurotic edema
- Infectious
  - Croup syndrome
  - Laryngotracheobronchitis
  - Epiglottitis

McMurray JS. Disorders of phonation in children. *Pediatr Clin North Am*. 2003;50:363–380.

B. Preoperative Evaluation and Preparation

B.1. What are the key points of the preanesthetic history and physical examination in this patient?

It is important to detect and address quickly any serious respiratory compromise. In the absence of severe respiratory distress, a detailed history should be obtained. A review of previous anesthetic experiences with particular emphasis on problems pertaining to airway management is a good starting point. Are there signs of airway obstruction? Does the patient have stridor? Does the patient snore at baseline? What position does the child sleep in? Sleep position can assist the team in maintaining airway patency particularly for mask ventilation. Weight, general health, associated comorbidities, recent respiratory infections, allergies, medications, and nothing by mouth (NPO) status are also important. An inquiry about serious adverse effects from IFN therapy should be made.

With respect to voice changes, a more in-depth investigation

may offer some clues regarding the suspected location. A low-pitched, coarse, fluttering voice suggests a subglottic lesion, whereas a high-pitched, cracking voice, aphonia, or breathy voice suggests a glottic lesion. Associated high-pitched stridor also suggests a glottic or subglottic lesion. Because of the precision of laryngeal mechanics, hoarseness can result from a remarkably small lesion. On the other hand, if the origin of the lesion is remote from the vocal cords, hoarseness can result from a significantly larger lesion.

The goal is to recognize a lesion that may result in a partial or complete airway obstruction during anesthetic induction. A preoperative flexible nasopharyngoscopic examination is now routinely performed in most ear, nose, and throat (ENT) offices. If, however, it has not already been done before the patient's arrival to the operating room, an immediate preoperative flexible nasopharyngoscopic examination should be considered.

Derkay CS. Recurrent respiratory papillomatosis. *Laryngoscope*. 2001;111:57–69.

B.2. What preoperative laboratory tests are necessary?

In recent years, the value of routine preoperative laboratory screening has been questioned. For a surgical procedure not associated with significant intraoperative blood loss in a child who is not at increased risk for severe anemia, no laboratory tests are required. This patient may however no longer fall into this latter category. Use of α-interferon is associated with serious side effects, such as neurotoxicity and myelosuppression. Because the effects of myelosuppression may not be diagnosed easily by history and physical examination, a preoperative complete blood count may be beneficial in this patient.

Coté CJ, Lerman J, Anderson MB, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2019:35–68.

B.3. How should this child be premedicated before coming to the operating room?

Children with RRP are often quite anxious and apprehensive coming back to the operating room for yet another reexcision. A reassuring preoperative visit by the anesthesiologist should help allay fears. Sedative premedication should be used very carefully, especially in the child with significant respiratory distress. It should not be administered without close monitoring and the immediate availability of oxygen, suction, and positive pressure ventilation. Dexmedetomidine, an α_2 adrenergic receptor agonist, given intranasally has minimal effect on respiration and has anxiolytic properties. Anticholinergic premedication can be used to reduce oral secretions.

Coté CJ, Lerman J, Anderson MB, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2019:35–68.

B.4. What are the special anesthetic considerations prior to inducing anesthesia in this patient?

Before the induction of anesthesia, the anesthesiologist should discuss the surgical plan with the surgeon. The anesthesiologist should have a thorough understanding of the surgical plan and closely communicate with the surgeon throughout the procedure. A strategy for maintaining oxygenation and ventilation during the case, while working around surgical needs, must be discussed. Special equipment (e.g., laser, jet ventilator, bronchoscopes) must be present and in working condition.

Equipment for securing a potentially difficult pediatric airway should be present in the operating room, which may include rigid bronchoscopes, a tracheostomy–cricothyrotomy set, as well as an experienced otolaryngologist.

The use of a laser greatly impacts airway management. The biggest concern here is prevention of an airway fire. The

anesthesiologist should also have an effective management plan should an airway fire occur. Operating room staff must wear protective eye gear when the laser is in use.

Derkay CS. Recurrent respiratory papillomatosis. *Laryngoscope*. 2001;111:57–69.

C. Intraoperative Management

C.1. What is a laser, and how does it work?

Electromagnetic radiation consists of photons, which have properties consistent with both particles and waves. Like radio waves and Roentgen waves, visible light is another form of electromagnetic radiation. The characteristic features of these different forms of radiation are their respective wavelengths. Visual light is electromagnetic radiation with wavelengths from 385 to 760 nm, shorter wavelengths are ultraviolet, and longer wavelengths are infrared.

Laser is an acronym for light amplification by stimulated emission of radiation. What makes laser special is the high energy density that it provides and its ability to quickly transfer large quantities of energy to remote locations, either through fiberoptic channels (e.g., with the KTP laser) or through free air, as is usually the case with the CO_2 laser.

Several concepts are important for a basic understanding of lasers:

- *The photoelectric effect*. Light of a certain wavelength (e.g., blue) causes metal to eject electrons at a rate proportional to the brightness of this light. Intense light of different colors (e.g., red, orange, yellow) cannot do that.
- *The orbital model*. Electrons circling the nuclei of atoms are limited to a few specific orbital patterns and radii. Each orbital has a specific energy level. The energy differences

between electron orbitals are characteristic for specific atoms. The only way an electron can move from one orbital to another of higher or lower energy is to either absorb or emit energy equivalent to the difference in energy between the two orbitals.

- *Stimulated absorption*. The process by which a photon's energy is captured by an electron, thereby lifting the electron into a higher energy orbital (the electrons get "excited").
- *Spontaneous emission*. The opposite phenomenon in which an electron drops to a lower orbital by emitting a photon to remove the excess energy.
- *Population inversion*. Many (as opposed to one) electrons achieve a higher energy level (higher orbital). Once initiated by a single photon, a chain reaction of stimulated emission occurs (amplification).

The necessary components of a laser system consist of a laser medium (gaseous or solid) containing the atoms whose electrons create the laser light, resonating mirrors to enhance laser efficiency, and an energy source to excite the atoms of the laser medium into generating laser light. An energy source provides the means for obtaining a population inversion of orbital electrons of the laser medium. A pair of axial mirrors permits repeated passes of collimated photons through the medium, allowing maximum amplification by stimulated emission. One of the mirrors is partially transmitting, finally allowing the laser beam to emerge.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2210–2235.

C.2. What are the characteristics of laser radiation?

The high energy density of a laser is the result of three characteristics:

- Monochromaticity, which means that all of the photons in a

laser beam have the same wavelength.

- Electromagnetic fields of all photons in the laser beam oscillate in identical phase. Unlike ordinary light where the electromagnetic fields are randomly phased, this phenomenon of synchronous oscillation is called *coherence*.
- Whereas ordinary light beams spread out in all directions from a point source, laser light remains in a narrow collimated beam with the elements of the laser beam parallel.

These characteristics permit lasers to deliver intense energy via powerful light beams efficiently and accurately through lenses to small targets.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2210–2235.

C.3. Discuss some advantages associated with the use of lasers for laryngeal surgery.

With laser light, tissue penetration is mostly a function of wavelength. Long-wavelength infrared laser light, such as that from CO_2 (operating at 10,600 nm), is completely absorbed by water in the first few layers of cells. The thermal effect is therefore largely limited to the point of entry into the target tissue. This results in explosive vaporization of the surface tissue of the target with surprisingly little damage to underlying cells. When coupled to an operating microscope, the laser vaporizes lesions with precision, causing minimal bleeding and edema, an obvious advantage, especially in small pediatric airways.

In certain situations, a laser-based resection technique is the surgical method of choice: Sessile lesions, lesions in scarred areas, and those located near or in the laryngeal ventricle often are treated with PDL. This laser has a shorter wavelength that typically *spares* the epithelium but targets the microvascular supply of the overriding lesion. This has obvious advantages, where the epithelium of one wall is in proximity to epithelium of

an opposing wall, such as is the case in the anterior laryngeal commissure. An added benefit at least in the adult population is that the PDL can be used with topical anesthesia alone (delivery is typically via fiberoptic scope), thereby avoiding many of the complicating considerations for laser surgery under general anesthesia.

Derkay CS. Recurrent respiratory papillomatosis. *Laryngoscope*. 2001;111:57–69.

Gallagher TQ, Derkay CS. Recurrent respiratory papillomatosis: update 2008. *Curr Opin Otolaryngol Head Neck Surg*. 2008;16:536–542.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2210–2235.

C.4. What are some disadvantages of lasers compared with microdebriders?

There are significant risks associated with the use of laser for laryngeal surgery. Extra staff is typically required for the safe operation of the laser equipment, adding to the overall cost of the procedure. Special eye protection for both patient and staff is required because the laser beam can cause serious retinal injury. Other body parts may need to be carefully protected from inadvertent laser exposure in order to prevent tissue injury (burns).

The biggest concern with laser use, however, is the risk of an airway fire through ignition of the ETT by inadvertent laser strike. This is a potentially fatal complication if not managed quickly. To minimize the risk of an airway fire, the oxygen concentration should be minimized as clinically feasible, generally aiming to keep the fraction of inspired oxygen (F_{IO_2}) below 30%. Nitrous oxide is not a suitable diluting gas because it also supports combustion.

Inappropriate and aggressive use of the laser may cause injury to mucosa that is unaffected by disease and create an

environment suitable for implantation of viral particles which can actually promote spread of the disease. Laser-induced pneumothorax has been reported after a laryngeal procedure. Although the thermal effect is largely limited to the point of entry into the target tissue, if not used judiciously especially near delicate structures such as the anterior or posterior laryngeal commissure, the laser may cause unacceptable scarring and subsequent abnormal vocal fold function.

Laser smoke contains water vapor and destroyed tissue. It has been found to contain active viral DNA, a potential source of infection for operating room personnel. Smoke may also obstruct the surgeon's view during the resection. Staff should protect themselves by wearing N95 face masks.

When comparing the microdebrider to the CO_2 laser, there is evidence suggesting that removing papillomata using the microdebrider is associated with better short-term improvement in voice quality and a shorter procedure time, which may ultimately translate to reduced operative cost. Heat-induced scarring of nearby tissues is not a concern; there is no need for protection from an inadvertent laser strike, and the risk for an airway fire is no higher than in a standard case.

Flint PW, Haughey BH, Lund VJ, et al, eds. *Cummings Otolaryngology: Head and Neck Surgery*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2015:3142–3157.

Gallagher TQ, Derkay CS. Recurrent respiratory papillomatosis: update 2008. *Curr Opin Otolaryngol Head Neck Surg*. 2008;16:536–542.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2210–2235.

Pasquale K, Wiatrak B, Woolley A, et al. Microdebrider versus CO_2 laser removal of recurrent respiratory papillomas: a prospective analysis. *Laryngoscope*. 2003;113(1):139–143.

Werkhaven JA. Microlaryngoscopy-airway management with anaesthetic techniques for CO_2 laser. *Paediatr Anaesth*. 2004;14:90–94.

C.5. How would you protect the external surface of a conventional endotracheal tube (ETT) for use during laser microlaryngoscopy?

An inadvertent laser strike can ignite any hydrocarbon material in the airway, including an ETT. Because of their proximity to the operative field, ETTs pose a serious fire hazard during laser use, especially in the oxygen-enriched environment of a general anesthetic.

All commonly used ETTs are potentially flammable, but flammability is a function of the material used to manufacture the tube. Unfortunately, the common clear polyvinylchloride (PVC) plastic tubes are more flammable than older red rubber tubes. Also, red rubber tubes produce less toxic combustion products once ignited.

In addition to limiting F_{IO_2}, another strategy to make conventional PVC tubes safer is to wrap them with reflective tape. Conventional aluminum or copper tape is an inexpensive (although not U.S. Food and Drug Administration [FDA]-approved) way to offer some protection against a brief laser strike. FDA-approved tape is also available (Merocel Laser-Guard, Medtronic, Minneapolis, MN).

According to a recent practice advisory published by the American Society of Anesthesiologists (ASA) for laser surgery, the ETT should be laser resistant. They also advise that the cuff should be inflated with saline rather than air when possible. The ASA also agreed that the addition of methylene blue to the saline would be beneficial to detect cuff rupture by the laser. They also recommended that for surgery involving the airway, a cuffed ETT should be used rather than an uncuffed ETT whenever possible.

Apfelbaum JL, Caplan RA, Barker SJ. Practice advisory for the prevention and management of operating room fires: an updated report by the American

Society of Anesthesiologists Task Force on Operating Room Fires. *Anesthesiology*. 2013;118(2):271–290.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2210–2235.

Wöllmer W, Schade G, Kessler G. Endotracheal tube fires still happen—a short overview. *Med Laser Appl*. 2010;25(2):118–125.

C.6. What special ETTs are available for laser surgery?

FDA-approved specialized tubes for laser surgery are commercially available. Although these laser-resistant ETTs may withstand laser strikes longer than conventional tubes, they will ignite with longer exposure. Laser-resistant tubes are made of metal or have a metallic overlay on a nonmetal core (**Fig. 35.2**).

The Laser-Shield II (Medtronic, Minneapolis, MN) has a silicone-based core wrapped with laser-reflective aluminum topped with a smooth fluoroplastic overwrap on the outside. Other laser-resistant tubes with a metallic overlay on a nonmetal core are the Sheridan Laser-Trach and the Rüsch Lasertubus (Teleflex, Morrisville, NC).

The Covidien Mallinckrodt Laser Oral/Nasal Tracheal Tube (Covidien, Boulder, CO) is a metal tube model; it has an airtight stainless steel spiral tube with two independent distal PVC cuffs. If one ruptures, the second unruptured cuff will still limit egress of oxygen-rich gas. Currently, there are no available ETTs with cuffs that remain inflated after puncture. Not surprisingly, the rigidity and bulkiness of these tubes are practical disadvantages that discourage their routine use, especially in pediatric patients.

FIGURE 35.2. Example of laser-resistant endotracheal tubes (ETTs). (*From Botney R. Fire Safety. In: Woodworth G, Kirsch JR, Sayers-Rana S, eds.* Anesthesia Technician and Technologist's Manual. *Philadelphia, PA: Wolters Kluwer; 2012:506.*)

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2210–2235.

Wöllmer W, Schade G, Kessler G. Endotracheal tube fires still happen—a short overview. *Med Laser Appl*. 2010;25(2):118–125.

C.7. How would you manage an airway fire?

In case of an airway fire, rapid and effective action is required. When suddenly faced with this crisis situation, the "4 *E*s" mnemonic provides focus:

- *E*xtract
- *E*liminate
- *E*xtinguish
- *E*valuate

All combustible materials (ETT, pledgets) must be *e*xtracted from the airway at once. Oxygen supply through the tube must be quickly *e*liminated by disconnection from the circuit. Continued flow through a burning tube would lead to a

blowtorch effect. Any residual fire needs to be *e*xtinguished with normal saline. Ventilation with 100% oxygen should then be provided by mask, and anesthesia should be continued. *E*valuation of the injury is then in order and should be done with direct laryngoscopy and rigid bronchoscopy to assess the upper and lower airway. Any apparent airway damage makes reintubation the most prudent approach. For severe injury, a low tracheotomy may be indicated.

According the most recent practice advisory from the ASA for the prevention and treatment of operating room fires, when a suspected airway fire has occurred and the fire has not been extinguished with the use of saline, a CO_2 fire extinguisher should be used. The ETT should also be examined and assessed to exclude any fragments left behind in the airway.

Apfelbaum JL, Caplan RA, Barker SJ. Practice advisory for the prevention and management of operating room fires: an updated report by the American Society of Anesthesiologists Task Force on Operating Room Fires. *Anesthesiology*. 2013;118(2):271–290.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2210–2235.

Werkhaven JA. Microlaryngoscopy-airway management with anaesthetic techniques for CO_2 laser. *Paediatr Anaesth*. 2004;14:90–94.

C.8. What is the Venturi effect?

The Venturi effect originally described the impact of constricted channels on fluid flow. As fluid passes through the constriction of a Venturi tube (a tube with two open ends and a narrowing in its midsection), it must speed up. At the same time, its hydrostatic pressure drops. This pressure drop is proportional to flow and can, for example, be used to measure flow in pipes without interfering with flow.

Ihra G, Aloy A. On the use of Venturi's principle to describe entrainment during jet ventilation. *J Clin Anesth*. 2000;12:417–419.

C.9. What is Venturi jet ventilation?

The jet injector technique of ventilation for upper airway surgery was introduced by Sanders in 1967. A high-pressure gas source is connected to a stiff, narrow cannula positioned at the inlet of the laryngoscope. With a manual switch, intermittent gas boluses are delivered. In the lumen of the laryngoscope, the high-velocity stream of gas encounters stationary gas, which it draws forward. Each jet bolus entrains ambient air through the open laryngoscope entrance, substantially augmenting the volume of the bolus and diluting the oxygen fraction of the jet.

Whether or not it is truly based on the phenomenon known as the *Venturi effect*, the jet injector provides a simple approach to delivering physiologic tidal volumes in a non–gas-tight delivery system. Venturi ventilation has become synonymous with jet ventilation.

Ihra G, Aloy A. On the use of Venturi's principle to describe entrainment during jet ventilation. *J Clin Anesth*. 2000;12:417–419.

McRae K. Anesthesia for airway surgery. *Anesthesiol Clin North Am*. 2001;19(3):497–541.

C.10. How would you institute and maintain manual jet ventilation?

Before effective jet ventilation can begin, the operating laryngoscope must be inserted, the larynx adequately exposed and evaluated for jet ventilation, the suspension system installed, and the jet injector needle attached to the laryngoscope in alignment with the axis of the trachea. This takes time in an anesthetized apneic patient. One option is to begin with laryngoscopy and intubation using a standard PVC ETT if the airway appears appropriate for jet ventilation. Uninterrupted ventilation can now be performed while the operating laryngoscope and jet injector are positioned. When ready, the ETT is removed, and jet ventilation begun. Alternatively,

following anesthesia induction and adequate mask airway ventilation, the patient is paralyzed and the operating laryngoscope and jet injector are inserted and positioned while the patient is apneic.

Ventilation begins with a jet pressure of 5 to 10 psi in infants and children and 15 to 20 psi in adults. The jet pressure is gradually increased until adequate chest excursions are evident. Jet ventilation should produce good clinical expansion of the chest at a rate appropriate for the patient's age. The inspiratory-to-expiratory (I:E) ratio should allow for complete passive exhalation in between jet applications. Monitoring of peripheral arterial saturation is mandatory as is monitoring ventilation both by auscultation and palpation.

Flint PW, Haughey BH, Lund VJ, et al, eds. *Cummings Otolaryngology: Head and Neck Surgery*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2015:3142–3157.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2210–2235.

C.11. How is anesthesia maintained during jet ventilation?

The leak around the scope is smaller in children having jet ventilation, but the delivery of inhalational anesthetics is not optimal because of operating room pollution and the inability to precisely regulate gas concentrations. Most clinicians, therefore, favor a total intravenous anesthesia technique. By combining a hypnotic agent such as propofol with a short-acting opioid (such as remifentanil), hypnosis, amnesia, and analgesia can all be achieved, while allowing for a rapid recovery of the patient at the end of the procedure. Temporary muscle relaxation can be achieved with either a short-acting or an intermediate-duration neuromuscular blocker.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2210–2235.

C.12. What are the complications of jet ventilation?

Complications associated with jet ventilation include dehydration of the mucosa, inadequate oxygenation and ventilation, gastric distention, regurgitation, and barotrauma. Pneumomediastinum and pneumothorax have been reported and seem to occur most frequently when jet ventilation is used in a patient with a (partially) obstructed airway. This is best avoided by using muscle relaxation during jet ventilation. In addition, particulate matter and virus particles can be spread down the distal airway. End-tidal CO2 measurements are also inaccurate.

Borland LM. Airway management for CO_2 laser surgery on the larynx: Venturi jet ventilation and alternatives. *Int Anesthesiol Clin*. 1997;35(3):99–106.

Jaquet Y, Monnier P, Van Melle G, et al. Complications of different ventilation strategies in endoscopic laryngeal surgery: a 10-year review. *Anesthesiology*. 2006;104(1):52–59.

C.13. Are there contraindications for the use of jet ventilation?

Jet ventilation is most suited for patients with normal, unobstructed airways and normal lung and chest wall compliance.

The ability to fully exhale in between jet applications is crucial. If this is not possible (glottic lesion, significant interarytenoid scarring, laryngospasm), jet ventilation may not be appropriate. Decreased chest wall compliance, such as in obese patients, may lead to inadvertent gastric distension, further worsening respiratory compliance. Advanced chronic obstructive pulmonary disease with its inherent prolonged exhalation phase may again make jet ventilation impractical and, in the presence of pulmonary bullae, even hazardous. Significant overbite especially when combined with retrognathia makes orolaryngotracheal alignment challenging and accidental gastric

hyperinflation likely.

Borland LM. Airway management for CO_2 laser surgery on the larynx: Venturi jet ventilation and alternatives. *Int Anesthesiol Clin*. 1997;35(3):99–106.

Jaquet Y, Monnier P, Van Melle G, et al. Complications of different ventilation strategies in endoscopic laryngeal surgery: a 10-year review. *Anesthesiology*. 2006;104(1):52–59.

C.14. Discuss airway management options during laryngeal papilloma resection.

In addition to (manual) Venturi jet ventilation, there are three different widely accepted methods for managing the airway during papilloma resection: controlled mechanical ventilation through a small ETT, spontaneous ventilation, and an apnea technique with intermittent ventilation.

Excluding the first option, all methods require an unsecured, unprotected airway during parts of the surgical resection. The use of an ETT during airway laser surgery, although reassuring, also presents the risk of an airway fire. In addition, surgical exposure to the larynx is often suboptimal in the presence of an ETT.

Access to all parts of the laryngeal mucosa using spontaneous ventilation without an additional airway device (e.g., tube, laryngeal mask airway) is naturally superior. Depending on the type of laser used, in the adult population, all that is sometimes required is *topical* anesthesia allowing for office-based treatments. In pediatric patients though, maintenance of spontaneous ventilation under general anesthesia is usually the most successful strategy. Since muscle relaxation is not an option, and the moving surgical field is somewhat of a challenge to using this technique.

Intermittent apnea offers a solution to this problem. During apnea with intermittent ventilation, the patient is repeatedly

hyperventilated, either by mask or after reintubation. Use of 100% oxygen will extend the tolerable apnea time. Inadvertent movement is best avoided using muscle relaxants. If an ETT is used, it is removed periodically, respirations are held while the surgeon operates for brief periods of time, and the peripheral oxygen saturation is closely monitored. Before desaturation occurs, the patient is then either reintubated or just masked and prepared for another period of apnea to allow for further resection as needed. Spreading the virus to more distal parts of the airway by repeated reintubations is a concern with this technique.

Spontaneous ventilation and intermittent apnea techniques seem to be favored by most members of the American Society of Pediatric Otolaryngology.

Flint PW, Haughey BH, Lund VJ, et al, eds. *Cummings Otolaryngology: Head and Neck Surgery*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2015:3142–3157.

Gallagher TQ, Derkay CS. Recurrent respiratory papillomatosis: update 2008. *Curr Opin Otolaryngol Head Neck Surg*. 2008;16:536–542.

Jaquet Y, Monnier P, Van Melle G, et al. Complications of different ventilation strategies in endoscopic laryngeal surgery: a 10-year review. *Anesthesiology*. 2006;104(1):52–59.

C.15. How would you plan to monitor this patient?

Routine monitors include a pulse oximeter, noninvasive blood pressure measurements, an electrocardiogram, a precordial stethoscope, a temperature probe, an oxygen analyzer, a CO_2 detector, and a neuromuscular blockade monitor. If using spontaneous ventilation, exposing the patient's chest can help the clinician assess adequate chest rise. In this otherwise healthy patient without the potential for significant blood loss or fluid shifts, no additional monitoring is necessary.

American Society of Anesthesiologists. Standards for basic anesthetic monitoring. Reaffirmed July 1, 2011. https://www.asahq.org/standards-and-

guidelines/standards-for-basic-anesthetic-monitoring. Accessed October 13, 2015.

C.16. How would you induce anesthesia for an intermittent apnea technique?

The choice of anesthetic induction is critically dependent on the presence of signs and symptoms suggesting possible airway compromise on induction. If present in an adult patient, an awake fiberoptic intubation can be performed, which not only secures the airway but also enables evaluation of the subglottic airway before ETT placement.

In children and uncooperative adults, an inhalational induction using sevoflurane is the next safest option. Maintenance of spontaneous ventilation is again critical. In this scenario, neuromuscular blockers are unsafe until it is clear that the patient can be ventilated and/or intubated.

Blind techniques (blind oral or nasal intubation) cannot be recommended in this setting because they carry the risk of bleeding and loss of the airway due to an obstructing lesion.

A word of caution: Papillomata are dynamic lesions in the sense that they can grow rapidly. The endoscopic airway examination should be current. Also, the absence of suggestive signs and symptoms does not truly guarantee a patent airway once anesthesia has been induced. Hence, extreme caution in managing these patients is essential.

If the patient truly has no airway compromise, any routine induction technique (intravenous or inhalational) can be used safely. An intermittent apnea technique will allow the surgeons to have a full view without an ETT in place.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2210–2235.

D. Postoperative Management

D.1. What are the common postoperative complications?

Laryngeal edema can occur early in the postoperative period and is usually manifested by chest retractions and inspiratory stridor. After microlaryngeal surgery, patients may benefit from humidified oxygen, intravenous steroids (e.g., dexamethasone), and inhalational racemic epinephrine. Laryngospasm can develop because of laryngeal hyperactivity. To reduce the incidence of laryngospasm, lidocaine can be sprayed on the vocal cords in the operating room. If laryngospasm develops postoperatively, it is treated with standard maneuvers, including a jaw thrust and positive pressure ventilation. Care must be taken not to insufflate the stomach with the use of greater than 20 cm H_2O airway pressure. Often, 5 to 10 cm H_2O airway pressure will suffice. More severe forms of laryngospasm may require the use of small doses of succinylcholine (one-tenth of a normal intubation dose, i.e., 0.2 mg per kg for pediatric patients and 0.1 mg per kg for adult patients intravenously). Pulmonary complications can result from retained secretions, atelectasis, or barotrauma (if jet ventilation was used).

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2210–2235.

Jaquet Y, Monnier P, Van Melle G, et al. Complications of different ventilation strategies in endoscopic laryngeal surgery: a 10-year review. *Anesthesiology*. 2006;104(1):52–59.

SECTION 10 Pediatrics

36 Tracheoesophageal Fistula

Jacques H. Scharoun

A 12-hour-old full-term infant weighing 2.5 kg presents with choking and cyanosis during his first feed. Neonatal intensive care unit (NICU) staff is unable to pass a feeding tube into the stomach. The baby also has copious oral secretions. Before birth, polyhydramnios was noticed.

A. Pathophysiology and Differential Diagnosis

1. What is the diagnosis? What are the clinical features of this disease?
2. What is the pathophysiology of this disease?
3. Describe the normal development of the trachea and esophagus.
4. How are tracheoesophageal fistula (TEF) and esophageal atresia (EA) inherited?
5. How are the different types of TEF/EA classified?
6. What other problems may this child have, and when should

these be investigated?
7. What should the parents be told regarding perioperative risk? Risk of recurrence?

B. Preoperative Evaluation and Preparation

1. What laboratory workup should be obtained before surgery?
2. Describe management in the NICU before surgery.
3. How is severe lung disease managed before repair?
4. Should this patient be intubated preoperatively for airway protection?

C. Intraoperative Management

1. What invasive lines and monitoring are appropriate before induction? After induction?
2. Discuss fluid and temperature management for this baby.
3. What are the options regarding induction and intubation?
4. What is the role of rigid and fiberoptic bronchoscopy in this patient prior to incision?
5. Describe the steps of an open repair of EA/TEF.
6. What are common intraoperative problems, and how can they be managed?
7. If the surgeon decides to proceed thoracoscopically, how will you perform your anesthetic? Is one-lung ventilation required? What are some complications unique to thoracoscopy in the newborn?

D. Postoperative Management

1. When should the baby be extubated?
2. What options are available for postoperative analgesia?
3. What are early and late complications of TEF repair?

A. Pathophysiology and Differential Diagnosis

A.1. What is the diagnosis? What are the clinical features

of this disease?

This patient has EA with a TEF. This occurs in 1 per 3,000 live births. The diagnosis is suspected prenatally by the presence of polyhydramnios, which is caused by the failure of the fetus to swallow amniotic fluid (secondary to EA). Polyhydramnios is a nonspecific prenatal finding. The combination of polyhydramnios and absent stomach bubble on prenatal ultrasound gives a 44% to 56% likelihood of EA/TEF. After birth, the neonate will have copious drooling from inability to swallow secretions. Attempts to feed the baby will result in coughing and cyanosis. An orogastric tube (OGT) will coil up in the upper esophageal pouch rather than pass into the stomach.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:506–507.

Knottenbelt G, Skinner A, Seefelder C. Tracheo-oesophageal fistula (TOF) and oesophageal atresia (OA). *Best Pract Res Clin Anaesthesiol*. 2010;24:387–401.

Pinheiro P, Simões e Silva AC, Pereira RM. Current knowledge on esophageal atresia. *World J Gastroenterol*. 2012;18:3662–3672.

A.2. What is the pathophysiology of this disease?

In this abnormality, there are two distinct problems: TEF and EA. In TEF, the trachea is connected to the esophagus through a fistula. This causes two problems. First, inhaled air can bypass the lungs through the fistula into the stomach and cause hypoventilation and gastric distension. If the lungs are especially noncompliant or the fistula is large, attempts to institute positive pressure ventilation (PPV) can lead to severely compromised ventilation due to gastric expansion or even rupture. Second, there is the continual risk of acidic stomach contents refluxing via the fistula back into the trachea causing aspiration pneumonitis. With EA, the esophagus is divided into a proximal and distal portion. The proximal portion ends in a blind pouch. Secretions from the hypopharynx pool here and cause drooling,

coughing, and choking with feeds. The child is unable to feed orally.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092–1099.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:506–508.

Knottenbelt G, Skinner A, Seefelder C. Tracheo-oesophageal fistula (TOF) and oesophageal atresia (OA). *Best Pract Res Clin Anaesthesiol*. 2010;24:387–401.

A.3. Describe the normal development of the trachea and esophagus.

The foregut arises first from primitive endoderm. This structure will eventually differentiate into trachea and esophagus. Lung buds form anteriorly at pharyngeal arch 6. Differential expression of various growth factors results in the anterior foregut developing into trachea and lung tissue, whereas the posterior portion develops into esophagus. The actual septation process is believed to arise at the level of the lung bud and proceed toward the pharynx. This process requires *multiple* gene signals, including Sonic hedgehog, Sox2, and NKX2.1. Errors in this process of separation of the trachea from the foregut results in a residual fistula between the esophagus and trachea.

Brosens E, Ploeg M, van Bever Y, et al. Clinical and etiological heterogeneity in patients with tracheo-esophageal malformations and associated anomalies. *Eur J Med Genet*. 2014;57:440–452.

Fausett SR, Klingensmith J. Compartmentalization of the foregut tube: developmental origins of the trachea and esophagus. *Wiley Interdiscip Rev Dev Biol*. 2012;1:184–202.

Stevenson RE, Hunter AGW. Considering the embryopathogenesis of VACTERL association. *Mol Syndromol*. 2013;4:7–15.

A.4. How are tracheoesophageal fistula (TEF) and esophageal atresia (EA) inherited?

TEF/EA is believed to be multifactorial in etiology and sporadic.

Rarely, it is associated with a specific genetic mutation or syndrome. These include trisomy 18, Hall-Hittner syndrome, anophthalmia-esophageal-genital (AEG) syndrome, Feingold syndrome, and 16q24.1 deletion syndrome. Most of the cases, however, are nonfamilial. There is a 1% chance of recurrence in each sibling of someone with EA. EA is twice as common in twins.

Brosens E, Ploeg M, van Bever Y, et al. Clinical and etiological heterogeneity in patients with tracheo-esophageal malformations and associated anomalies. *Eur J Med Genet*. 2014;57:440–452.

Pinheiro P, Simões e Silva AC, Pereira RM. Current knowledge on esophageal atresia. *World J Gastroenterol*. 2012;18:3662–3672.

Shaw-Smith C. Genetic factors in esophageal atresia, tracheo-esophageal fistula and the VACTERL association: roles for FOXF1 and the 16q24.1 FOX transcription factor gene cluster, and review of the literature. *Eur J Med Genet*. 2010;53:6–13.

A.5. How are the different types of TEF/EA classified?

There are five types of TEF according to the classic Gross classification (**Fig. 36.1**). Type A is pure EA with no involvement of the respiratory tree; this occurs in 8% of cases. Gross type B has EA and a fistula connecting the proximal esophageal pouch to the trachea; this occurs in less than 1%. The most common is type C, with EA and fistula linking the distal esophagus to the trachea; this occurs in 75% to 80% of cases. Rarely, type D occurs with two fistula connecting both proximal and distal esophagus to the trachea (2%). Type E, known as an H-type fistula, has no atresia. Instead, an intact esophagus has a linkage with trachea through a fistula, and it occurs in 4%.

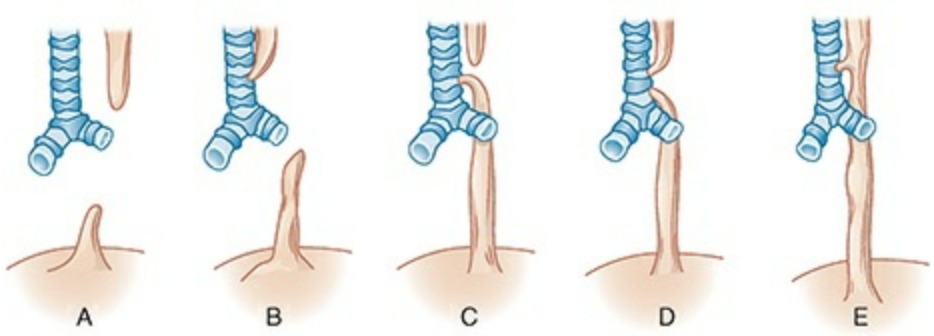

FIGURE 36.1. Gross classification of EA and TEF. (*Modified from Gregory GA, ed.* Pediatric Anesthesia. *2nd ed. New York: Churchill Livingstone; 1989:921, with permission.*)

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092–1099.

Pinheiro P, Simões e Silva AC, Pereira RM. Current knowledge on esophageal atresia. *World J Gastroenterol*. 2012;18:3662–3672.

A.6. What other problems may this child have, and when should these be investigated?

Fifty percent of children with EA/TEF will have additional anomalies. Most often, they occur in the spectrum known as *VACTERL* (formerly known as *VATER*):

V = vertebral anomalies (10%)

A = anal canal defect (anal atresia) (14%)

C = cardiac malformations (29%), including ventricular septal defect, atrial septal defect, tetralogy of Fallot, right-sided arch, patent ductus arteriosus

TE = tracheoesophageal fistula

R = renal dysplasia

L = limb defect (radial aplasia)

A patient is considered to have VACTERL association with the presence of three or more of these lesions. Nearly one-third of TEF patients will have an additional VACTERL lesion, and an additional one-fifth will have two. Other possible gastrointestinal problems include malrotation of the midgut and duodenal atresia. Renal problems can include malposition, hydronephrosis, and ureteral abnormalities.

Because the existence of these associated defects may alter the surgical or anesthetic plan, and because the TEF is an urgent but not emergent procedure, these other possible defects should be assessed *prior* to TEF repair.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092–1099.

Husain M, Dutra-Clarke M, Lemieux B, et al. Phenotypic diversity of patients diagnosed with VACTERL association. *Am J Med Genetics*. 2018;176:1830–1837.

A.7. What should the parents be told regarding perioperative risk? Risk of recurrence?

The survival of TEF babies has improved over the years because of the improvements in intensive care unit care, anesthesia, and surgical technique. Risk of perioperative mortality remains well stratified by the Spitz Classification in a recent series of 248 neonates over a 20-year period.

- Spitz group I: birth weight more than 1.5 kg, no major cardiac disease, survival 96%
- Spitz group II: birth weight less than 1.5 kg, or major cardiac disease, survival 79%
- Spitz group III: birth weight less than 1.5 kg and major cardiac disease, survival 38%

Peters RT, Ragab H, Columb MO, et al. Mortality and morbidity in oesophageal atresia. *Pediatr Surg Int*. 2017;33:989–994.

Spitz L. Oesophageal atresia. *Orphanet J Rare Dis*. 2007;2:24.

B. Preoperative Evaluation and Preparation

B.1. What laboratory workup should be obtained before surgery?

- First, a plain chest x-ray is used to assess the presence and severity of pulmonary disease, especially looking for

aspiration pneumonia and respiratory distress associated with prematurity. It may also show the presence of congestive heart failure in the setting of associated cardiac disease, which may be optimized by administering a diuretic. A radiopaque OGT will be seen coiled in the proximal esophageal pouch, whereas an abdominal x-ray may show air in the bowels entering through the fistula. Because of the risk of aspiration, the use of contrast dye to delineate the fistula should be used only when there is diagnostic uncertainty. Of note, an OGT that appears to enter the stomach may in fact have passed through an esophageal perforation caused by repeated traumatic insertion attempts.

- Second, an echocardiogram is *mandatory* because major cardiac defects strongly influence survival and may have an impact on anesthetic management. If the child has severe tetralogy of Fallot, he may require placement of a temporary shunt between the systemic arterial and pulmonary circulation prior to repair of the TEF. In addition, one wants to look for presence of a right-sided aortic arch because this will require positioning the infant with the opposite side down from usual.
- Spinal plain films should be done to exclude vertebral anomalies, especially if epidural pain management is being considered. Renal ultrasound should be done to rule out abnormalities, especially hydronephrosis.
- In addition, complete blood count (CBC), arterial blood gas, and electrolytes should be drawn, and at least 1 unit of packed red blood cells should be type and crossed.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092–1099.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:506–508.

Knottenbelt G, Skinner A, Seefelder C. Tracheo-oesophageal fistula (TOF)

and oesophageal atresia (OA). *Best Pract Res Clin Anaesthesiol*. 2010;24:387–401.

B.2. Describe management in the NICU before surgery.

After the diagnosis of TEF is established, the baby should not be fed, and intravenous (IV) replacement of fluid and glucose provided. A drainage tube should be placed in the proximal esophageal pouch and kept on intermittent suction to minimize aspiration of oral secretions. He should be positioned either prone or supine with the head up 30 degrees to minimize reflux of gastric fluids into the lungs via the fistula. Antibiotics to treat aspiration pneumonia should be given when appropriate. Ensure that blood is available from the blood bank. Because the patient will require a thoracotomy with lung retraction and intermittent compression of the trachea and great vessels, an arterial catheter is mandatory for the case. This should ideally be placed in the NICU. An umbilical artery catheter may be conveniently placed by a qualified neonatologist. Two additional IV catheters should also be placed. A central venous catheter is not necessary. Avoid placing IV access in the right arm because this arm will most likely be elevated during right thoracotomy and access to it may be limited.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092–1099.

Knottenbelt G, Skinner A, Seefelder C. Tracheo-oesophageal fistula (TOF) and oesophageal atresia (OA). *Best Pract Res Clin Anaesthesiol*. 2010;24:387–401.

Pinheiro P, Simões e Silva AC, Pereira RM. Current knowledge on esophageal atresia. *World J Gastroenterol*. 2012;18:3662–3672.

B.3. How is severe lung disease managed before repair?

Very early primary repair is considered standard of care. However, there remains a subset of neonates with either severe pneumonia or respiratory distress syndrome (from prematurity), who are poor anesthetic and surgical risks (Waterston type C)

and who need to be intubated because of respiratory disease. The baby can be intubated conventionally while a simple gastrostomy is simultaneously placed to relieve gastric distension that can occur with PPV in the setting of a type C TEF. This procedure can be performed under local anesthesia. The problem with this approach is that by decompressing the stomach, gas from the trachea can now bypass the lungs and exit through the stomach. This is especially a concern if the baby's lungs are noncompliant from pneumonia or respiratory distress syndrome. This can make it difficult or impossible to ventilate the baby adequately. Alternately, the baby can be ventilated using a high-frequency oscillator, which has the advantage of providing oxygenation and carbon dioxide (CO_2) removal while minimizing the peak inspiratory pressure and therefore gastric distension.

Ho AM, Dion JM, Wong JC. Airway and ventilatory management options in congenital tracheoesophageal fistula repair. *J Cardiothorac Vasc Anesth*. 2016;30:515–520.

Holcomb GW III. Thoracoscopic surgery for esophageal atresia. *Pediatr Surg Int*. 2017;33:475–481.

B.4. Should this patient be intubated preoperatively for airway protection?

Unless mandated by severe pulmonary disease, the child is not intubated preoperatively to minimize the possibility of gastric distension from PPV through the fistula. Intubation does not protect the child from aspiration of gastric contents through the fistula.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092–1099.

C. Intraoperative Management

C.1. What invasive lines and monitoring are appropriate before induction? After induction?

- At least one peripheral IV should be in place before induction. A second may be placed after the patient is anesthetized. If the surgeon intends to give the child total parenteral nutrition postoperatively, a central line may be placed. An arterial catheter for blood gas and hemodynamic monitoring should be in place before incision. It is especially useful if thoracoscopy is planned. If a peripheral arterial is not feasible, an umbilical arterial line may be placed by a skilled NICU practitioner.
- Electrocardiogram, oxygen saturation, end-tidal CO_2, and rectal temperature should also be monitored. A precordial stethoscope should be placed over the left axilla to assess breath sounds in case of inadvertent movement of the endotracheal tube (ETT) during surgical retraction or positioning. A second stethoscope placed over the stomach may be useful to assess if the fistula is being ventilated.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092–1099.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:507–508.

Knottenbelt G, Skinner A, Seefelder C. Tracheo-oesophageal fistula (TOF) and oesophageal atresia (OA). *Best Pract Res Clin Anaesthesiol*. 2010;24:387–401.

C.2. Discuss fluid and temperature management for this baby.

As with all neonates undergoing surgery, meticulous attention to fluid management and temperature is essential. Limited subcutaneous fat renders the neonate prone to hypothermia. Hypothermia is dangerous because it will increase pulmonary vascular resistance and may result in a reversion to transitional

circulation, greatly complicating intraoperative care. The child should be transported to the operating room (OR) in a warmed isolette, with a stocking cap on his head to minimize heat loss. The OR should be prewarmed to at least 30°C. Surgical irrigation and RBCs should be warmed. Using a forced-air convective warming system is strongly recommended.

The baby will require intraoperative glucose infusion. One must remember that once infused, the glucose will be rapidly metabolized, leaving behind a potentially hypotonic solution. In the past, free water was routinely infused in the form of a hypotonic glucose solution such as D10/0.2 normal saline (NS) administered at a rate of 4 mL/kg/hr. This was sufficient to prevent hypoglycemia. Recent studies have focused on the role of increased antidiuretic hormone (ADH) secretion, which occurs during surgery. This ADH secretion renders the infant at a fivefold increased risk of severe hyponatremia when given free water. Current recommendations including infusing *isotonic* glucose solution for maintenance. Insensible losses should be estimated at 3 to 4 mL/kg/hr and replaced with an isotonic (non–glucose-containing) solution. Urine output (ideally 1 mL/kg/hr) may be difficult to assess accurately in a low birth weight baby.

Nkilly GE, Michelet D, Hilly J, T et al. Postoperative decrease in plasma sodium concentration after infusion of hypotonic intravenous solutions in neonatal surgery. *Br J Anaesth*. 2014;112:540–545.

Thomas J. Reducing the risk in neonatal anesthesia. *Pediatr Anaesth*. 2014;24:106–113.

Wang J, Xu E, Xiao Y. Isotonic versus hypotonic maintenance IV fluids in hospitalized children: a meta-analysis. *Pediatrics*. 2014;133:105–113.

C.3. What are the options regarding induction and intubation?

The goal is to intubate the baby to allow adequate gas exchange with the lowest possible inspiratory pressure needed to inflate the lungs, avoid atelectasis, and minimize gas flow through the

fistula. One-lung ventilation is generally not required. The most important aspect of the intubation is the correct positioning of the ETT. The goal is to have the tip of the ETT distal to the fistula yet proximal to the carina. If the tube is deliberately placed deep (into the right mainstem) with the bevel facing forward, then slowly pulled back just until breath sounds occur on the left equal to the right, the tube is likely to be in good position. Keep in mind the following options:

1. Avoidance of PPV until the fistula is ligated will decrease the risk of gastric distension. One can intubate awake or after inhalation induction while maintaining spontaneous ventilation. Awake intubation can be associated with the risk of increased intracranial pressure or intraventricular hemorrhage in the premature infant and discomfort to the child. If one chooses to intubate after induction, this will require deep anesthesia with spontaneous ventilation using an inhalation anesthetic. The lowest inspiratory pressure assistance is used to prevent atelectasis while minimizing distension of the stomach. If the lungs are suspected of being poorly compliant due to pneumonia or prematurity, then mask ventilation should be avoided. Good intubating conditions can be achieved with a volatile agent, but maintaining adequate ventilation and surgical conditions during a thoracotomy without muscle relaxant may be challenging.
2. Rapid sequence IV induction and placement of the ETT below the fistula is another option. If the ETT is in good position, then muscle relaxants can be given and normal PPV maintained. The difficulty lies in maintaining good position of the ETT during surgical manipulation and turning the patient lateral. Alabbad et al. describe a disastrous scenario in which a neonate with TEF was intubated and ETT position confirmed by breath sounds; yet

after turning the patient, the ETT migrated *into* the fistula without being recognized. This resulted in failure to ventilate the baby and eventual cardiac arrest.

3. Another option, to avoid the risk of ETT malposition, is to deliberately keep the tip of the tube *above* the fistula (if it is shown by bronchoscopy to be small) and keep ventilation pressures low until the fistula is ligated. This comes with a high risk of gastric distension.
4. In cases where the lung compliance is poor, or the fistula is located near the carina, high-frequency oscillating ventilation (HFOV) can be used because it provides gas exchange with a much lower inspiratory pressure. This technique is technically cumbersome and requires utilization of a total IV anesthetic technique.

Alabbad SI, Shaw K, Puligandla PS, et al. The pitfalls of endotracheal intubation beyond the fistula in babies born with type C esophageal atresia. *Semin Pediatr Surg*. 2009;18(2):116–118.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092–1099.

Ho AM, Dion JM, Wong JC. Airway and ventilatory management options in congenital tracheoesophageal fistula repair. *J Cardiothorac Vasc Anesth*. 2016;30:515–520.

C.4. What is the role of rigid and fiberoptic bronchoscopy in this patient prior to incision?

Perioperative bronchoscopy before commencing TEF repair allows assessment of the size and location of the fistula. A cervical level fistula does not require a thoracotomy to repair. A low-lying or subcarinal fistula will predict difficult in placing an ETT that does not ventilate the fistula. The presence of a second fistula can be ruled out. If deemed appropriate, the fistula can be occluded using a no. 3 French Fogarty occlusion catheter, thereby allowing normal PPV without distending the abdomen. Following placement of the balloon, the rigid bronchoscope is

removed and the child intubated with a microcuff ETT *alongside* the catheter. There is a real possibility that during positioning or surgical manipulation, the Fogarty balloon may slide back into the trachea. This could precipitate immediate complete airway obstruction if not promptly recognized and treated.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092–1099.

Ho AM, Dion JM, Wong JC. Airway and ventilatory management options in congenital tracheoesophageal fistula repair. *J Cardiothorac Vasc Anesth*. 2016;30:515–520.

Knottenbelt G, Skinner A, Seefelder C. Tracheo-oesophageal fistula (TOF) and oesophageal atresia (OA). *Best Pract Res Clin Anaesthesiol*. 2010;24:387–401.

Rinkel R, Van Poll D, Sibarani-Ponsen R, et al. Bronchoscopy and Fogarty balloon insertion of distal tracheo-oesophageal fistula for oesophageal atresia repair with video illustration. *Ann Otol Rhinol Laryngol*. 2017;126:6–8.

C.5. Describe the steps of an open repair of EA/TEF.

First, the patient is positioned in the lateral position, left side down. If the patient has a right-sided aortic arch (rare), the surgeon will position the patient with right side down. A retropleural approach is used, which minimizes the danger from an anastomotic leak. The azygos vein is ligated to better visualize the fistula. The fistula is exposed and ligated, leaving a little stump; this usually occurs within 45 minutes. It is important to remember that a fistula stump remains after repair, at least initially. When the patient returns for follow-up surgery (e.g., esophageal dilations), during intubation, the ETT may be observed to pass through the vocal cords yet the tip end up in the stump, precluding effective ventilation. An anterior posterior chest x-ray (AP CXR) will not show this, but a lateral film will. This possibility should always be entertained if unable to ventilate one of these patients despite apparent successful

intubation. If the patient is stable, then normal PPV can commence while the repair of the esophagus begins. The upper esophagus is mobilized, then the distal esophagus. The esophagus is joined together. Following this, a feeding tube is placed across the anastomosis to allow feeding (if the patient does not have a gastrostomy). The lung should be carefully reexpanded to eliminate atelectasis before closure. Chest tubes are not routinely placed following repair.

Knottenbelt G, Skinner A, Seefelder C. Tracheo-oesophageal fistula (TOF) and oesophageal atresia (OA). *Best Pract Res Clin Anaesthesiol*. 2010;24:387–401.

Pinheiro P, Simões e Silva AC, Pereira RM. Current knowledge on esophageal atresia. *World J Gastroenterol*. 2012;18:3662–3672.

C.6. What are common intraoperative problems, and how can they be managed?

Interference with ventilation is the most common problem and can have many causes. Lung retraction with resulting atelectasis leads to frequent desaturation. It may be difficult if not impossible to maintain normocarbia. The partial pressure of arterial carbon dioxide ($PaCO_2$) may rise to 70 to 80 mmHg despite all attempts to optimize ventilation. If the patient has a Fogarty catheter in the fistula, it may be displaced into the trachea causing total airway obstruction. Surgical manipulation of the soft trachea makes the ETT vulnerable to kinking or displacement distally into right mainstem or proximally above the fistula. Frequent compression of vital structures in the mediastinum can lead to profound hemodynamic compromise. Blood and secretions are a constant problem, which risk obstructing the tube. The ETT should be suctioned frequently, more so if blood is seen. The retracted lung may need to be intermittently re-expanded to avoid severe hypoxia. Severe gastric distension before ligation of the TEF may require

emergent gastric needle decompression. It is crucial to maintain close communication with the surgeon. Avoid hypothermia.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092–1099.

Ho AM, Dion JM, Wong JC. Airway and ventilatory management options in congenital tracheoesophageal fistula repair. *J Cardiothorac Vasc Anesth*. 2016;30:515–520.

Knottenbelt G, Skinner A, Seefelder C. Tracheo-oesophageal fistula (TOF) and oesophageal atresia (OA). *Best Pract Res Clin Anaesthesiol*. 2010;24:387–401.

C.7. If the surgeon decides to proceed thoracoscopically, how will you perform your anesthetic? Is one-lung ventilation required? What are some complications unique to thoracoscopy in the newborn?

Thoracoscopy to repair TEF/EA has gained increasing popularity over the past decade. Three major advantages are described. First, the approach provides excellent visualization of the fistula, which allows rapid ligation and stabilization of ventilation. Second, avoidance of thoracotomy results in less pain. Third, avoiding posterolateral thoracotomy results in better chest wall symmetry and less long-term scoliosis. A meta-analysis by Borruto et al. showed that the anastomosis leak rate was not increased in the thoracoscopic group.

To perform this anesthetic, an arterial line is mandatory due to the significant gradient between end-tidal and arterial CO_2. Concerns regarding intubation, PPV, paralysis, fluid, and temperature management are identical to that for an open repair. Opioid requirements may be reduced. Isolating the right lung is *not* required for a successful thoracoscopy. One lung ventilation is helpful but not necessary and may not be tolerated well in the neonate. Deliberate left mainstem ETT intubation to collapse the right lung may result in prolonged left upper lobe lung collapse.

Exposure of the fistula is attained by insufflation of the right chest cavity with CO_2 to a pressure of 5 mmHg. Hypercapnia and acidosis are expected with both open repair and thoracoscopic repair, but the degree of hypercapnia and acidosis is worse with thoracoscopy ($PaCO_2$ 59 mmHg vs. 51 mmHg in one study). The potentially impact of the raised intrathoracic pressure and hypercapnia associated with thoracoscopy on neonatal brain oxygenation has been explored. One single-center study found no significant effect on brain cerebral oximetry measurement in infants having repair thoracoscopically compared to open repair, provided mean arterial pressure was maintained with a combination of fluid and inotropic support.

Borruto FA, Impellizeri P, Montalto AS, et al. Thoracoscopy versus thoracotomy for esophageal atresia and tracheoesophageal fistula repair: review of the literature and meta-analysis. *Eur J Pediatr Surg*. 2012;22:415–419.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092–1099.

Dingemann C, Ure BM. Minimally invasive repair of esophageal atresia: an update. *Eur J Pediatr Surg*. 2013;23:198–203.

Tytgat SH, van Herwaarden MY, Stolwijk LJ, et al. Neonatal brain oxygenation during thoracoscopic correction of esophageal atresia. *Surg Endosc*. 2016;30:2811–2817.

Zani A, Lamas-Pinheiro R, Paraboschi I, et al. Intraoperative acidosis and hypercapnia during thoracoscopic repair of congenital diaphragmatic hernia and esophageal atresia/tracheoesophageal fistula. *Paediatr Anesth*. 2017;27:841–848.

D. Postoperative Management

D.1. When should the baby be extubated?

Although some surgeons prefer to have the baby extubated immediately in the OR to minimize tension on the suture line, this can be risky. Many infants with TEF have a deficiency of tracheal cartilage at the level of the fistula predisposing to

tracheomalacia. This can result in airway obstruction requiring immediate reintubation. Many of the children have significant lung disease from prematurity or aspiration pneumonia; they should stay intubated. If opioid-based postoperative analgesia is planned, mechanical ventilation is preferred due to the risk of hypoventilation. If early extubation is planned, an epidural technique might be helpful. However, if the child is to remain intubated, care should be made to limit inspiratory pressure to protect the repair from disruption.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092–1099.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:510.

Knottenbelt G, Skinner A, Seefelder C. Tracheo-oesophageal fistula (TOF) and oesophageal atresia (OA). *Best Pract Res Clin Anaesthesiol*. 2010;24:387–401.

D.2. What options are available for postoperative analgesia?

For patients who are to remain intubated postoperatively, a narcotic anesthetic technique with fentanyl at 10 to 20 μg per kg with muscle relaxant will give hemodynamic stability and allow analgesia to be continued in the postoperative period. For experienced practitioners, an epidural catheter can also be placed. An epidural catheter threaded through the caudal space can be easily threaded up to the thoracic dermatomes. The position of the catheter placed in this way should be confirmed with fluoroscopy or ultrasound prior to use. This technique should only be undertaken by one who is experienced in regional anesthesia for children.

Broemling N, Campbell F. Anesthetic management of congenital tracheoesophageal fistula. *Paediatr Anaesth*. 2011;21:1092–1099.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:510.

Knottenbelt G, Skinner A, Seefelder C. Tracheo-oesophageal fistula (TOF) and oesophageal atresia (OA). *Best Pract Res Clin Anaesthesiol*. 2010;24:387–401.

D.3. What are early and late complications of TEF repair?

Early anastomosis leakage occurs in up to 15% of patients. This may require immediate exploration or may be managed expectantly. Esophageal dysmotility and gastroesophageal reflux disease (GERD) are common. The dysmotility may be from abnormal innervation of the distal esophagus or may be related to vagal nerve injury during the repair. Stricture of the esophageal anastomosis may require repeated dilatations. Tracheomalacia may be evident postoperatively, and vocal cord paresis has been reported.

Pinheiro P, Simões e Silva AC, Pereira RM. Current knowledge on esophageal atresia. *World J Gastroenterol*. 2012;18:3662–3672.

Wu Y, Kuang H, Ly T, et al. Comparison of clinical outcomes between open and thoracoscopic repair for esophageal atresia with tracheoesophageal fistula: a systematic review and meta-analysis. *Pediatr Surg Int*. 2017;33:1147–1157.

37 Congenital Diaphragmatic Hernia

Dana L. Gurvitch and Fun-Sun F. Yao

A full-term male baby was born with respiratory distress and cyanosis. Physical examination showed barrel chest and scaphoid abdomen. The breath sounds were absent in the left side of the chest; the heart sounds were best heard in the right side of the chest. Labored respiration, nasal flaring, and sternal retraction were found. The baby weighed 2,800 g. Blood pressure was 60/30 mmHg; heart rate, 160 beats per minute; respiration, 70 breaths per minute; and temperature, 36°C (96.8°F). Arterial blood gas analysis on room air showed the following: pH, 7.20; $Paco_2$, 55 mmHg; Pao_2, 35 mmHg; and CO_2 content, 19 mEq per L.

A. Medical Disease and Differential Diagnosis

1. What differential diagnoses are compatible with these signs and symptoms?
2. Describe the incidence and classification of congenital diaphragmatic hernia (CDH).
3. What are the causes of hypoxemia in patients with CDH?
4. How do you assess the severity of pulmonary hypoplasia?
5. How do you make a diagnosis of right-to-left shunting through

the patent ductus arteriosus?

6. What other congenital anomalies are usually associated with CDH?

B. Preoperative Evaluation and Preparation

1. How would you interpret the following arterial blood gas analyses: pH, 7.20; $Paco_2$, 55 mmHg; Pao_2, 35 mmHg; and CO_2 content, 19 mEq per L? How would you correct them?
2. What immediate treatment should be given to improve the newborn's respiratory status preoperatively?
3. Should CDH be repaired urgently once the diagnosis is made and confirmed?
4. What are the effects of nitric oxide (NO) on pulmonary and systemic circulation?
5. What is the current role of extracorporeal membrane oxygenation (ECMO) in the management of CDH?

C. Intraoperative Management

1. What monitors would you use for this neonate during surgery?
2. How would you induce and maintain anesthesia?
3. Would you use nitrous oxide for anesthesia? Why?
4. How would you ventilate the patient?
5. Is the infant with CDH more at risk from hypothermia?
6. The surgeon returned the intrathoracic stomach and intestine to the peritoneal cavity and the ipsilateral lung was found to be hypoplastic and collapsed. The resident anesthesiologist tried to expand the collapsed lung manually with positive airway pressure. Five minutes after the abdomen was closed, the blood pressure suddenly dropped from 70/40 to 30/20 mmHg, the heart rate from 150 to 80 beats per minute, and the pulse oximeter from 95% down to 60% saturation. What would you immediately do?
7. Discuss fluid therapy in this patient.

8. At the conclusion of surgery, would you extubate the patient in the operating room?

D. Postoperative Management

1. What is the mortality rate in patients with CDH? What postoperative problems would you expect in this patient?

A. Medical Disease and Differential Diagnosis

A.1. What differential diagnoses are compatible with these signs and symptoms?

The differential diagnosis of cyanosis and respiratory distress in the newborn is broad and includes respiratory distress syndrome, meconium aspiration, diaphragmatic hernia, persistent pulmonary hypertension (PPH) of the newborn, cyanotic congenital heart disease, choanal atresia, airway abnormalities, and bronchopulmonary sequestration. However, CDH should be suspected in any infant with respiratory distress, shift of cardiac sounds to the right, decreased breath sounds ipsilateral to the side of the hernia, bowel sounds heard in the chest and a concave/scaphoid abdomen. Confirmation of diagnosis includes a chest x-ray demonstrating herniation of abdominal contents into the hemithorax, little or no visible aerated lung on affected side and mediastinal shift (**Fig. 37.1**). If in doubt, a radiopaque dye may be injected through a nasogastric tube to delineate the stomach and intestine in the chest cavity. If the CDH is right sided, the liver may be the only herniated organ and appear as a thoracic soft tissue mass. The internal abdominal view of CDH is shown in **Figure 37.2**.

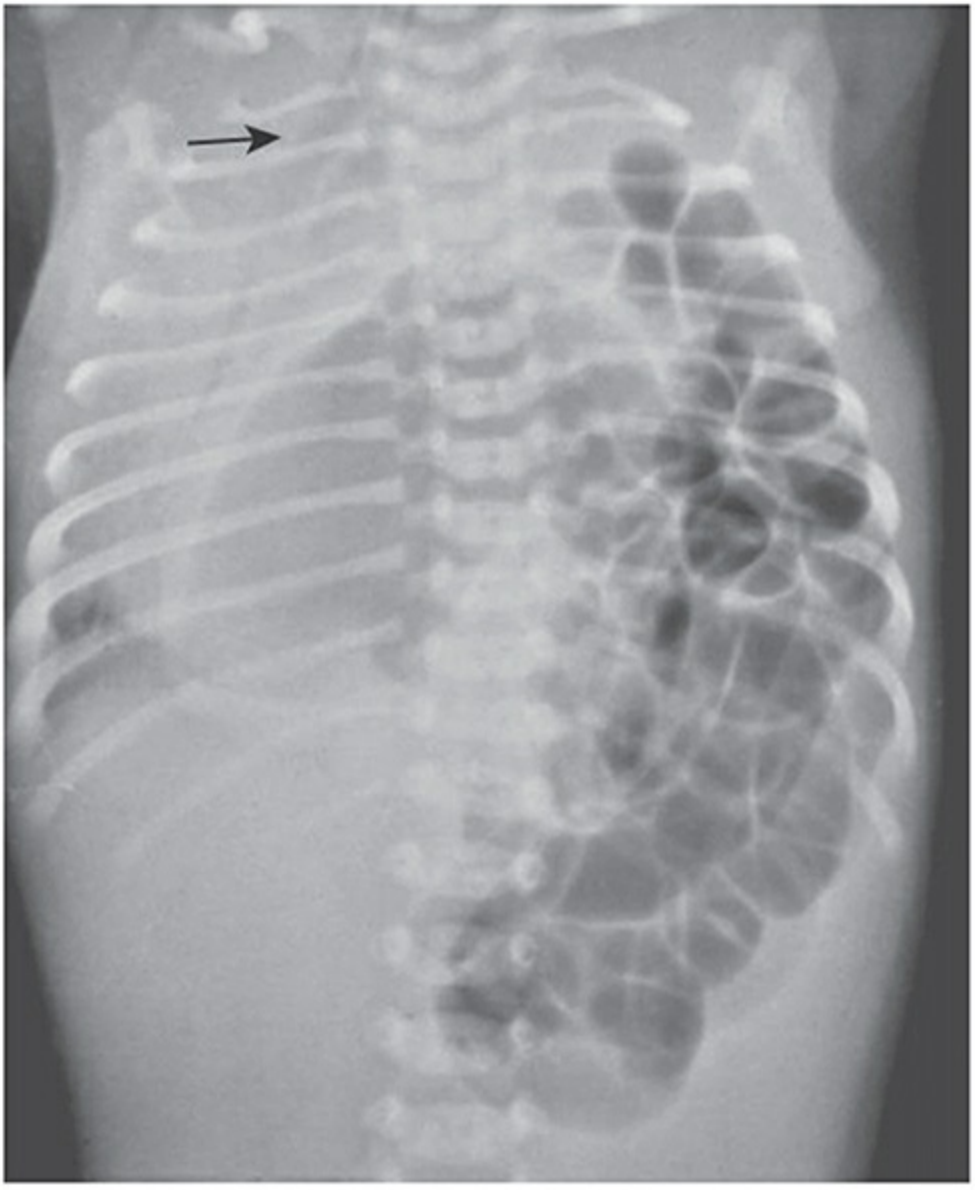

FIGURE 37.1. Chest radiograph of a neonate with a left diaphragmatic hernia. Note shifting of the trachea and bronchi into the right chest (*arrow*). (*Reprinted from Cote CJ, Lerman J, Anderson BJ, eds*. Cote and Lerman's A Practice of Anesthesia for Infants and Children. *6th ed. Philadelphia, PA: Saunders/Elsevier; 2018:859.e2. Copyright © 2018 Elsevier. With permission.*)

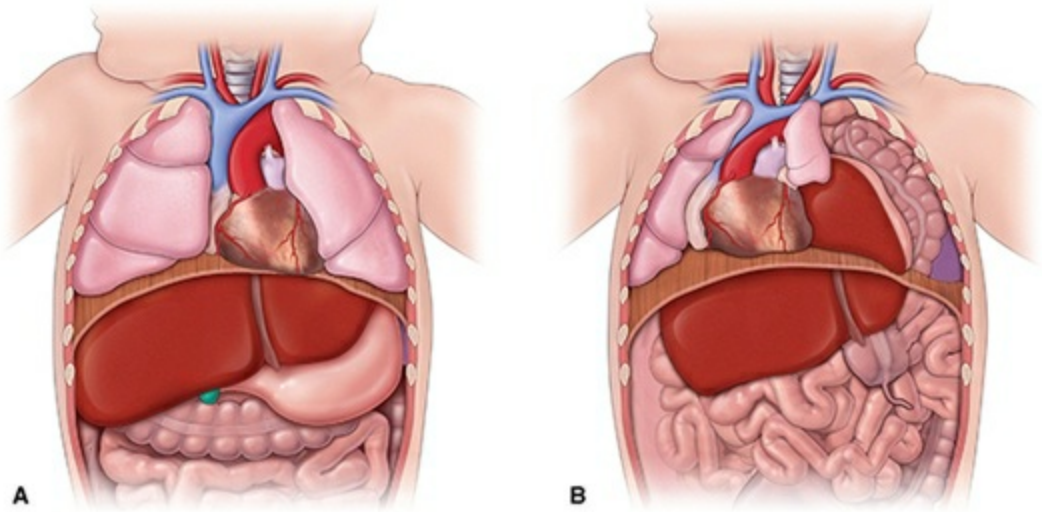

FIGURE 37.2. CDH internal abdominal view. The diaphragm **(left)** is a sheet of flat muscle that separates the heart and lungs from the abdominal cavity. In CDH, a hole in the diaphragm **(right)** allows abdominal organs to move into the chest and restrict lung development.

Hines RL, Maschall KE. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:642–643.

Kliegman RM, Stanton BF, St Geme JW, et al, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:894.

A.2. Describe the incidence and classification of congenital diaphragmatic hernia (CDH).

The incidence of CDH is between 1 per 2,000 and 1 per 3,000 births. Eighty-five percent of defects are left sided and <5% are bilateral. Ninety percent of defects are posterolateral (Bochdalek hernia). Anteromedial and paraesophageal hernias and eventrations make up the remainders (**Fig. 37.3**). There is no difference in mortality between left- and right-sided herniations, although right sided may have a higher incidence of pulmonary complications. Associated anomalies can include central nervous system (CNS) lesions, esophageal atresia, omphalocele, and cardiovascular lesions. In addition, trisomy 21, trisomy 13, trisomy 18, and tetrasomy 12p are examples of syndromes associated with CDH.

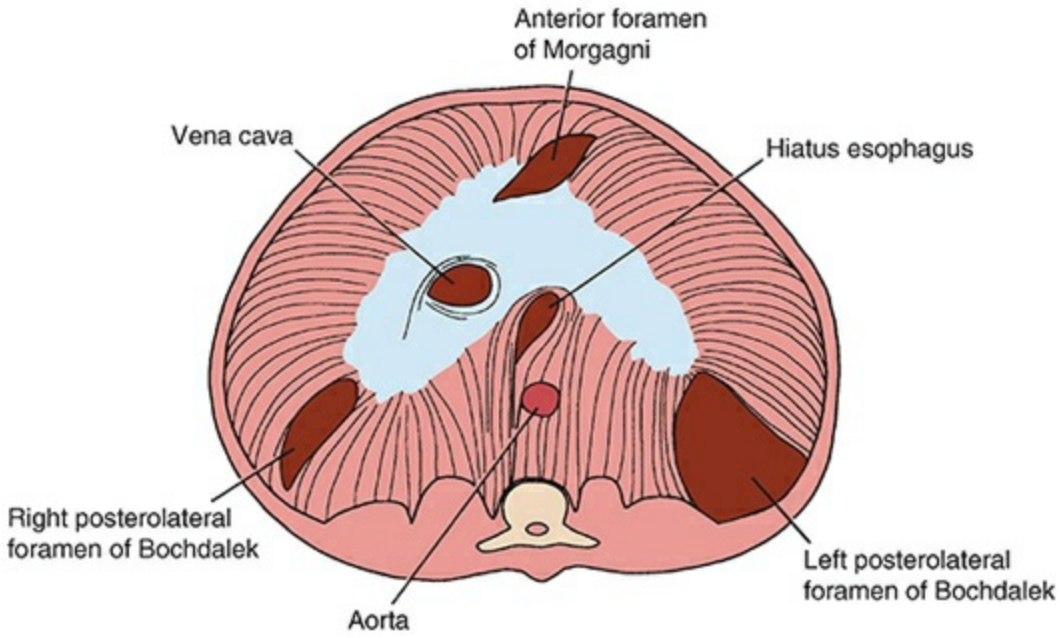

FIGURE 37.3. Potential sites of CDH.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Saunders/Elsevier; 2018:859–860.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2016;567–574.

Partidge EA, Peranteau WH, Herkert L, et al. Right- versus left-sided congenital diaphragmatic hernia: a comparative outcomes analysis. *J Pediatr Surg*. 2016;51(6):900–902.

Pober BR, Russell MK, Ackerman KG. Congenital diaphragmatic hernia overview. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. *Gene Reviews*. Seattle, WA: University of Washington; 1993–2018.

A.3. What are the causes of hypoxemia in patients with CDH?

Infants with CDH have deficient bilateral major airway and vessel branching not explained by simple compression of the ipsilateral and contralateral lungs. The severity of pulmonary vascular hypoplasia correlates with mortality in CDH. Airway maldevelopment leads to reduced total number of bronchi and alveoli at birth with resulting decreased lung compliance and decreases in both ventilation and surface area for gas exchange.

Oxygenation is thus impaired. Pulmonary vascular hypoplasia results in pulmonary hypertension, causing right-to-left shunting through the patent ductus arteriosus, with resultant hypoxemia.

Bancalari E, ed. *The Newborn Lung: Neonatology Questions and Controversies*. 2nd ed. Philadelphia, PA: Elsevier; 2012:381–406.

A.4. How do you assess the severity of pulmonary hypoplasia?

The majority of infants with CDH are diagnosed prenatally by ultrasound, which demonstrates herniated viscera with or without liver in the fetal thorax. The degree of pulmonary hypoplasia is estimated by calculating the lung-to-head ratio where a high ratio (>1.4) indicates good lung size and predicts a good outcome compared to a low ratio (<1.0). In addition, color flow Doppler can be used to assess positioning of the umbilical and portal veins, which are indicative of liver herniation. Fetal magnetic resonance imaging (MRI) is increasingly being used for confirmation of CDH and for anatomy delineation as well as fast spin echo MRI for lung volume calculation and thus further assessment of pulmonary hypoplasia.

Postnatally, the degree of pulmonary hypoplasia can be assessed by the degree of respiratory distress, hypoxemia, acidosis, and ensuing PPH in the newborn. Severe hypoplasia necessitates immediate intubation and mechanical ventilation and ECMO for neonates with critical cardiopulmonary deterioration. Inability to resuscitate in the delivery room is a marker of lethal lung hypoplasia and most centers will not attempt emergency ECMO in this situation.

Bancalari E, ed. *The Newborn Lung: Neonatology Questions and Controversies*. 2nd ed. Philadelphia, PA: Elsevier; 2012:381–406.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Saunders/Elsevier; 2018:859–860.

Gorincour G, Bouvenot J, Mourot MG, et al. Prenatal prognosis of congenital diaphragmatic hernia using magnetic resonance imaging measurement of fetal lung volume. *Ultrasound Obstet Gynecol*. 2005;26:738–744.

Hedrick HL, Crombleholme TM, Flake AW, et al. Right congenital diaphragmatic hernia: prenatal assessment and outcome. *J Pediatr Surg*. 2004;39:319–323.

A.5. How do you make a diagnosis of right-to-left shunting through the patent ductus arteriosus?

Clinical signs of ductal patency include murmur, tachycardia, bounding peripheral pulses with wide pulse pressure, congestive heart failure, and unexplained metabolic acidosis. Preductal (upper extremity) and postductal (lower/umbilical arteries) oxygen saturation measurements by pulse oximetry demonstrate a 10% or higher gradient difference (with preductal saturation being higher). The gold standard for diagnosis is with Doppler echocardiogram to demonstrate the size of the ductal opening and the shunt and allow estimation of mean pulmonary pressure.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2016:723–726.

Fuhrman B, Zimmerman J, Clark R, et al, eds. *Fuhrman & Zimmerman's Pediatric Critical Care*. 5th ed. Philadelphia, PA: Elsevier; 2016:449.

Mariani G, Dik PB, Ezquer A, et al. Pre-ductal and post-ductal O2 saturation in healthy term neonates after birth. *J Pediatr*. 2007;150:418–421.

A.6. What other congenital anomalies are usually associated with CDH?

About one-third of patients born with CDH have major congenital abnormalities.

- 10% having a chromosome abnormality, most commonly trisomy 18 and isochromosome 12p
- 25% having cardiovascular malformations including ventricular septal defect (VSD), autism spectrum disorder (ASD), tetralogy of Fallot (TOF), and hypoplastic left heart syndrome

- 28% having CNS abnormalities including neural tube defects, hydrocephalus, agenesis of corpus callous, and sensorineural hearing loss
- 15% having genitourinary abnormalities including undescended testis and hypospadias
- 20% having gastrointestinal malformations including malrotation, atresia, omphalocele, and gastroesophageal reflux

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. New York: Churchill Livingstone; 2012:510–512.

B. Preoperative Evaluation and Preparation

B.1. How would you interpret the following arterial blood gas analyses: pH, 7.20; $PaCO_2$, 55 mmHg; PaO_2, 35 mmHg; and CO_2 content, 19 mEq per L? How would you correct them?

The blood gas analyses demonstrate a mixed respiratory and metabolic acidosis with severe hypoxemia. In this patient, the severe hypoxemia is due to the pulmonary pathology and PPH. As alveolar P_{O_2} decreases below a threshold of 50 mmHg at normal P_{CO_2}, ventilation increases initially and respiratory alkalosis followers. However, if hypoxemia is not corrected, patient fatigue results in CO_2 retention and a respiratory acidosis. In addition, the hypoxemia results in anaerobic metabolism and a concomitant lactic acidosis.

Treatment includes mechanical ventilation with control of oxygenation and ventilation. Metabolic acidosis should be corrected by administration of sodium bicarbonate and improvement of circulation/perfusion with fluid therapy.

Kliegman RM, Stanton BF, St Geme JW, et al, eds. *Nelson Textbook of*

Pediatrics. 21st ed. Philadelphia, PA: Elsevier; 2019:410–421.

Pittman RN. *Regulation of Tissue Oxygenation*. San Rafael, CA: Morgan & Claypool Life Sciences; 2011:33–35.

B.2. What immediate treatment should be given to improve the newborn's respiratory status preoperatively?

Immediate treatment should include intubation and ventilation and decompression of the intrathoracic bowel with a nasogastric tube. Barotrauma and further pulmonary damage must be avoided by maintaining peak inspiratory pressures under 25 cm H_2O and fraction of inspired oxygen (FIO_2) adjusted to preductal arterial saturations >85%. Institution of pressure support ventilation, use of high-frequency oscillatory ventilation, permissive hypercarbia, and even ECMO are modes to optimize the oxygenation status.

Bancalari E, ed. *The Newborn Lung: Neonatology Questions and Controversies*. 2nd ed. Philadelphia, PA: Elsevier; 2012:381–406.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Saunders/Elsevier; 2018:859–860.

King H, Booker PD. Congenital diaphragmatic hernia in the neonate. *Contin Educ Anaesth Crit Care Pain*. 2005;5:171–174.

B.3. Should CDH be repaired urgently once the diagnosis is made and confirmed?

Surgical repair of CDH was treated as a surgical emergency. However, improvement in gas exchange, thoracic compliance, or $PaCO_2$ was not proven from immediate surgery. This has resulted in delay for clinical stabilization of the neonate's respiratory and cardiovascular status and ensuring adequate end-organ perfusion, as evidenced by improved oxygenation, decreasing pulmonary vascular hypertension, and correction of metabolic acidosis.

Boloker J, Bateman DA, Wung JT, et al. Congenital diaphragmatic hernia in 120 infants treated consecutively with permissive hypercapnia/spontaneous respiration/elective repair. *J Pediatr Surg*. 2002;37(3):357–366.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Saunders/Elsevier; 2018:859–860.

Mohseni-Bod H, Bohn D. Pulmonary hypertension in congenital diaphragmatic hernia. *Semin Pediatr Surg*. 2007;16(2):126–133.

Wung JT, Sahni R, Moffitt ST, et al. Congenital diaphragmatic hernia: survival treated with very delayed surgery, spontaneous respiration, and no chest tube. *J Pediatr Surg*. 1995;30(3):406–409.

B.4. What are the effects of nitric oxide (NO) on pulmonary and systemic circulation?

In vivo, NO is an endothelium-derived relaxing factor, which causes smooth muscle relaxation and vasodilation. Inhaled NO (iNO) is unique in that it is a selective pulmonary vasodilator and has no effect on systemic circulation. In low concentrations, iNO diffuses into pulmonary smooth muscle, raises the concentration of current good manufacturing practice (cGMP), which induces selective vasodilation and decreased vascular tone. Unfortunately, most neonates with CDH with pulmonary hypertension plus lung hypoplasia do not have a dramatic response to iNO. A Cochrane review concluded that iNO does not improve outcomes in neonates with CDH and may, in fact, worsen outcomes.

Campbell BT, Herbst KW, Briden KE, et al. Inhaled nitric oxide use in neonates with congenital diaphragmatic hernia. *Pediatrics*. 2014;134(2):e420–e426.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2016:592–593.

Finer N, Barrington KJ. Nitric oxide for respiratory failure in infants born at or near term. *Cochrane Database Syst Rev*. 2006;(4):CD000399. doi:10.1002/14651858.CD000399.pub2.

B.5. What is the current role of extracorporeal membrane

oxygenation (ECMO) in the management of CDH?

Despite wide use over many decades, survival of patients with CDH treated with ECMO remains unchanged at 50%. A recent United Kingdom study showed infants who received ECMO for CDH had significant mortality in the first year of life and there was long-term physical and neurodevelopmental morbidity in the majority of survivors. Consensus of significant risks associated with ECMO, such as bleeding, intracranial hemorrhage, and sepsis, have shifted the implementation of ECMO, as a rescue therapy for infants with persistent preductal hypoxemia and acidosis despite inotropic and ventilator support.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2016:593.

Davis PJ, Firmin RK, Manktelow B, et al. Long-term outcome following extracorporeal membrane oxygenation for congenital diaphragmatic hernia: the UK experience. *J Pediatr*. 2004;144:309–315.

Kays DW. ECMO in CDH: is there a role? *Semin Pediatr Surg*. 2017;26(3):166–170.

C. Intraoperative Management

C.1. What monitors would you use for this neonate during surgery?

Respiratory

- Two pulse oximeters, for preductal and postductal oxygen saturation
- Capnometry
- Inspiratory pressure measurement
- Inspiratory oxygen concentration
- Intraoperative arterial blood gas analysis

Cardiovascular

- Five-lead electrocardiogram

- Blood pressure cuff
- Arterial line: right radial artery for preductal Pao_2
- Central venous pressure (CVP) line for evaluating volume status and right ventricular performance

Thermoregulatory

- Esophageal or rectal temperature probe

C.2. How would you induce and maintain anesthesia?

In general, the preoperative care of the neonate is continued into the operating room with the addition of high-dose opioids and nondepolarizing muscle relaxant. Ventilation strategies focus on permissive hypercarbia (60 to 65 mmHg), preductal oxygen saturation of 90% to 95%, and peak pressures <25 cm H_2O.

Volatile agents may be instituted with precaution because systemic vascular resistance may decrease more than pulmonary vascular resistance (PVR) resulting in worsening of right-to-left shunt. Frequent blood gas sampling will guide changes in respiratory management and assessment of acid–base status. Availability of agents to maintain blood pressure support should be readily available and include isotonic fluids and inotropes such as dopamine and/or dobutamine and hydrocortisone. Meticulous attention to temperature is essential because hypothermia can increase PVR and thus increase right-to-left shunting.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Saunders/Elsevier; 2018:860.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2016:595.

C.3. Would you use nitrous oxide for anesthesia? Why?

Nitrous oxide is avoided because it will expand air-filled cavities (such as bowel) and potentially further compress

functioning lung tissue and because it limits the inspired oxygen concentration, which can be provided to a compromised neonate.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Saunders/Elsevier; 2018:860.

C.4. How would you ventilate the patient?

The goals of ventilation and oxygenation in the operating room are the same as preoperative: Avoid volutrauma by using small tidal volumes and low-peak inspiratory pressures, adequate oxygenation with the goal of saturations in the low to mid 90s, and permissive hypercapnia with maintenance of pH >7.25.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Saunders/Elsevier; 2018:860.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2016:594–595.

C.5. Is the infant with CDH more at risk from hypothermia?

All neonates are susceptible to heat loss because of a high ratio of surface area to body weight, reduced subcutaneous fat, and an underdeveloped ability to shiver (thermogenesis) in response to cold. However, infants with CDH have increased morbidity and mortality secondary to hypothermia because the resulting increased PVR can cause decreased oxygen delivery, worsening acidosis, shunting, and continued increases in PVR. Concentrated efforts to maintain normothermia are mandatory and include maintaining ambient operating room temperature >23°C, use of warmed intravenous fluids, passive insulation with drapes and blankets, forced-air warming, and passive humidification of inspired anesthetic gases.

Bajwa SJS, Swati. Perioperative hypothermia in pediatric patients: diagnosis, prevention and management. *Anaesth Pain Intensive Care*. 2014;18(1):97–100.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2016:594–595.

C.6. The surgeon returned the intrathoracic stomach and intestine to the peritoneal cavity and the ipsilateral lung was found to be hypoplastic and collapsed. The resident anesthesiologist tried to expand the collapsed lung manually with positive airway pressure. Five minutes after the abdomen was closed, the blood pressure suddenly dropped from 70/40 to 30/20 mmHg, the heart rate from 150 to 80 beats per minute, and the pulse oximeter from 95% down to 60% saturation. What would you immediately do?

Any sudden deterioration in blood pressure, heart rate, oxygen saturation, or pulmonary compliance is suggestive of tension pneumothorax. Auscultation of the chest, particularly the contralateral side, should be done immediately. If absent or diminished breath sounds confirm the diagnosis, a chest tube should be inserted immediately. A large-bore intravenous catheter with needle may be inserted to release the tension pneumothorax if a chest tube is not immediately available.

The tension pneumothorax is usually on the contralateral side because the high airway pressure required to inflate the hypoplastic lung may rupture the normal alveoli on the contralateral side, resulting in pneumothorax. Moreover, the ipsilateral chest usually already has a chest tube after surgery.

If there is no pneumothorax, or if deterioration is not improved after insertion of a chest tube, inferior vena cava compression (resulting in decreased venous return and decreased cardiac output) should be considered. The abdominal cavity is

often underdeveloped and unable to fully accommodate the returned abdominal organs, which increases the intra-abdominal pressure, displaces the diaphragm cephalad, and ultimately decreases pulmonary compliance (in the healthy lung). The net result clinically is desaturation, hypercarbia, and overall instability. In this circumstance, the abdominal wound should be reopened to relieve the compression on the great vessels and displacement of the diaphragm. A patch closure of the abdomen can be attempted or a Silo pouch is placed until growth allows safe return to the abdominal cavity.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Saunders/Elsevier; 2018:860.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2016:594–595.

C.7. Discuss fluid therapy in this patient.

Fluid and electrolyte management in newborns should be focused on maintaining homeostasis while recognizing the impact of gestational age, physiologic changes in renal function, redistribution of total body water, water loss secondary to environmental factors, underlying medical condition of neonate, and surgical stress on fluid requirements. Neonates are obligate sodium losers, and therefore, exogenous sodium should be supplied. In addition, urine concentrating ability is limited in the newborn and as a result, the risk of volume depletion is increased due to the inability to maximally concentrate urine, decreased response to antidiuretic hormone (ADH), limited sodium reabsorption due to tubular immaturity, and reduced responsiveness to aldosterone.

The preoperative fluid deficit may be evaluated by careful history taking, signs and symptoms of dehydration, urine output, and CVP monitoring. Maintenance fluids consisting of 5%

dextrose in one-fourth to one-half strength saline are given at 4 mL/kg/hr. Intraoperative evaporative and third-space losses are replaced with lactated Ringer's, Plasma-Lyte, or saline at approximately 6 to 8 mL/kg/hr. Each milliliter of blood loss is replaced with 3 mL of lactated Ringer's or 1 mL of 5% albumin. Blood pressure, heart rate, urine output, CVP, hematocrit, and electrolytes should guide fluid therapy.

Feld LG, Neuspiel DR, Foster BA, et al. Clinical practice guideline: maintenance intravenous fluids in children. *Pediatrics*. 2018;142:e20183083.

Kliegman RM, Stanton BF, St. Geme JW, et al, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:425–428.

C.8. At the conclusion of surgery, would you extubate the patient in the operating room?

No, the patient should remain intubated at the conclusion of surgery. Varying degrees of pulmonary dysfunction, fluid shifts, and changes in abdominal compliance must be anticipated, and the need for postoperative mechanical ventilation and stabilization is mandatory.

D. Postoperative Management

D.1. What is the mortality rate in patients with CDH? What postoperative problems would you expect in this patient?

Despite advances in medical and surgical treatment, the mortality rate in patients with CDH has remained at approximately 20% to 30% over the past two decades. Pulmonary hypoplasia and PPH are the two main prognosticators. Survival is complicated by both restrictive and obstructive lung disease patterns and BPD is often documented radiographically. Curiously, by childhood or adolescence, survivors of CDH seem to recover and remodel achieving near-

normal lung volumes and mechanics. Gastroesophageal reflux disease, intestinal obstruction, delayed growth, neurocognitive defects, sensorineural hearing loss, and musculoskeletal abnormalities (mainly scoliosis and pectus excavatum) also complicate long term survival.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2016:595–598.

Kliegman RM, Stanton BF, St. Geme JW, et al, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:894.

38 Tetralogy of Fallot

David Whiting and James A. DiNardo

A 5-month-old infant is being evaluated for stable persistent cyanosis with arterial oxygen saturation (Sa_{O_2}) of 70% to 80% since birth. She eats well and is in the 70th percentile for weight (6.5 kg). A transthoracic echocardiogram done before her arrival at your institution suggests that she has tetralogy of Fallot (TOF). Although she has never been noted to have a "Tet spell," her Sa_{O_2} was noted to decrease to 60% during a recent febrile illness. A repeat echocardiogram reveals TOF with severe valvar pulmonary stenosis (PS) and mild subvalvar PS secondary to anterior deviation of the conal septum into the right ventricle outflow tract (RVOT). There is a peak instantaneous pressure gradient of 70 mmHg across the RVOT, as determined by continuous wave Doppler.

A. Medical Disease and Differential Diagnosis

1. What is TOF?
2. What is the pathophysiology of TOF/PS?
3. What is shunting, and how is Q_P:Q_S calculated?
4. What is the pathophysiology of TOF with pulmonary atresia?
5. How is Sa_{O_2} determined in single ventricle physiology?
6. What is a "pink Tet"?

7. What are hypercyanotic spells? How are they treated?
8. What palliative surgical procedures are available for treating patients with TOF/PS?
9. What palliative catheter-based procedures are available for patients with TOF?
10. What definitive surgical procedures are available for treating patients with TOF/PS?
11. What palliative and definitive surgical procedures are available for patients with TOF with pulmonary atresia?
12. What are the long-term outcomes of patients with TOF?

B. Preoperative Evaluation and Preparation

1. What preoperative history and physical examination information do you want?
2. Which other abnormalities need to be considered in this patient?
3. What premedication will you give to a child with congenital heart disease?

C. Intraoperative Management

1. How will you induce anesthesia in this patient if intravenous (IV) access cannot be obtained?
2. Why would end-tidal carbon dioxide (Et_{CO_2}) monitoring be of particular use in a patient with TOF/PS?
3. What is near-infrared spectroscopy (NIRS) and what does it measure?
4. What are the important management issues during creation of a palliative shunt?
5. What is the effect of inhalation anesthetics on airway reflexes, myocardial contractility, systemic vascular resistance (SVR), and pulmonary vascular resistance (PVR) in children?
6. What are the pre-cardiopulmonary bypass (pre-CPB) anesthetic goals for a patient undergoing definitive surgical correction of TOF/PS?

7. What interventions will reliably reduce PVR?
8. How does heparin administration and activated coagulation time (ACT) monitoring for CPB differ in children as compared with adults?
9. How is heparin reversed?
10. What is the incidence of protamine reactions in children?
11. What is the role of transesophageal echocardiography (TEE) in this patient?
12. What effect would a residual ventricular septal defect (VSD) have in this patient following separation from CPB?

D. Postoperative Management

1. How should postoperative ventilation be managed in this patient following placement of a transannular patch for TOF/PS?
2. Following complete repair of TOF/PS in an infant, what Sao_2 is acceptable?
3. Following placement of a modified Blalock-Taussig shunt (MBTS) for TOF/PS in an infant, what Sao_2 is acceptable?
4. What is junctional ectopic tachycardia (JET)?

A. Medical Disease and Differential Diagnosis

A.1. What is TOF?

In 1888, French physician Étienne-Louis Arthur Fallot described a congenital heart defect with four characteristics: (1) large VSD, (2) right ventricular (RV) outflow obstruction, (3) overriding aorta, and (4) right ventricle hypertrophy (RVH). Broadly defined, TOF is a complex of anatomic malformations consisting of a large malaligned conoventricular VSD; rightward and anterior displacement of the aorta such that it overrides the VSD; and a variable degree of subvalvar RVOT obstruction due to anterior, superior, and leftward deviation of the conal

(infundibular) ventricular septum. In addition, RV abnormalities in the septal and parietal bands of the crista supraventricularis exacerbate the infundibular RVOT obstruction. RVH is the result of chronic RVOT obstruction. The most common associated lesion is a right aortic arch with mirror image arch vessel branching that occurs in 25% of patients with TOF. In this lesion, the innominate artery gives rise to the left carotid and left subclavian arteries and the right carotid and subclavian arteries arise separately. TOF/PS and TOF with pulmonary atresia are two broad subsets of TOF. A third rare variant of TOF occurs when the pulmonary valve is absent.

Tetralogy of Fallot with Pulmonary Stenosis

TOF/PS has the four features of TOF in conjunction with varying degrees of valvar PS. At one end of the spectrum, the pulmonary valve annulus is mildly hypoplastic with minimal fusion of the pulmonary valve leaflets (**Fig. 38.1A**). At the other end of the spectrum, the pulmonary annulus is very small and the pulmonary valve leaflets are nearly fused. RVOT from valvar PS is fixed, whereas the subvalvar component of RVOT obstruction is dynamic. If left uncorrected, compensatory RVH from valvar or subvalvar components of the RVOT increases the mass of the RV and the infundibulum and worsens subvalvar obstruction. The anatomy of TOF/PS can usually be definitively delineated by two-dimensional transthoracic echocardiography, so further imaging with cardiac catheterization is rarely necessary or indicated.

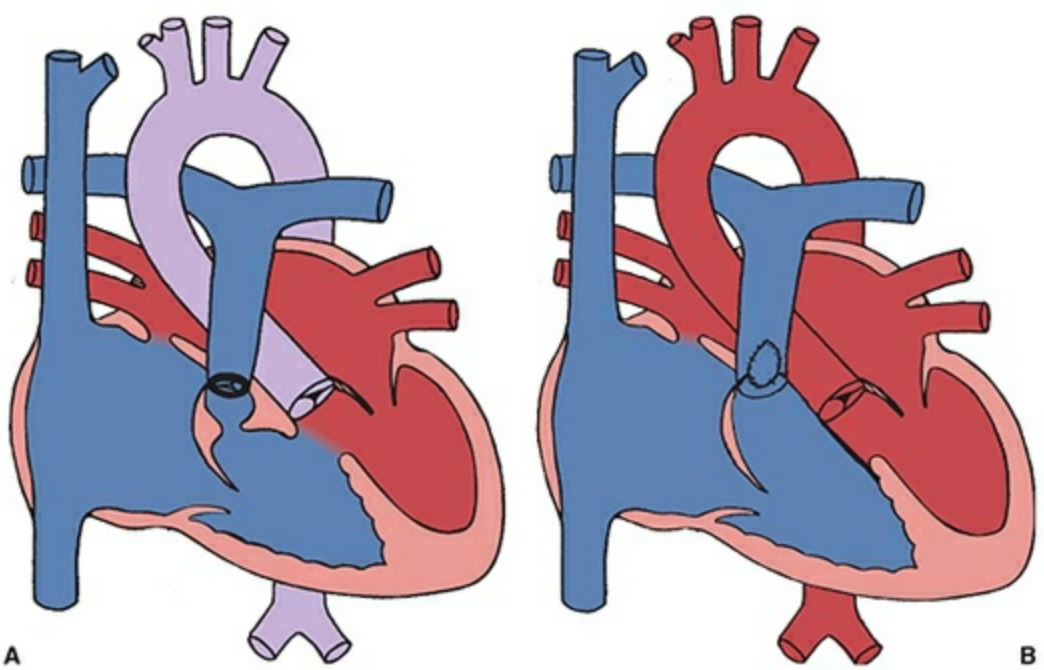

FIGURE 38.1. A. Uncorrected tetralogy of Fallot with pulmonary stenosis (TOF/PS) demonstrating malalignment ventricular septal defect (VSD) with aortic override, valvular and subvalvular (dynamic) PS. There is a left aortic arch. **B.** Definitively repaired TOF/PS with VSD closure creating left ventricle to aortic continuity, resection of subvalvular muscle bundles and deviated conal septum, and creation of a transannular patch (with pulmonary valvectomy) creating pulmonary insufficiency. A small atrial-level communication has been left.

Tetralogy of Fallot with Pulmonary Atresia

TOF with pulmonary atresia has the features of TOF with infundibular and pulmonary valvar atresia in conjunction with varying degrees of pulmonary artery (PA) atresia. TOF with pulmonary atresia patients are divided into four groups based on the degree of PA atresia. *Group 1* patients have isolated infundibular and pulmonary valve atresia with main PA and branch PAs of near-normal size and architecture. In some of these patients, the main PA may extend to the atretic infundibulum. In others, atresia involves a short segment of the main PA (**Fig. 38.2**). Patients in this group have pulmonary blood flow supplied from a patent ductus arteriosus (PDA). In *group 2* patients, the main PA is absent, but the left and right PAs are in continuity and supplied by a PDA. *Group 3* patients have severely hypoplastic native PAs, and the left and right PAs

may not be in continuity. Pulmonary blood flow is from collateral vessels from the aorta to the PAs, known as major aortopulmonary collateral arteries (MAPCAs). A PDA may be present as well. Some segments of lung may be perfused from MAPCAs, some only by the native PAs, and others by both sources (**Fig. 38.3**). *Group 4* patients have no native PAs, and all pulmonary blood flow is derived entirely from MAPCAs.

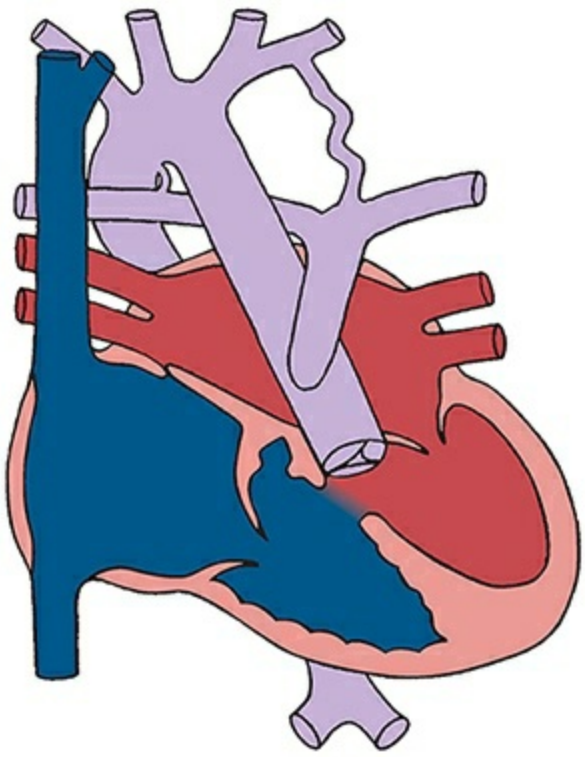

FIGURE 38.2. Illustration of TOF with pulmonary atresia group 1 with short segment pulmonary artery (PA), good-sized PAs in continuity supplied by a right-sided patent ductus arteriosus, and one major aortopulmonary collateral artery from the left subclavian artery. There is a right aortic arch with mirror image arch vessel branching.

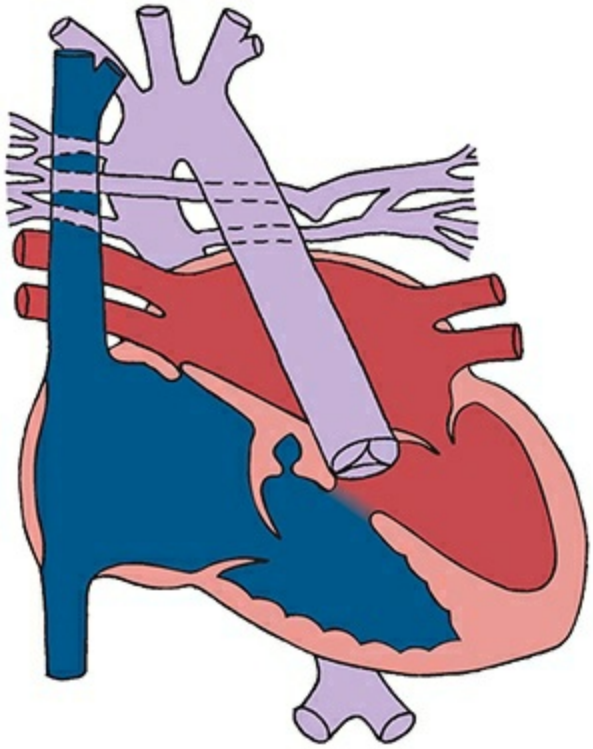

FIGURE 38.3. Illustration of TOF with pulmonary atresia group 3 with no main pulmonary artery (PA), small branch PAs in continuity supplied by major aortopulmonary collateral arteries (MAPCAs). Some lung segments are supplied by the native PAs, whereas others are supplied directly by MAPCAs. There is a right aortic arch with mirror image arch vessel branching.

The anatomy of MAPCAs in TOF with pulmonary atresia can almost never be clearly delineated by two-dimensional transthoracic echocardiography alone. Cardiac catheterization and/or magnetic resonance imaging or magnetic resonance angiography are usually necessary to delineate collateral anatomy and determine Q_P:Q_S.

Jonas RA, ed. Tetralogy of Fallot with pulmonary atresia. In: *Comprehensive Surgical Management of Congenital Heart Disease*. 2nd ed. Boca Raton, FL: CRC Press; 2014:585–602.

Nasr VG, DiNardo JA, eds. *The Pediatric Cardiac Anesthesia Handbook*. Hoboken, NJ: Wiley; 2017.

Tetralogy of Fallot with Absent Pulmonary Valve

TOF with absent pulmonary valve is the least common variant of TOF and accounts for only 3% to 6% of cases of TOF. These

patients have a displaced infundibulum, VSD, and varying degrees of RVOT obstruction as well as aneurysmal dilation of the main and branch PAs from in utero pulmonary regurgitation. The pathophysiology of TOF is complicated by symptoms of tracheobronchial compression that are similar to those caused by an anterior mediastinal mass. These patients usually must be positioned on their sides even when mechanically ventilated.

A.2. What is the pathophysiology of TOF/PS?

The pathophysiology of TOF/PS is a right-to-left (R-L) shunt characterized by the presence of an interventricular communication (VSD) and partial obstruction to RV outflow caused by RV infundibular and valvar stenosis. This is a complex shunt because resistance to RV outflow is a combination of the resistance from the obstructive lesions and the PVR. If the resistance from the RV obstructive lesions is high, changes in PVR will have little effect on shunt magnitude and direction. In most patients with TOF/PS, there is a fixed (valvar) and dynamic (variations in caliber of the RV infundibulum) component to RVOT obstruction. In addition, because the aorta overrides the VSD and the RV, desaturated systemic venous blood tends to stream out of the RV directly to the aorta, even in the presence of mild RVOT obstruction resulting in further systemic desaturation.

The degree of cyanosis is related to the percentage of desaturated hemoglobin. A markedly hypoxemic child with baseline arterial saturations in the 70% range who is anemic may appear less cyanotic than another child with similar oxygen saturation and a hematocrit of 65%. The Sa_{O_2} is determined by the relative volumes and saturations of recirculated systemic venous blood and effective systemic blood flows that have mixed and reached the aorta. This is summarized in the following equation:

$$\text{Aortic } Sao_2 = \frac{[(\text{pulmonary venous } O_2 \text{ saturation} \times \text{effective systemic blood flow}) + (\text{systemic venous } O_2 \text{ saturation} \times \text{recirculated systemic venous blood flow})]}{(\text{total systemic blood flow})}$$

This is demonstrated in **Figure 38.4**. Notice that the patient has a Q_P:Q_S = 0.5:1.

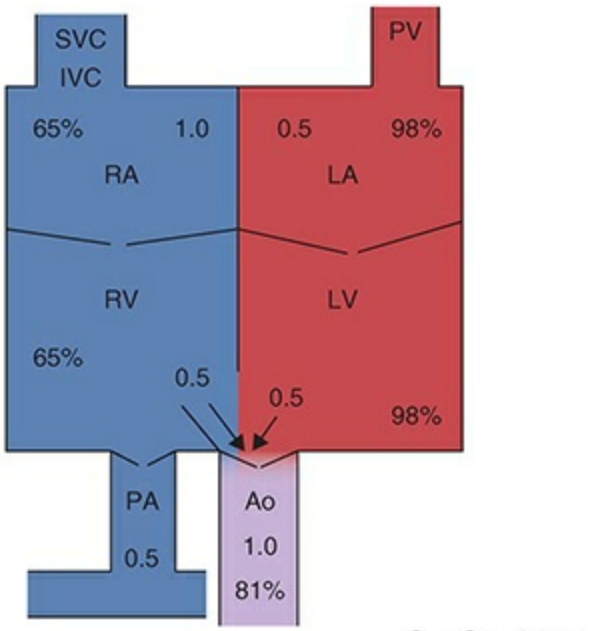

FIGURE 38.4. Chamber oxygen saturations and relative flows for a patient with uncorrected tetralogy of Fallot with pulmonary stenosis (TOF/PS). Arterial oxygen saturation (SaO_2) and Q_P:Q_S are illustrated. Ao, aorta; IVC, inferior vena cava; LA, left atrium; LV, left ventricle; PA, pulmonary artery; PV, pulmonary vein; RA, right atrium; RV, right ventricle; SVC, superior vena cava.

A.3. What is shunting, and how is Q_P:Q_S calculated?

Shunting is the process whereby venous return from one circulatory system is recirculated into the arterial outflow of the same circulatory system. Flow of blood from the systemic venous atrium (right atrium) to the aorta produces a physiologic R-L shunt with recirculation of systemic venous blood. Flow of blood from the pulmonary venous atrium (left atrium) to the PA produces a physiologic left-to-right (L-R) shunt with

recirculation of pulmonary venous blood. A physiologic R-L or L-R shunt is usually caused by a communication (orifice) at the level of the cardiac chambers or great vessels; however, physiologic shunts can exist in the absence of an anatomic shunt; transposition physiology is the best example.

Effective blood flow is the quantity of venous blood from one circulatory system reaching the arterial system of the other circulatory system. Effective pulmonary blood flow is the volume of systemic venous blood reaching the pulmonary circulation, whereas effective systemic blood flow is the volume of pulmonary venous blood reaching the systemic circulation. Effective pulmonary and effective systemic blood flows are always equal, no matter how complex the lesions. Effective blood flow usually is the result of a normal pathway through the heart, but it may occur as the result of an anatomic R-L or L-R shunt.

Total pulmonary blood flow (Q_P) is the sum of effective pulmonary blood flow and recirculated pulmonary blood flow. Total systemic blood flow (Q_S) is the sum of effective systemic blood flow and recirculated systemic blood flow. Total pulmonary blood flow and total systemic blood flow do not have to be equal because the amount of recirculated systemic or pulmonary venous blood do not have to equal. Q_S (systemic cardiac output) tends to remain constant to maintain end-organ blood supply, even in the presence of a physiologic R-L shunt (systemic venous recirculation), although the Sa_{O_2} will be lower. Conversely, a physiologic L-R shunt (pulmonary recirculation) causes pulmonary volume overload.

The calculation of Q_P:Q_S can be made by the Fick equation, where the pulmonary and systemic blood flows (Q_P and Q_S) are calculated individually by dividing the rate of oxygen extraction by the change in oxygen content in the arterial and venous side

of each circulation. The rate of oxygen extraction is the same as effective systemic or pulmonary blood flow and must be equal, so these numbers cancel out in the equation. The calculation of oxygen content is simplified when the determination is made using low inspired concentrations of oxygen (fraction of inspired oxygen [F_{IO_2}]), the contribution of oxygen carried in solution ($P_{O_2} \times 0.003$) can be ignored, so calculation of Q_P:Q_S can be simplified using oxygen saturations. Failure to account for the contribution of oxygen carried in solution, when calculation oxygen content of blood, will introduce substantial error.

$$(S_AO_2 - S_{SVC}O_2) / (S_{PV}O_2 - S_{PA}O_2)$$

where A = arterial, SVC = superior vena cava, PV = pulmonary vein that can be assumed to be 98% in the absence of significant pulmonary disease, and PA = pulmonary artery.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

38.

A.4. What is the pathophysiology of TOF with pulmonary atresia?

The pathophysiology of TOF with pulmonary atresia is characterized as single ventricle physiology because there is a VSD and little or no antegrade flow from the RV. In single ventricle physiology, there is complete mixing of pulmonary venous and systemic venous blood at the atrial or ventricular level and the ventricle(s) distributes output to both the systemic and pulmonary vascular beds. As a result of this physiology, the following are observed:

- Ventricular output is the sum of pulmonary blood flow (Q_P) and systemic blood flow (Q_S).
- Distribution of systemic and pulmonary blood flow is

dependent on the relative resistances to flow (both intracardiac and extracardiac) into the two parallel circuits.

- Oxygen saturations are the same in the aorta and the PA.

Single ventricle physiology can exist with one hypoplastic ventricle and one well-developed ventricle or with two well-formed anatomic ventricles when there is atresia or near atresia of outflow from one of the ventricles.

Examples include the following:

- TOF with pulmonary atresia where pulmonary blood flow is supplied through a large PDA or MAPCAs
- Truncus arteriosus
- Severe neonatal aortic stenosis and interrupted aortic arch; in both lesions, a substantial portion of systemic blood flow is supplied through a PDA.
- Heterotaxy syndrome

In cases where there is a single anatomic ventricle, there is complete or near-complete obstruction to inflow and/or outflow from the hypoplastic ventricle, so there must be an alternate source of either systemic or pulmonary blood flow to ensure postnatal survival. An example of alternate source of blood flow is in ductal-dependent circulation where a PDA forms a direct connection between the aorta and the PDA is the alternate (sole) source of systemic blood flow in hypoplastic left heart syndrome or of pulmonary blood flow in PA with intact ventricular septum. In other instances of a single anatomic ventricle, intracardiac pathways provide both systemic and pulmonary blood flow as in tricuspid atresia with normally related great vessels, a nonrestrictive VSD and minimal or absent PS.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

A.5. How is SaO_2 determined in single ventricle

physiology?

The Sa_{O_2} is determined by the relative volumes and saturations of pulmonary venous and systemic venous blood flows that have mixed and reached the aorta. This is summarized in the following equation:

$$\text{Aortic } O_2 \text{ saturation} = \frac{\begin{array}{c}[(\text{systemic venous saturation})(\text{total systemic venous blood flow}) \\ + (\text{pulmonary venous saturation})(\text{total pulmonary venous blood flow})]\end{array}}{(\text{total systemic blood flow} + \text{total pulmonary venous blood flow})}$$

The primary goal in the management of patients with single ventricle physiology is the optimization of systemic oxygen delivery and perfusion pressure to prevent end-organ (myocardial, renal, hepatic, splanchnic) dysfunction, so the systemic and pulmonary circulations must be balanced. The term balanced circulation is used because both laboratory and clinical evaluations have demonstrated that maximal systemic oxygen delivery (the product of systemic oxygen content and systemic blood flow) is achieved for single ventricle lesions when Q_P:Q_S is at or just below 1:1. Increases in Q_P:Q_S in excess of 1:1 are associated with a progressive decrease in systemic oxygen delivery because the subsequent increase in systemic oxygen content is more than offset by the progressive decrease in systemic blood flow and by diastolic hypotension due to runoff into the pulmonary circulation. Decreases in Q_P:Q_S below 0.7 to 0.8:1 are associated with a precipitous decrease in systemic oxygen delivery because the subsequent increase in systemic blood flow is more than offset by the dramatic decrease in systemic oxygen content.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

A.6. What is a "pink Tet"?

The term pink Tet refers to any patient with TOF/PS or TOF with pulmonary atresia who is not cyanotic. In these patients, Q_P:Q_S is sufficiently high (usually greater than 0.8:1 in the presence of a normal mixed venous saturation and pulmonary vein saturations) to maintain a deoxyhemoglobin concentration less than 5 g per dL with Sao_2 generally >80%. Examples are TOF/PS patients with minimal valvar and subvalvar PS and all patients with TOF with pulmonary atresia where pulmonary blood flow is supplied from a large PDA and/or MAPCAs.

DiNardo JA, Zvara DA. Congenital heart disease. In: DiNardo JA, Zvara DA, eds. *Anesthesia for Cardiac Surgery*. 3rd ed. Oxford: Blackwell; 2008:167–251.

A.7. What are hypercyanotic spells? How are they treated?

Hypercyanotic or "Tet" spells are sudden episodes of profound cyanosis in TOF patients that may be life-threatening. These spells occur more frequently in patients who are severely cyanotic at baseline but may occur in any patient with TOF. The peak frequency of spells is between 2 and 3 months of age. The onset of spells usually prompts urgent surgical intervention, so the anesthesiologist may care for an infant who is at great risk for spells during the perioperative period. The etiology of spells is not completely understood, but acute infundibular spasm that acutely decreases flow through the RV outflow tract and increased the magnitude of the R-L shunt through the VSD is thought to be causal. Crying, defecation, feeding, fever, and awakening from sleep all can be precipitating events. Paroxysmal hyperpnea is the initial finding with an increase in the rate and depth of respirations followed by increasing cyanosis and potential syncope, convulsions, or death. During a spell, the infant will appear pale and limp secondary to poor cardiac output. Hyperpnea maintains and worsens hypoxic spells

by increasing oxygen consumption and lowering the mean intrathoracic pressure, which increases systemic venous return. RV volume and pressure increase because there is an obstruction to RV outflow increasing the R-L shunt and the degree of cyanosis. During a spell, the infant will appear pale and limp secondary to poor cardiac output. Hyperpnea has several deleterious effects that can maintain and worsen a hypoxic spell. Hyperpnea increases oxygen consumption through the increased work of breathing. Hypoxia induces a decrease in SVR, which further increases the magnitude of the R-L shunt. Treatment of a "Tet spell" is focused on increasing pulmonary blood flow and decreasing the magnitude of the R-L shunt. It includes the following:

- Administration of 100% oxygen
- Compression of the femoral arteries or placing the patient in a knee-chest position to transiently increase SVR and reduce the magnitude of the R-L shunt
- Manual compression of the abdominal aorta to increase SVR and reduce the R-L shunt. This maneuver is particularly effective in the anesthetized patient. A cardiac surgeon can manually compress the ascending aorta to increase impedance to left ventricle (LV) ejection and reduce the R-L shunt.
- Administration of IV morphine sulfate (0.05 to 0.1 mg per kg) for sedation reduces oxygen demand and reduces hyperpnea by depressing the respiratory drive.
- Administration of 15 to 30 mL per kg of a crystalloid solution IV. Increasing preload to the heart increases the diameter of the RVOT and reduces dynamic RVOT obstruction.
- Administration of sodium bicarbonate to treat the severe metabolic acidosis that can be seen during a spell. Correction of the metabolic acidosis will help normalize SVR and reduce hyperpnea. Empiric administration of sodium bicarbonate (1

to 2 mEq per kg IV) in the absence of a blood gas determination should be considered during a spell.

- Phenylephrine (5 to 10 μg per kg IV or 2 to 5 μg/kg/min as an infusion) can be used to increase SVR and reduce R-L shunting. In the presence of severe RV outflow obstruction, phenylephrine-induced increases of PVR will have little or no effect on RV outflow resistance. Treatment with phenylephrine increases SVR and may decrease R-L shunting across the VSD and augment preload by decreasing unstressed venous volume, but the underlying cause of the spell is not treated.
- β-Adrenergic agonists are absolutely contraindicated. By increasing contractility, they will cause further narrowing of the stenotic infundibulum.
- Administration of β-adrenergic antagonists such as propranolol (0.1 mg per kg IV) or esmolol (0.5 mg per kg IV followed by an infusion of 50 to 300 μg/kg/min) may reduce infundibular spasm by depressing contractility. In addition, slowing of heart rate may increase preload by improving diastolic filling, increasing heart size, and the diameter RV outflow tract. Caution is warranted when administering β-adrenergic agonists after administering α-adrenergic agonists because the LV may not tolerate the increased SVR after β-mediated reduction in contractility.
- Extracorporeal membrane oxygenation resuscitation is another alternative in refractory episodes when immediate operative intervention is not possible.

Nasr VG, DiNardo JA, eds. *The Pediatric Cardiac Anesthesia Handbook*. Hoboken, NJ: Wiley; 2017.

A.8. What palliative surgical procedures are available for treating patients with TOF/PS?

Palliative shunt procedures to increase pulmonary blood flow

and relieve cyanosis are used when complicated surgical anatomy or institutional practice precludes definitive repair at the time of presentation. The palliative shunts are systemic-to-pulmonary artery (L-R) shunts that increase pulmonary blood flow. The volume load imposed on the LV by these shunts parallels the increases in pulmonary flow that they produce. The progressive hypertrophy of the body and infundibulum of the RV that is characteristic of TOF is unchanged, so RV outflow tract obstruction increases in the interval from shunt placement to definitive repair. The shunts can be summarized as follows:

Waterston shunt: a side-to-side anastomosis between the ascending aorta and the right PA. This procedure is performed through a right thoracotomy without CPB.

Potts shunt: a side-to-side anastomosis between the descending aorta and the left PA. This procedure is performed through a left thoracotomy without CPB.

Waterston and Potts shunts are of historic interest only. These shunts were difficult to size—too small of an orifice overly restricted pulmonary blood flow, whereas too large an orifice resulted in pulmonary overperfusion and congestion and predisposed the patient to development of unilateral pulmonary vascular obstructive disease. Furthermore, these shunts were difficult to take down at the time of the procedure and frequently distorted PA anatomy making definitive repair more difficult.

Central shunt: a synthetic tube graft between the ascending aorta and the main or branch PA. This shunt can be performed with or without CPB through a thoracotomy or median sternotomy. It is usually only used when prior shunt procedures have failed.

Blalock-Taussig shunt (BTS): an end-to-side anastomosis of the right or left subclavian artery to the ipsilateral branch PA. Currently, a modification of this procedure known as the MBTS is used. A Gore-Tex tube graft (usually 3.5 to 4.0 mm diameter

in infants) is interposed between the subclavian or innominate artery and the branch PA. These shunts usually are performed on the side opposite the aortic arch through a thoracotomy without CPB (**Fig. 38.5**).

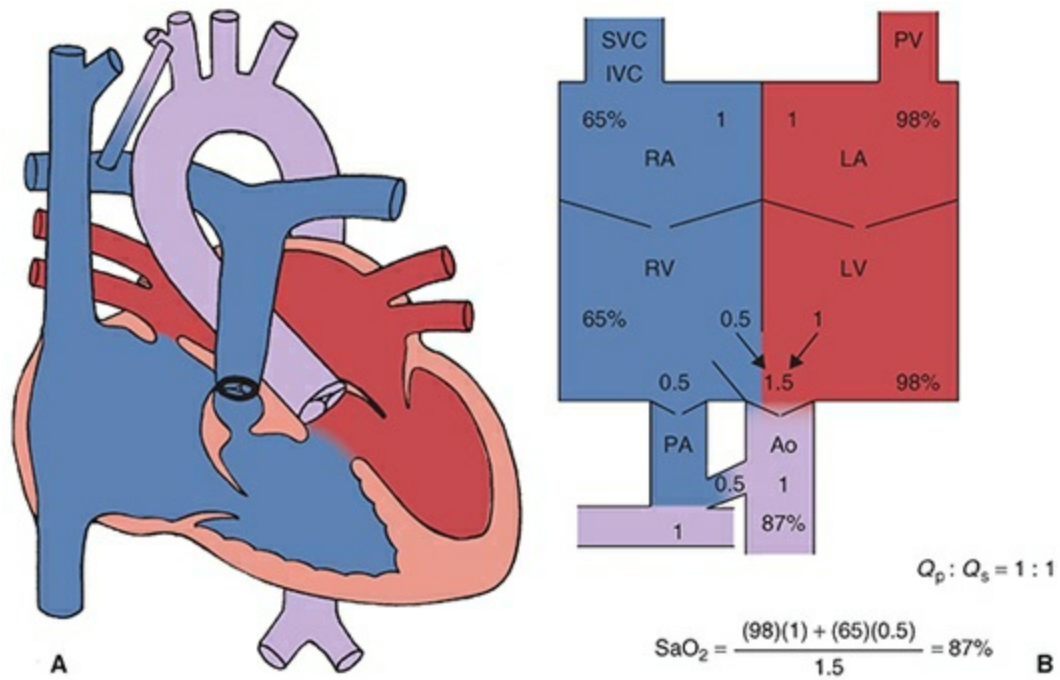

FIGURE 38.5. A. Palliative modified Blalock-Taussig shunt (MBTS) for tetralogy of Fallot with pulmonary stenosis (TOF/PS). Shunt is seen to connect the innominate artery to the right pulmonary artery (PA). This patient has a left aortic arch. **B.** Chamber oxygen saturations and relative flows for a patient with MBTS and TOF/PS. Arterial oxygen saturation (SaO_2) and Q_P:Q_S are illustrated. Ao, aorta; IVC, inferior vena cava; LA, left atrium; LV, left ventricle; PV, pulmonary vein; RA, right atrium; RV, right ventricle; SVC, superior vena cava.

Nasr VG, DiNardo JA, eds. *The Pediatric Cardiac Anesthesia Handbook*. Hoboken, NJ: Wiley; 2017.

A.9. What palliative catheter-based procedures are available for patients with TOF?

A catheter-based palliative RVOT stent is an alternative to a systemic-to-pulmonary artery shunt in patients who are not candidates for a complete repair. These patients are usually symptomatic low birth weight infants with multiple comorbidities or infants with unfavorable anatomy (small PAs).

The procedure is performed in the cardiac catheterization lab or an operating room with biplane fluoroscopy. The stent is placed through a femoral vein or a hybrid perventricular approach where the apex of the RV is approached through a subxiphoid incision. The indications for the procedure are not clearly defined and vary from institution to institution. Results including early morbidity, time to complete repair, and rate of PA growth have been encouraging when compared to an MBTS.

Quandt D, Ramchandani B, Penford G, et al. Right ventricular outflow tract stent versus BT shunt palliation in tetralogy of Fallot. *Heart*. 2017;103(24):1985–1991.

A.10. What definitive surgical procedures are available for treating patients with TOF/PS?

Most patients with TOF/PS have an elective full correction between the ages of 2 and 10 months. Definitive repair for TOF/PS in the neonatal period is done in some centers if favorable anatomy is present, whereas other centers delay surgery as long as possible until cyanotic episodes require urgent repair. Surgery is aimed at relieving the RV outflow obstruction by resection of the hypertrophied muscles that obstruct the RV outflow tract and enlargement of the RV outflow tract with a pericardial patch. A transannular pericardial patch is placed across the pulmonary valve annulus and into the main PA unless the pulmonic annulus is near-normal size and the pulmonary valve is only mildly stenotic. A transannular patch is avoided if possible because the pulmonary valve is rendered insufficient and free pulmonary regurgitation is present until the valve is repaired or replaced at an older age. If stenosis of the PA extends to the bifurcation, the pericardial patch can be extended beyond the bifurcation of the PAs. In neonates, the VSD is closed through the right ventriculotomy that was created for resection of the RVOT obstruction and placement of the

transannular patch. In infants and older children, the VSD can be closed through the right atrium and the tricuspid valve.

An important surgical consideration for patients with TOF/PS is the presence of coronary artery abnormalities. Approximately 8% of patients have either the left main coronary artery or the left anterior descending artery as a branch of the right coronary artery. In these cases, a right ventriculotomy to enlarge the RVOT could endanger the left coronary artery. In such cases, an extracardiac conduit (RV to main PA) may be necessary to bypass the outflow tract obstruction and avoid injury to the coronary artery.

Jonas RA. Early primary repair of tetralogy of Fallot. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu*. 2009;12:39–47.

Jonas RA, ed. Tetralogy of Fallot with pulmonary stenosis. In: *Comprehensive Surgical Management of Congenital Heart Disease*. 2nd ed. Boca Raton, FL: CRC Press; 2014:347–368.

Nasr VG, DiNardo JA, eds. *The Pediatric Cardiac Anesthesia Handbook*. Hoboken, NJ: Wiley; 2017.

A.11. What palliative and definitive surgical procedures are available for patients with TOF with pulmonary atresia?

Patients with TOF with pulmonary atresia in groups 1 and 2 are dependent on prostaglandin E_1 (PGE_1) to maintain pulmonary blood flow through a PDA so surgery to establish a reliable source of pulmonary blood flow must be performed in the neonatal period. These patients may undergo a palliative shunt procedure or a definitive procedure. A definitive procedure includes placement of an RV to PA and closure of VSD, usually through the ventriculotomy used for the proximal attachment of the RV to PA conduit.

Patients in groups 3 and 4 are more challenging to manage. These patients have single ventricle physiology with a tendency

toward excessive pulmonary blood flow (Q_P:Q_S >2 to 3:1) as the PVR drops in the neonatal period. In group 3 patients, neonatal repair with placement of an RV to PA conduit is undertaken to place the PAs in continuity with the RV in an effort to promote native PA growth. In this circumstance, the VSD is left open as a source of R-L shunting and delivery of desaturated blood to the systemic circulation because the RV cannot deliver an adequate cardiac output to the left atrium across the hypoplastic pulmonary vascular bed. These infants then undergo multiple cardiac catheterization procedures in order to dilate and stent the hypoplastic native PAs and to embolize MAPCAs, which provide pulmonary blood flow that is competitive to the blood flow supplied by native PAs. MAPCAs that provide pulmonary blood flow to segments of lung not supplied by native PAs must be unifocalized to the proximal pulmonary circulation. Unifocalization involves removal of the collateral vessel from the aorta with anastomosis to the RV to PA conduit or a proximal PA branch. This establishes antegrade blood flow from the RV to the pulmonary vascular bed. Usually, 80% to 90% of the pulmonary vascular bed (10 to 12 bronchopulmonary segments) must be in direct continuity with the RV to ensure that adequate cardiac output can cross the pulmonary bed and the VSD can be closed. In group 4 patients, the initial intervention may be to create an RV to PA conduit and unifocalize several large collaterals to the distal end of conduit from the RV. Alternatively, several large collaterals can be unifocalized to an MBTS or central shunt. These procedures serve to promote pulmonary vascular growth, prevent the development of pulmonary vascular obstructive disease, and control the Q_P:Q_S.

Bauser-Heaton H, Borquez A, Han B, et al. Programmatic approach to management of tetralogy of Fallot with major aortopulmonary collateral arteries: a 15-year experience with 458 patients. *Circ Cardiovasc Interv*.

2017;10:e004952.

Hofferberth SC, Esch JJ, Zurakowski D, et al. Pulmonary atresia with ventricular septal defect and major aortopulmonary collaterals: collateral vessel disease burden and unifocalisation strategies. *Cardiol Young*. 2018;28:1091–1098.

A.12. What are the long-term outcomes of patients with TOF?

Complete surgical repair of TOF has been performed for over 40 years with actuarial survival of 85% at 30 to 35 years. Most patients are largely asymptomatic and RV dysfunction may only be evident on echocardiography and exercise stress testing. Factors that adversely affect long-term survival include older age at initial repair, initial palliative procedures, and presence of residual PS and/or pulmonary regurgitation. RV dysfunction from chronic pressure and volume overload as well as the development of ventricular dysrhythmias may prompt pulmonary valve repair or replacement.

Geva T. Indications for pulmonary valve replacement in repaired tetralogy of Fallot: the quest continues. *Circulation*. 2013;128:1855–1857.

B. Preoperative Evaluation and Preparation

B.1. What preoperative history and physical examination information do you want?

The medical history and review of systems should include an assessment of ability to perform age-appropriate activities that will aid in the evaluation of cardiac function and reserve. The observation by a parent that the patient cannot keep the same pace as siblings is often a reliable clinical sign that cyanosis or congestive heart failure is worsening. Symptoms of low cardiac reserve include sweating, dyspnea, and circumoral cyanosis that may first occur during feeding, which is a strenuous activity for a newborn. Interpretation of vital signs must be age specific.

Growth curves also are useful because congestive heart failure will inhibit age-appropriate gains in weight, height, and head circumference. It is not unusual for patients with severe congestive heart failure to weigh less at 3 or 4 months of age than at birth. Interestingly, cyanotic children often do not manifest this failure to thrive.

It is often difficult to differentiate signs and symptoms of congestive heart failure from a mild upper respiratory tract infection in infants and children, so surgery may need to proceed even when the diagnosis is not clear. Children and infants with increased pulmonary blood flow are predisposed to multiple respiratory tract infections so surgery may need to proceed in these patients to reduce pulmonary blood flow and the propensity for chronic lung infections.

Physical examination might reveal cyanosis, clubbing, or signs of congestive heart failure similar to those seen in adults, such as hepatomegaly, ascites, edema, or tachypnea. Some manifestations of congestive heart failure such as rales may not be heard in infants and children, so the severity of heart failure may be more reliably assessed by the signs and symptoms outlined previously.

Physical examination should include an evaluation of the limitations to vascular access and monitoring sites imposed by previous surgeries. A child who has undergone a BT or MBT palliative shunt procedure may have a diminished pulse or unobtainable blood pressure in the ipsilateral arm, preventing accurate blood pressure and pulse oximetry measurement in that extremity. Venous access should also be assessed preoperatively because this may affect the mode of induction of anesthesia.

Nasr VG, DiNardo JA, eds. *The Pediatric Cardiac Anesthesia Handbook*. Hoboken, NJ: Wiley; 2017.

B.2. Which other abnormalities need to be considered in

this patient?

Approximately 8% of children with congenital heart disease have other congenital abnormalities. Patients with TOF/PS or TOF with pulmonary atresia have a higher incidence of 22q11.2 deletion syndrome. Different phenotypes of this syndrome include DiGeorge syndrome, velocardiofacial syndrome, and conotruncal anomaly face syndrome. These syndromes are characterized by hypocalcemia; immunodeficiency; facial dysmorphia; palate anomalies; velopharyngeal dysfunction; renal anomalies; possible tracheoesophageal fistula; as well as speech, feeding, neurocognitive, behavioral, and psychiatric disorders. Many of these defects may complicate airway management.

McDonald-McGinn DM, Sullivan KE, Marino B, et al. 22q11.2 deletion syndrome. *Nat Rev Dis Primers*. 2015;1:15071.

Nasr VG, DiNardo JA, eds. *The Pediatric Cardiac Anesthesia Handbook*. Hoboken, NJ: Wiley; 2017.

B.3. What premedication will you give to a child with congenital heart disease?

Premedication alleviates anxiety and eases separation of children from parents. In infants, premedication facilitates placement of an IV catheter for induction of anesthesia, alone or in combination with inhaled anesthetics. Midazolam (1 mg per kg PO) may be sufficient in infants and young children, but the addition of ketamine (3 to 5 mg per kg PO) is sometimes necessary in older children with heightened anxiety or in patients who are tolerant to benzodiazepines from previous procedures. Intramuscular (IM) ketamine (2 to 3 mg per kg) and glycopyrrolate (10 μg per kg) alone or in combination with midazolam (0.1 mg per kg) works well in children who will not take oral medications.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

C. Intraoperative Management

C.1. How will you induce anesthesia in this patient if intravenous (IV) access cannot be obtained?

Induction of anesthesia with IM ketamine (3 to 5 mg per kg IM), succinylcholine (5 mg per kg IM), and glycopyrrolate (10 μg per kg IM) is an alternative to IV induction in infants and neonates with difficult peripheral IV access. Glycopyrrolate is an important adjunct to reduce airway secretions associated with ketamine administration and to prevent the bradycardia, which may be associated with succinylcholine. This technique provides prompt induction of anesthesia, allowing for immediate control of the airway with endotracheal intubation. This is useful in circumstances where it is anticipated that initial IV access will have to be obtained through the external jugular vein, femoral vein, or internal jugular vein. IM rocuronium (1 mg per kg IM) can be substituted for the succinylcholine, but the time to adequate intubating conditions and duration of action is variable.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017: 633–698.

C.2. Why would end-tidal carbon dioxide ($EtCO_2$) monitoring be of particular use in a patient with TOF/PS?

$EtCO_2$ monitoring is particularly helpful in patients with congenital heart disease because the difference between arterial CO_2 and alveolar CO_2 reflects physiologic dead space ventilation and is indicative of changes in lung perfusion. An

acute reduction in pulmonary blood flow (decreased cardiac output, pulmonary embolus, or increased intracardiac R-L shunting) will increase this gradient. In a patient with TOF/PS, a gradual reduction in Et_{CO_2} often precedes a decrease in Sa_{O_2} as the first manifestation of the increased R-L intracardiac shunting during a "Tet spell."

Levy RJ. Anesthesia for congenital heart surgery. In: Jonas RA, ed. *Comprehensive Surgical Management of Congenital Heart Disease*. 2nd ed. Boca Raton, FL: CRC Press; 2014:19–36.

C.3. What is near-infrared spectroscopy (NIRS) and what does it measure?

NIRS is a real-time, online monitor of cerebral tissue oxygenation. This technology is based on the physical principle that light of an appropriate wavelength passing through a solution of a colored compound (chromophore) will be absorbed by the compound. As a result of this absorption, the intensity of the light emerging from the solution will be lower than the intensity of the light projected into the solution. This principle through application of the Beer-Lambert equation "$\log [I_O / I] = c\, \alpha\, d$" allows quantification of the concentration (c) of a chromophore if the emergent light intensity (I) is measured and the following are known:

- Extinction coefficient (α), a constant that describes the absorption characteristics of a particular chromophore at a given wavelength of light
- Thickness of the solution (d)
- Incident light intensity (I_O)

NIRS technology is particularly suited to use in neonates and infants because the thin skull and small head allow light to be transmitted through one side of the head and detected on the other side, a technique known as *transmission spectrometry*.

Cerebral oxygen saturation (Sc_{O_2}) as measured by all NIRS

technology is the combined oxygen saturation of an uncertain mix of arterioles, capillaries, and venules. Traditional pulse oximetry differs in this respect from NIRS because it is capable of isolating and measuring the arteriole component by gating measurements to arterial pulsatility. It has been previously assumed that Sco_2 represented contributions of cerebral arterial and venous blood in a ratio of 25:75, with the contribution of capillary blood felt to be negligible. More recent data suggest that in children, the average ratio is 15:85. The issue is further complicated by the fact that there is significant variability in the ratio (from 0:100 to 40:60) between patients.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

Ferradal SL, Yuki K, Vyas R, et al. Non-invasive assessment of cerebral blood flow and oxygen metabolism in neonates during hypothermic cardiopulmonary bypass: feasibility and clinical implications. *Sci Rep*. 2017;7:44117.

C.4. What are the important management issues during creation of a palliative shunt?

- Unilateral lung retraction will be required for surgical exposure if a thoracotomy approach is used. The resulting atelectasis may severely compromise ventilation and worsen oxygenation and CO_2 removal.
- The main or branch PAs will have to be partially occluded by a clamp to allow creation of the distal anastomosis of all palliative systemic to PA shunts. The resulting increase in physiologic dead space and $PaCO_2$ and $EtCO_2$ gradients may compromise oxygenation and CO_2 removal. Efforts to optimize ventilation, reduce PVR, and increase pulmonary blood flow should be initiated before PA occlusion.
- Partial occlusion of the aorta with a clamp will be necessary

during creation of Waterston, Potts, and central shunts. The resulting increase in LV afterload may compromise LV systolic function, and inotropic support may need to be initiated.

- All of the palliative shunts impose a volume load on the LV. Inotropic support may be necessary to ensure systemic and shunt perfusion after shunt creation.
- Palliative shunts are mildly restrictive simple shunts. It is important to maintain SVR and reduce PVR to maintain pulmonary blood flow in these patients.
- Be prepared to treat an episode of hypercyanosis.

Nasr VG, DiNardo JA, eds. *The Pediatric Cardiac Anesthesia Handbook*. Hoboken, NJ: Wiley; 2017.

C.5. What is the effect of inhalation anesthetics on airway reflexes, myocardial contractility, systemic vascular resistance (SVR), and pulmonary vascular resistance (PVR) in children?

Sevoflurane, isoflurane, and desflurane induce a dose-dependent reduction in cardiac output and SVR with mild depression of contractility at 1 and 1.5 minimal alveolar concentration (MAC). At these concentrations, sevoflurane and isoflurane do not alter the ratio of PVR to SVR enough to induce any change in Q_P:Q_S.

Isoflurane and desflurane are not good choices for inhalational induction because their pungency is responsible for a high incidence of airway complications in children. Sevoflurane has cardiovascular effects similar to isoflurane and is a good agent for inhalational induction.

Laird TH, Stayer SA, Rivenes SM, et al. Pulmonary-to-systemic blood flow ratio effects of sevoflurane, isoflurane, halothane, and fentanyl/midazolam with 100% oxygen in children with congenital heart disease. *Anesth Analg*. 2002;95:1200–1206.

Nasr VG, DiNardo JA, eds. *The Pediatric Cardiac Anesthesia Handbook*.

Hoboken, NJ: Wiley; 2017.

C.6. What are the pre-cardiopulmonary bypass (pre-CPB) anesthetic goals for a patient undergoing definitive surgical correction of TOF/PS?

- Maintain heart rate, contractility, and preload to maintain cardiac output. Maintaining euvolemia is important to prevent exacerbation of dynamic RVOT obstruction from hypovolemia and reflex increases in heart rate and contractility.
- Avoid increases in the PVR:SVR ratio. Increases in PVR relative to SVR and decreases in SVR relative to PVR will increase R-L shunting, reduce pulmonary blood flow, and produce or worsen cyanosis. This effect is more pronounced when the RV outflow obstruction is not severe.
- Maintain or increase SVR. This is particularly important when RV outflow obstruction is severe, and changes in PVR will have little or no effect on shunt magnitude and direction.
- Treat episodes of hypercyanosis.
- Maintain contractility. Depression of contractility, particularly in the face of severe RV outflow obstruction, may produce RV afterload mismatch and drastically reduce pulmonary blood flow. The exception to this is a patient in whom the dynamic component of infundibular obstruction is active. Reducing contractility in these patients may reduce RV outflow obstruction through relaxation of the infundibulum.

Nasr VG, DiNardo JA, eds. *The Pediatric Cardiac Anesthesia Handbook*. Hoboken, NJ: Wiley; 2017.

C.7. What interventions will reliably reduce PVR?

Increase P_{O_2}. High levels of inspired O_2 reduce elevated PVR, whereas alveolar hypoxia and arterial hypoxemia induce

pulmonary vasoconstriction. An arterial O_2 tension lower than 50 mmHg increases PVR over a wide range of arterial pH values. This effect is most pronounced when the pH is lower than 7.40.

Reduce P_{CO_2}. Consistent reductions in PVR and increases in pulmonary blood flow and P_{O_2} are seen in children with R-L shunts who are hyperventilated to a P_{CO_2} near 30 mmHg and a pH near 7.50. Hypocarbia reduces PVR through production of an alkalosis, but hypercarbia increases PVR independent of changes in arterial pH. Patient with preoperative pulmonary hypertension who are hyperventilated post-CPB to a P_{CO_2} of 30 to 35 mmHg and a pH of 7.50 to 7.56 have a reduction in PVR when compared with ventilation that produces normocarbia or hypercarbia.

Reduce *pH*. Both respiratory and metabolic alkalosis reduce PVR, whereas respiratory and metabolic acidosis increase PVR.

Variation in lung volumes. At small lung volumes, atelectasis compresses extra-alveolar vessels, whereas at high lung volumes, hyperinflation of alveoli compresses intra-alveolar vessels. Therefore, PVR is normally lowest at lung volumes at/or near the functional residual capacity. Positive end-expiratory pressure (PEEP) may cause an increase in PVR by increasing alveolar pressure through hyperinflation. However, a decrease in PVR generally is seen in situations in which PEEP works to recruit atelectatic alveoli and increase arterial P_{O_2}.

Vasodilator agents. PGE_1, prostaglandin I_2 (PGI_2), nitroglycerin, sodium nitroprusside, and tolazoline are IV drugs that induce pulmonary vasodilation as well as systemic vasodilation. There is no IV drug that selectively acts as a pulmonary vasodilator. Inhaled nitric oxide, PGE_1, and PGI_2 are the only specific pulmonary vasodilators available.

Nasr VG, DiNardo JA, eds. *The Pediatric Cardiac Anesthesia Handbook*. Hoboken, NJ: Wiley; 2017.

C.8. How does heparin administration and activated coagulation time (ACT) monitoring for CPB differ in children as compared with adults?

Adequate anticoagulation, usually defined as an ACT greater than 400 seconds, is necessary before cannulation and the commencement of CPB. Most of the evidence for assessing the adequacy of anticoagulation in children during heart surgery has been extrapolated from the adult literature. The ACT will overestimate the antifactor IIa and Xa effects of heparin in children because the ACT is also prolonged by hypothermia, hemodilution, platelet dysfunction, and low coagulation factor levels. These factors are more significant in children than in adults during CPB because of their small size relative to the CPB circuits.

Most institutions use an age- or weight-based protocol to administer the initial pre-CPB dose of heparin. An example of a simple weight-based protocol is all patients weighing less than 30 kg receive 300 IU heparin per kg and patients greater than 30 kg receive 400 IU per kg. The large circuit prime volume to blood volume ratio in infants and children would be expected to decrease plasma heparin levels with initiation of CPB unless an appropriate quantity of heparin is added to the CPB prime. Most institutions add heparin to the CPB prime as follows: 3.0 IU heparin added per mL of CPB prime for patients less than 30 kg and 2.5 IU heparin added per mL of CPB prime in patients greater than 30 kg.

Heparin should always be given into a central line through which venous return can be demonstrated easily or directly into the heart by the surgeon. This is necessary to ensure that the heparin dose has reached the central circulation. An ACT can be

drawn within minutes of heparin administration as peak arterial ACT prolongation occurs within 30 seconds and peak venous ACT prolongation within 60 seconds.

Matte GS. The bypass plan. In: Matte GS. *Perfusion for Congenital Heart Surgery: Notes on Cardiopulmonary Bypass for a Complex Patient Population*. Hoboken, NJ: Wiley; 2015:33–65.

Matte GS, DiNardo JA. Pediatric cardiopulmonary bypass. In: Gravlee GP, Davis RF, Hammon JW, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2015:655–682.

C.9. How is heparin reversed?

Systemic heparin is reversed with protamine, a polyvalent cation derived from salmon sperm. Protamine normally is given once the patient's hemodynamics have stabilized after termination of CPB and the team is satisfied with the repair. The cardiotomy suction should not be used and the arterial and venous cannulas should be removed before protamine neutralization of heparin begins. This prevents contamination of the heparinized CPB circuit with protamine so that prompt reinstitution of CPB is possible, if necessary.

There are several approaches to the neutralization of heparin with protamine, all with reportedly good clinical results. Some centers titrate the amount of protamine to the amount of heparin determined to exist at the termination of CPB using the in vitro protamine-heparin neutralization ratio of 1.3:1.0. This method had been criticized because the amount of heparin present post-CPB is calculated based on the ACT, and the ACT can be affected by factors other than the concentration of heparin, such as CPB-induced platelet dysfunction, hypothermia, and hemodilution. This may result in an overestimation of the heparin present at the termination of CPB and results in a larger than necessary calculated protamine dose. Other centers administer a fixed dose of protamine based on the patient's

weight (3 to 4 mg per kg IV) regardless of the ACT or heparin dose administered, whereas others administer 1.0 to 1.3 mg of protamine for each 100 units of heparin administered prior to and during CPB.

Matte GS. The bypass plan. In: Matte GS. *Perfusion for Congenital Heart Surgery: Notes on Cardiopulmonary Bypass for a Complex Patient Population*. Hoboken, NJ: Wiley; 2015:33–65.

Matte GS, DiNardo JA. Pediatric cardiopulmonary bypass. In: Gravlee GP, Davis RF, Hammon JW, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2015:655–682.

C.10. What is the incidence of protamine reactions in children?

The incidence of protamine reactions in children following cardiac surgery is substantially lower than in adults. Acute reactions to protamine may be mild with transient erythema and hypotension or severe with bronchoconstriction, PA hypertension, and cardiovascular collapse. The mechanism has not been fully characterized. A recent retrospective analysis of 1,249 children showed the incidence of hypotension (defined as a 25% decrease in mean arterial pressure) following protamine administration to be 1.76% to 2.88%, depending on the stringency of criteria linking the hypotensive episode to protamine administration. In this series, no episodes of pulmonary hypertension or RV dysfunction were noted. Clinical experience indicates that pulmonary hypertensive episodes in children following protamine administration are very rare.

Matte GS, DiNardo JA. Pediatric cardiopulmonary bypass. In: Gravlee GP, Davis RF, Hammon JW, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2015:655–682.

C.11. What is the role of transesophageal

echocardiography (TEE) in this patient?

TEE has a major impact on post-CPB decision making, such as return to CPB to repair residual lesions in approximately 15% of cases when it is used nonselectively in children. In the subset of patients undergoing valve repair and outflow tract reconstruction (such as this patient), the impact of TEE would be expected to be greater by providing immediate assessment of the adequacy of the operative procedure and directing the revision, if necessary. Although detection of retained intracardiac air is facilitated by the use of intraoperative TEE, it remains to be determined what role TEE will play in improving cardiac de-airing algorithms particularly in neonates/infants.

The role of TEE in the detection of residual VSDs following repair of both simple and complex defects deserves some discussion. Residual defects smaller than 3 mm are detectable by TEE but generally do not require immediate reoperation because they are hemodynamically insignificant. The majority (75%) of these small defects are not present at the time of hospital discharge as determined by transthoracic echocardiography. Residual defects greater than 3 mm detected by TEE require immediate reoperation only when intraoperative assessment suggests that the defect will be hemodynamically significant. Examples of concerning findings are elevated left atrial pressure and/or PA pressure in the presence of good ventricular function, right atrium to PA oxygen saturation step-up with $F_{IO_2} \leq 0.50$, and oximetric measurement of $Q_P:Q_S > 1.5$.

Yang SG, Novello R, Nicolson S, et al. Evaluation of ventricular septal defect repair using intraoperative transesophageal echocardiography: frequency and significance of residual defects in infants and children. *Echocardiography*. 2000;17:681–684.

C.12. What effect would a residual ventricular septal defect (VSD) have in this patient following separation

from CPB?

A residual VSD is likely to be poorly tolerated in patients with repaired TOF/PS. There is potential for a large L-R shunt through a residual VSD because RVOT obstruction will be completely or near completely eliminated postrepair and the PVR is likely to be low and the pulmonary vasculature very compliant. This will acutely place a large volume load on both the LV and RV. The RV is not likely to tolerate the volume load because the RV compliance is reduced from the preoperative concentric hypertrophy and the function may be impaired postbypass and from the ventriculotomy. The most likely manifestation will be low cardiac output associated with an elevated heart rate, elevated left atrial pressure, and elevated PA pressure (low cardiac output syndrome).

Nasr VG, DiNardo JA, eds. *The Pediatric Cardiac Anesthesia Handbook*. Hoboken, NJ: Wiley; 2017.

D. Postoperative Management

D.1. How should postoperative ventilation be managed in this patient following placement of a transannular patch for TOF/PS?

The inspiratory phase of mechanical positive pressure ventilation should be adjusted to minimize mean airway pressure. The inspiratory phase of mechanical positive pressure ventilation increases impedance to RV ejection and RV afterload by elevating alveolar pressure and creating more West zone I (alveolar pressure greater than arterial and venous pressure) and West zone II (alveolar pressure greater than venous pressure) lung segments. This is directly related to the duration of inspiration (respiratory rate and inspiratory-to-expiratory [I:E] ratio) and to mean airway pressure. Increasing RV afterload will

impede antegrade pulmonary blood flow and exacerbate the extent of pulmonary insufficiency induced by the transannular patch. RV afterload will also be increased by elevations in PVR.

As discussed in section C.7, ventilation and gas mixture should be adjusted to minimize PVR. This is usually accomplished with a tidal volume of 10 to 15 mL per kg, 3 to 5 mmHg of PEEP, and a respiratory rate and I:E ratio adjusted to minimize mean airway pressure.

Nasr VG, DiNardo JA, eds. *The Pediatric Cardiac Anesthesia Handbook*. Hoboken, NJ: Wiley; 2017.

D.2. Following complete repair of TOF/PS in an infant, what SaO_2 is acceptable?

Following complete repair of TOF/PS with no residual lesions and minimal intrapulmonary shunt, the Sa_{O_2} should be 100%. The surgeon may choose to leave a small (3 to 4 mm) atrial level communication or patent foramen ovale in infants and small children, particularly in those patients with pulmonary insufficiency as the result of a transannular patch and those expected to have restrictive RV function as a result of a ventriculotomy and/or extensive RV hypertrophy. This will allow intracardiac R-L shunting, with the ability to augment systemic cardiac output at the expense of systemic oxygen saturation in the setting of RV dysfunction by allowing direct delivery of desaturated venous blood to the left atrium. In these patients, a Pa_{O_2} of 40 to 50 mmHg and a Sa_{O_2} of 70% to 80% are acceptable until RV function improves over the course of days.

Nasr VG, DiNardo JA, eds. *The Pediatric Cardiac Anesthesia Handbook*. Hoboken, NJ: Wiley; 2017.

D.3. Following placement of a modified Blalock-Taussig

shunt (MBTS) for TOF/PS in an infant, what SaO_2 is acceptable?

As illustrated in **Figure 38.5B**, the expected Sao_2 would be 80% to 90% in the presence of some antegrade pulmonary blood flow. In the absence of any antegrade pulmonary blood flow, single ventricle physiology exists and a Sao_2 of 70% to 80% would be expected. Sao_2 is determined by the relative volumes and saturations of recirculated systemic venous blood and effective systemic blood flows that have mixed and reached the aorta. This is summarized in the following equation:

$$\text{Aortic } SaO_2 = \frac{[(\text{pulmonary venous saturation} \times \text{effective systemic blood flow}) + (\text{systemic venous saturation} \times \text{recirculated systemic venous blood flow})]}{(\text{total systemic blood flow})}$$

This is demonstrated in **Figure 38.5B**.

Three variables will ultimately affect Sao_2:

1. *The ratio of total pulmonary to total systemic blood flow* (Q_P:Q_S). A greater proportion of the arterial blood will consist of saturated blood (pulmonary venous blood) than of desaturated blood (systemic venous blood) when Q_P:$Q_S \geq$ 1:1. Q_P:Q_S will be increased when systemic arterial blood pressure is high and PVR is low.
2. *Systemic venous saturation*. For a given Q_P:Q_S and pulmonary venous saturation, a decrease in systemic venous saturation will result in a decreased arterial saturation. Decreases in systemic venous saturation occur as the result of decreases in systemic oxygen delivery or increases in systemic oxygen consumption. Recall that systemic oxygen delivery is the product of systemic blood flow and arterial oxygen content. Arterial oxygen content, in turn, is dependent on the hemoglobin concentration and the arterial saturation. Efforts should be made to increase hematocrit

into the range of 35% to 45%, increase cardiac output with inotropes, and reduce systemic O_2 consumption with appropriate levels of sedation/anesthesia and muscle relaxation if necessary.

3. *Pulmonary venous saturation.* For any given systemic venous saturation and Q_P:Q_S, a reduction in pulmonary venous saturation will result in a decreased arterial saturation. In the absence of large intrapulmonary shunts and/or ventilation/perfusion mismatch, pulmonary venous saturation should be close to 100% when breathing room air. In the presence of pulmonary parenchymal disease, pulmonary venous saturation may be reduced. The mismatched component of pulmonary venous desaturation will be largely eliminated with an F_{IO_2} of 1.0, whereas the intrapulmonary shunt contribution will not be eliminated.

Nasr VG, DiNardo JA, eds. *The Pediatric Cardiac Anesthesia Handbook*. Hoboken, NJ: Wiley; 2017.

D.4. What is junctional ectopic tachycardia (JET)?

Postoperative JET is a transient tachyarrhythmia that can occur immediately following congenital heart surgery. A rare form of congenital JET exists as well. JET is due to enhanced automaticity in the area of the atrioventricular (AV) node or proximal His bundle. Patients who develop JET have a higher than average incidence of postoperative AV block. The incidence of JET following TOF/PS repair may be as high as 20% and is felt to be secondary to trauma from surgical retraction near the AV node that is necessary to expose the VSD and RVOT from across the tricuspid valve.

JET typically manifests with a junctional rate only slightly faster than the sinus node rate. It is the only narrow complex tachycardia in which the atrial rate is less than the ventricular rate (A:V ratio <1:1). In fewer than 10% of cases of JET, there

may be retrograde activation of the atrium with inverted P waves and an A:V ratio of 1:1. Cardiac output is reduced because there is a loss of AV synchrony, which reduces the atrial transport factor (atrial kick). In many instances, this arrhythmia is well tolerated, but JET with heart rate greater than 170 beats per minute is associated with hemodynamic instability and increased postoperative mortality.

The most effective therapy for JET is atrial pacing at a rate slightly faster than the junctional rate such that AV synchrony is reinitiated. This therapy is effective unless the junctional rate is very high (>160 to 170 beats per minute), at which point atrial pacing at a faster rate is unlikely to improve hemodynamics because the reinitiation of AV synchrony is offset by the dramatic reduction in diastolic filling time present at these rates. In this circumstance, the most effective therapy is multimodal. The goal of multimodal therapy is to terminate JET or reduce the rate to the point where atrial pacing can be reinitiated. Note that cardioversion and adenosine are not effective.

The following modalities are applied in this order:

- Fever is aggressively treated with antipyretics.
- Sedation and hemodynamics are optimized.
- Doses of inotropic agents are reduced because most of these agents have positive chronotropic effects. This may be difficult in the setting of hemodynamic instability and low cardiac output syndrome.
- Mild systemic hypothermia is introduced. A cooling blanket and icepacks are used to reduce patient temperature to 32°C (89.6°F) to 35°C (95°F). This usually requires sedation and paralysis to prevent shivering.
- Procainamide or amiodarone therapy is initiated.

JET requiring aggressive treatment prolongs postoperative ventilation times and intensive care unit stay.

Walsh EP. Automatic atrial and junctional tachycardias. In: Walsh EP, Saul JP, Triedman JK, eds. *Cardiac Arrhythmias in Children and Young Adults with Congenital Heart Disease.* Philadelphia, PA: Lippincott Williams & Wilkins; 2001:115–135.

39 Transposition of the Great Arteries

David Whiting and James A. DiNardo

A 3-day-old, full-term, 3.4-kg male is scheduled for an arterial switch operation (ASO). Shortly after birth, he demonstrated reverse differential cyanosis with right arm arterial saturation of 40% and lower extremity saturation of 60%, despite prostaglandin E_1. A bedside balloon atrial septostomy was performed with resolution of reverse differential cyanosis and improvement of arterial saturation to 75%. Prostaglandin E_1 was discontinued 4 hours after the septostomy. He is breathing spontaneously with 0.5 L per minute supplemental oxygen through nasal cannula. His arterial oxygen saturation (Sao_2) is 75%; blood pressure, 63/37 mmHg; pulse, 145 beats per minute; and respiration, 46 breaths per minute.

A. Medical Disease and Differential Diagnosis

1. What defines the cardiac situs?
2. What is transposition of the great arteries (D-TGA)?
3. What additional cardiac lesions are associated with D-TGA?
4. What is the natural history of D-TGA?
5. What is the pathophysiology of D-TGA?
6. What determines the oxygen saturation in patients with D-

TGA?

7. Why did this infant have reverse differential cyanosis?
8. What are the preoperative issues pertaining to the coronary arteries in D-TGA?
9. What are the clinical subsets of D-TGA?
10. What is the differential diagnosis of D-TGA and how is the diagnosis made?
11. What preoperative interventions can help stabilize a patient with D-TGA?
12. What are the surgical options for repair? Why is one chosen over the others?

B. Preoperative Evaluation and Preparation

1. What information is important to prepare for this case?
2. What are the anesthetic goals before cardiopulmonary bypass (CPB)?
3. What is the plan for glucose management in this patient?

C. Intraoperative Management

1. How would you monitor this infant?
2. What would be the best method of induction for this patient?
3. Is CPB in infants and children different from adults?
4. What is modified ultrafiltration (MUF)?
5. Briefly describe the surgical techniques of the Mustard/Senning, ASO, and Rastelli procedures.
6. What is hypothermia, and how is it classified? What is low-flow cardiopulmonary bypass (LFCPB)? What is deep hypothermic circulatory arrest (DHCA)?
7. Why is hypothermia beneficial to the brain during LFCPB and DHCA?
8. Explain the difference between α-stat and pH-stat blood gas management.
9. What are the immediate post-CPB issues following ASO?

D. Postoperative Management

1. How is myocardial ischemia addressed in the intensive care unit (ICU) following the ASO?
2. What immediate postoperative problems would be anticipated following the Rastelli procedure?
3. What intermediate and long-term surgical problems are seen after ASO?
4. What are the long-term outcomes after ASO?
5. What are the long-term outcomes after Rastelli repair for patients with D-TGA with left ventricular outflow tract (LVOT) obstruction?
6. What is long-term neurologic outcome like after ASO?

A. Medical Disease and Differential Diagnosis

A.1. What defines the cardiac situs?

Cardiac situs refers to the orientation of the morphologic right atrium (RA). If the RA is to the right of midline, cardiac situs is "solitus"; otherwise, the cardiac situs is "inversus" (morphologic RA to the left atrium [LA]) or "ambiguous" when the situs is indeterminate. Cardiac structures may not be in the expected location, so echocardiography can help characterize the anatomy of the atria, atrioventricular (AV) valves, ventricles, ventriculoarterial (VA) valves, and great arteries. A few anatomic characteristics are consistent. The RA receives the vena cava and coronary sinus. There is always concordance (agreement) between the AV valves and the ventricle, so the tricuspid valve is always the inflow valve for the right ventricle (RV) and the mitral valve the inflow valve for the left ventricle (LV). A muscular conus (infundibulum) always separates the AV (tricuspid) and VA (pulmonary) valves of the RV and the inflow/AV (mitral) and VA (aortic) valves of the LV are always in fibrous continuity.

Kloesel B, DiNardo JA, Body SC. Cardiac embryology and molecular mechanisms of congenital heart disease: a primer for anesthesiologists. *Anesth Analg*. 2016;123:551–569.

Williams GD, Feng A. Heterotaxy syndrome: implications for anesthesia management. *J Cardiothorac Vasc Anesth*. 2010;24:834–844.

A.2. What is transposition of the great arteries (D-TGA)?

D-TGA is a common congenital heart lesion accounting for 5% to 7% of all congenital cardiac defects, second in frequency only to isolated ventricular septal defects (VSDs). In D-TGA, there is concordance of the AV connections and discordance of the VA connections. The segmental anatomy is S, D, D, with atrial situs *S*olitus, *D*-loop ventricles, and *D*-loop great arteries. A right-sided RA connects through a right-sided tricuspid valve and RV to a right-sided and anterior aorta. A left-sided LA connects through a left-sided mitral valve and LV to a left-sided and posterior pulmonary artery (PA). As a result, there is fibrous continuity between the mitral and pulmonic valves with a lack of fibrous continuity (conus) between the tricuspid and aortic valves. The combination of AV concordance (RA to RV and LA to LV) and VA discordance (RV to aorta and LV to PA) produces a parallel rather than a normal series circulation.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

A.3. What additional cardiac lesions are associated with D-TGA?

The most commonly associated cardiac anomalies are a persistent patent foramen ovale (PFO), patent ductus arteriosus (PDA), VSD, and subpulmonic stenosis resulting in LVOT obstruction. Approximately 50% of patients with D-TGA will present with a PDA before prostaglandin E_1 administration and diagnosis of D-TGA. There is almost always a PFO, but a true

secundum atrial septal defect (ASD) exists in approximately 5% of patients. Although angiographically detectable, VSDs occur in 30% to 40% of patients, only approximately one-third of these defects are hemodynamically significant. Therefore, for practical purposes, 75% of patients have an intact ventricular septum (IVS). LVOT obstruction is present in approximately 30% of patients with VSD and is most often due to an extensive subpulmonic fibromuscular ring or posterior malposition of the outlet portion of the ventricular septum.

Allen HD, Shaddy RE, Penny DJ, et al, eds. *Moss and Adams' Heart Disease in Infants, Children, and Adolescents, Including the Fetus and Young Adult*. 9th ed. Philadelphia, PA: Wolters Kluwer; 2016:1163–1186.

A.4. What is the natural history of D-TGA?

Survival in the neonatal period is dependent on sufficient mixing of the parallel systemic and pulmonary circulations at the atrial, ventricular, or arterial level. Patency of the ductus arteriosus can be maintained with prostaglandin E_1, allowing for mixing at the arterial level. An emergent Rashkind-Miller balloon atrial septostomy can be performed to increase mixing at the atrial level in those infants who do not have adequate mixing through the PDA or VSD. Forty-five percent of patients with D-TGA will die within the first month, and 90% will die within the first year of life without intervention, despite being largely free from other extracardiac defects. Following stabilization, as a neonate, many of these infants can be offered the ASO, a definitive surgical procedure that will give them a quality of life similar to that of normal children. Infants with D-TGA who have anatomy that is not favorable for the ASO are offered palliative surgeries.

Hypoxia and intractable congestive heart failure (CHF) are the two primary causes of death in infants without intervention who survive the neonatal period. Infants with D-TGA are at particular risk for early-onset accelerated pulmonary artery

hypertension (PAH). The etiology is most likely related to systemic hypoxemia, the presence of bronchopulmonary collaterals (which deliver deoxygenated blood to the precapillary pulmonary arterioles), polycythemia, and platelet aggregation. Infants with D-TGA and a large VSD without LVOT obstruction are at highest risk for the early development of PAH due to exposure of the pulmonary vascular bed to systemic pressures with unrestricted flow. Advanced, nonreversible pulmonary hypertension reduces the corrective surgical options available to the patient.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

A.5. What is the pathophysiology of D-TGA?

Systemic and pulmonary circulations are in a parallel with varying degrees of intercirculatory mixing. Deoxygenated systemic venous blood recirculates through the systemic circulation (a physiologic right-to-left shunt) and oxygenated pulmonary venous blood recirculates through the pulmonary circulation (a physiologic left-to-right shunt). The physiologic shunt fraction or the percentage of venous blood from one system that recirculates in the arterial outflow of the same system is 100% for both circuits in parallel. This is why there must be a connection at the atrial, ventricular, or arterial level to allow for any survival, even in the neonatal period.

The sites available for intercirculatory mixing in D-TGA can be intracardiac (PFO, ASD, VSD) or extracardiac (PDA, bronchopulmonary collaterals). Several factors affect the amount of intercirculatory mixing. The number, size, and position of anatomic communications are important. One large nonrestrictive communication will provide better mixing than two or three restrictive communications. The position of the

communication is also important because poor mixing can occur with large anterior muscular VSDs if their orientation is not favorable. Reduced ventricular compliance and elevated systemic and pulmonary vascular resistance (SVR and PVR) tend to reduce intercirculatory mixing by impeding flow across the anatomic communications. In the presence of anatomically adequate intercirculatory mixing sites, mixing is directly related to the total pulmonary blood flow. Patients with reduced pulmonary blood flow secondary to subpulmonic stenosis or PAH will have reduced intercirculatory mixing.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

A.6. What determines the oxygen saturation in patients with D-TGA?

Arterial saturation (Sa_{O_2}) is determined by the relative volumes and saturations of the recirculated systemic and effective systemic blood flows reaching the aorta. This is summarized in the following equation:

$$\text{Arterial saturation} = \frac{\begin{array}{c}[(\text{systematic venous saturation})\ (\text{recirculated systemic blood flow})] \\ +\ [(\text{pulmonary venous saturation})\ (\text{effective systemic blood flow})]\end{array}}{(\text{total systemic blood flow})}$$

The anatomic left-to-right shunt produces effective systemic blood flow, which is the volume of pulmonary venous blood reaching the systemic circulation. The anatomic left-to-right shunt is the result of intercirculatory mixing at the atrial, ventricular, and arterial levels and must equal the amount of the right-to-left shunt at the same sites. The greater the effective systemic blood flow (intercirculatory mixing) relative to the recirculated systemic blood flow, the greater the Sa_{O_2}. For a given amount of intercirculatory mixing and total systemic

blood flow, a decrease in systemic venous or pulmonary venous saturation will result in a decrease in Sao_2.

Total systemic blood flow is the sum of recirculated systemic venous blood plus effective systemic blood flow. Likewise, total pulmonary blood flow is the sum of recirculated pulmonary venous blood plus effective pulmonary blood flow. Recirculated blood makes up the largest portion of total pulmonary and systemic blood flow, with effective blood flows contributing only a small portion of the total flows. This is particularly true in the pulmonary circuit where the total pulmonary blood flow and the volume of the pulmonary circuit (LA, LV, PA) is three to four times larger than the total systemic blood flow and the volume of the systemic circuit (RA, RV, aorta). The net result is transposition physiology, where the PA oxygen saturation is greater than the aortic oxygen saturation. **Figure 39.1** further elucidates these concepts.

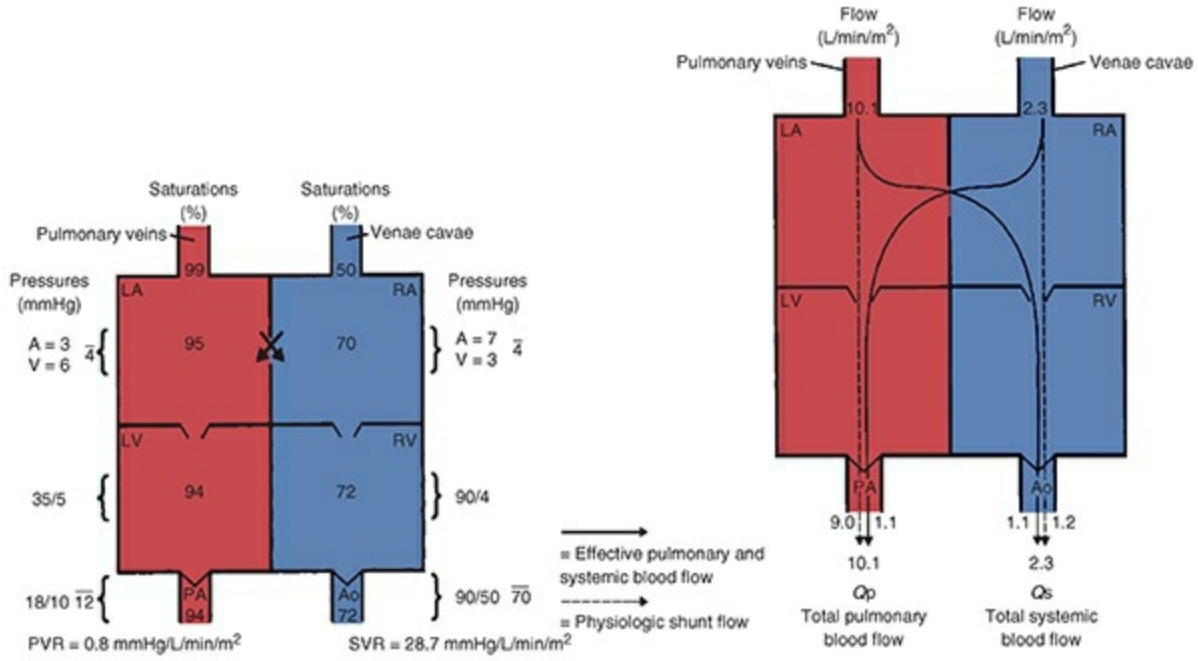

FIGURE 39.1. Depiction of saturations, pressures, and blood flows in complete transposition of the great vessels with intercirculatory mixing at the atrial level and a small LVOT gradient. It is apparent that total pulmonary blood flow (10.1 L/min/m^2) is almost five times the total systemic blood flow (2.3 L/min/m^2). Effective pulmonary and effective systemic blood flow are equal (1.1 L/min/m^2)

and are the result of an anatomic shunt at the atrial level. The physiologic left-to-right shunt is 9 L/min/m^2; this represents blood recirculated from the pulmonary veins to the pulmonary artery (PA). The physiologic right-to-left shunt is 1.2 L/min/m^2; this represents blood recirculated from the systemic veins to the aorta. In this depiction, pulmonary vascular resistance is low (approximately 1/35 of systemic vascular resistance), and there is a small (17 mm peak to peak) gradient from the left ventricle to the PA. These findings are compatible with the high pulmonary blood flow depicted. A, artery; Ao, aorta; LA, left atrium; LV, left ventricle; PVR, pulmonary vascular resistance; *Q*p, total pulmonary blood flow; *Q*s, total systemic blood flow; RA, right atrium; RV, right ventricle; SVR, systemic vascular resistance; V, vein. (*Modified with permission from Freed MO, Keane JF. Profiles in congenital heart disease. In: Grossman W, ed*. Cardiac Catheterization and Angiography. *Philadelphia, PA: Lea & Febiger; 1986:463*.)

$$SaO_2 = [(50)(1.2)] + [(99)(1.1)] / 2.3 = 73\%$$

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

A.7. Why did this infant have reverse differential cyanosis?

In D-TGA with IVS, the anatomic mixing sites are usually a PDA and a PFO. The dynamics of intercirculatory mixing in D-TGA with IVS are complex. Anatomic shunting at the atrial level is ultimately determined by the size of the atrial communication and the cyclic pressure variations between the left and right atria. The volume and compliance of the atria, ventricles, and vascular beds in each circuit as well as heart rate (HR) and phase of respiration influence this relationship. Shunting is from the RA to the LA during diastole as the result of the reduced ventricular and vascular compliance of the systemic circuit (RV and systemic arterial circuit). In systole, shunt is from the LA to the RA primarily because of the large volume of blood returning to the LA as a result of the high volume of recirculated pulmonary blood flow.

The direction of shunting across the PDA largely depends on the PVR and the size of the intra-atrial communication. When the PVR is low and the intra-atrial communication is

nonrestrictive, shunting is predominantly from the aorta to the PA through the PDA (effective pulmonary blood flow) and predominantly from the LA to RA across the atrial septum (effective systemic blood flow). When PVR is elevated, shunting across the PDA is likely to be bidirectional that in turn encourages bidirectional shunting across the atrial septum. When PVR is high and PA pressure exceeds aortic pressure, shunting at the PDA will be predominantly from the PA to the aorta. This will create reverse differential cyanosis—physiology wherein the preductal arterial saturation (right arm) is lower than the postductal arterial saturation (legs). This physiology is usually the result of a restrictive atrial communication producing left atrial hypertension and is associated with low effective blood flows (poor mixing) and hypoxemia. A balloon atrial septostomy can be lifesaving in this setting. Decompression of the LA promotes mixing at the atrial level and also reduces PVR and PA pressure promoting mixing at the PDA. Other causes of reverse differential cyanosis to be considered in D-TGA are the presence of an interrupted aortic arch or severe aortic coarctation.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

A.8. What are the preoperative issues pertaining to the coronary arteries in D-TGA?

As in normally related great vessels, the coronary arteries in D-TGA arise from the aortic sinuses that face the PA. In normally related vessels, these sinuses are located on the anterior portion of the aorta, whereas in D-TGA, they are located posteriorly. In most D-TGA patients (70%), the right sinus is the origin of the right coronary artery, whereas the left sinus is the origin of the left main coronary artery. In the remainder of cases, there is

considerable variability, with the most common variations being shown in **Figure 39.2**.

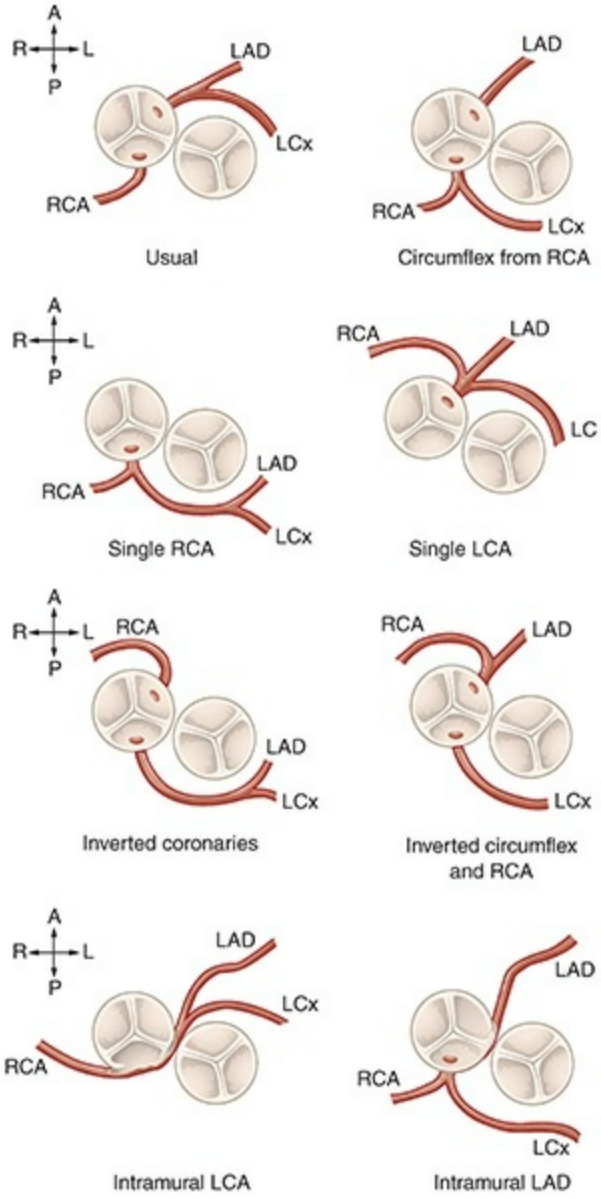

FIGURE 39.2. Depiction of the most common coronary artery patterns in transposition of the great vessels. The aorta is depicted anterior and to the right of the PA. LAD, left anterior descending coronary artery; LCA, left coronary artery; LCx, left circumflex coronary artery; RCA, right coronary artery. (*Adapted with permission from Mayer JE Jr, Sanders SP, Jonas RA, et al. Coronary artery pattern and outcome of arterial switch operation for transposition of the great arteries*. Circulation. *1990;82[5 suppl]:144*.)

Most patients with D-TGA have coronary anatomy that is suitable for the coronary reimplantation necessary in the ASO.

Patients with certain types of coronary anatomy (intramural coronaries, single coronary artery) are at risk for postoperative myocardial ischemia and early mortality because reimplantation can result in the distortion of the coronary ostia or the narrowing of the artery itself. Patients with intramural coronaries generally require resuspension of the posterior leaflet of neopulmonary valve once the coronaries and a surrounding tissue cuff are excised.

The presence of a single coronary artery or intramural coronary arteries is a risk factor for mortality, and this risk has persisted over the last two decades despite improvement in surgical technique.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

Pasquali SK, Hasselblad V, Li JS, et al. Coronary artery pattern and outcome of the arterial switch operation for transposition of the great arteries: a meta-analysis. *Circulation*. 2002;106(20):2575–2580.

A.9. What are the clinical subsets of D-TGA?

The four clinical subsets of D-TGA are characterized by differences in anatomy, amount of pulmonary blood flow, and sites of intercirculatory mixing. These are summarized in **Table 39.1**.

TABLE 39.1 Clinical Subsets of Transposition of Great Arteries

Anatomy	Pulmonary Blood Flow	Intercirculatory Mixing
D-TGA with IVS	Increased	Small
D-TGA with IVS; nonrestrictive atrial septum or PDA	Increased	Large
D-TGA with VSD	Increased	Large
D-TGA with VSD and LVOT obstruction	Reduced	Small
D-TGA with PAH	Reduced	Small

D-TGA, transposition of great arteries; IVS, intact ventricular septum; LVOT, left ventricular outflow tract; PAH, pulmonary artery hypertension; PDA, patent ductus arteriosus; VSD, ventricular septal

defect.
Reprinted with permission from DiNardo JA. Transposition of the great vessels. In: Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:357–380.

A.10. What is the differential diagnosis of D-TGA and how is the diagnosis made?

Figure 39.3 delineates the differential diagnosis for D-TGA in the cyanotic newborn.

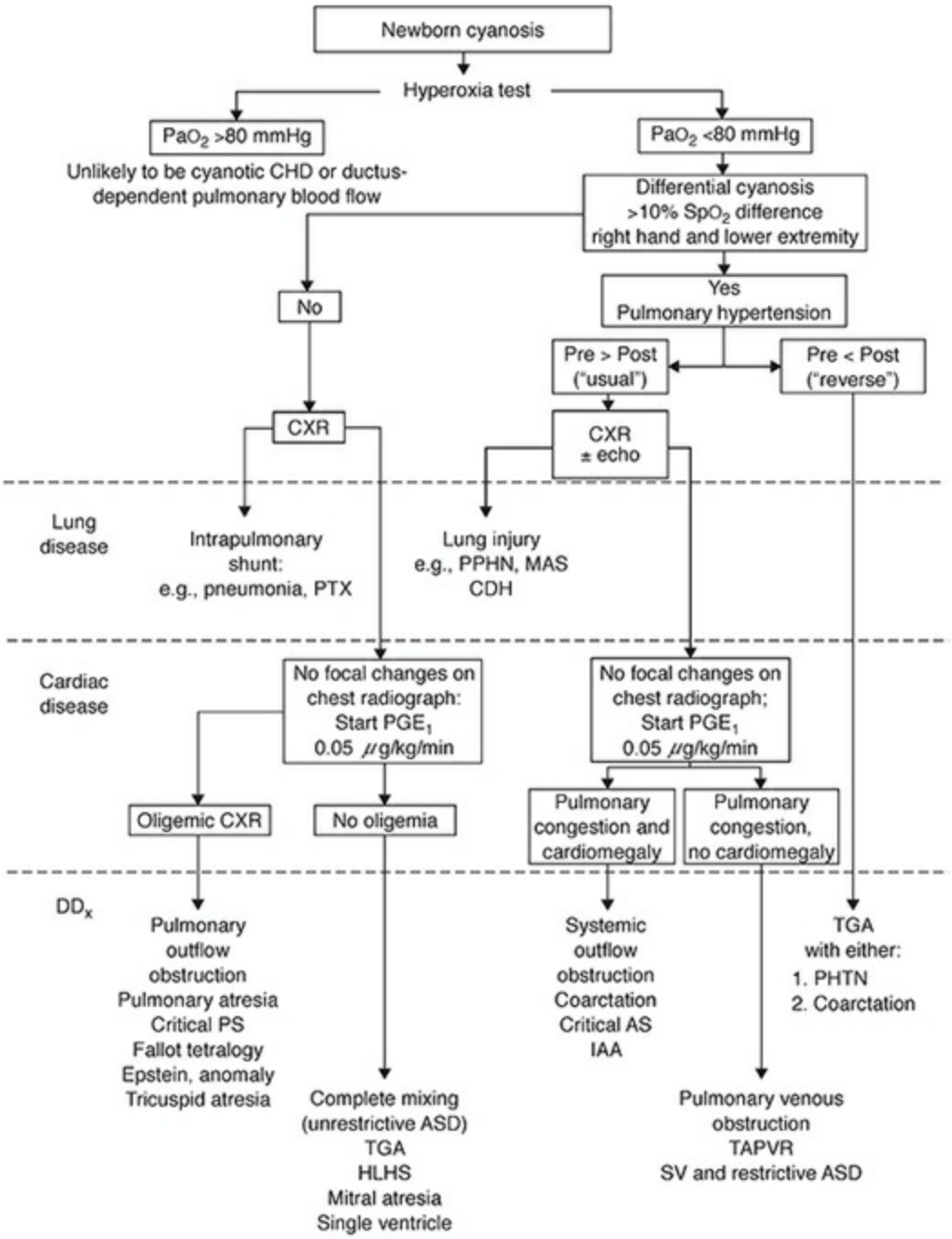

FIGURE 39.3. The differential diagnosis of transposition of the great arteries. AS, aortic stenosis; ASD, atrial septal defect; CDH, congenital diaphragmatic hernia; CHD, congenital heart disease; CXR, chest radiograph; DD_X, differential diagnosis; HLHS, hypoplastic left heart syndrome; IAA, interrupted aortic arch; MAS, meconium aspiration syndrome; PGE_1, prostaglandin E_1; PHTN, pulmonary hypertension; PPHN, persistent pulmonary hypertension of the newborn; PS, pulmonary stenosis; PTX, pneumothorax; Spo_2, peripheral oxygen saturation; SV, single ventricle; TAPVR, total anomalous pulmonary venous return; TGA, transposition of great arteries.

D-TGA may be associated with either cyanosis or CHF. Cyanosis is severe in patients with limited intercirculatory mixing. Infants with a large quantity of intercirculatory mixing have increased pulmonary blood flow, mild cyanosis, and symptoms of CHF.

Chest radiographs may appear normal in the first few weeks of life in infants with D-TGA and IVS. Eventually, the triad of an enlarged egg-shaped heart (large RA and RV), narrow superior mediastinum, and increased pulmonary vascular markings evolve. In patients with D-TGA and VSD without LVOT obstruction, a large cardiac silhouette and prominent pulmonary vascular markings are seen at birth. Right axis deviation and right ventricular hypertrophy are the electrocardiographic (ECG) findings in D-TGA with IVS, whereas right axis deviation, LV hypertrophy, and RV hypertrophy are seen with D-TGA and VSD.

Two-dimensional echocardiography is the diagnostic modality of choice in the diagnosis and assessment of infants with D-TGA. It accurately establishes the diagnosis of D-TGA and reliably identifies associated abnormalities, such as VSD, mitral valve, and tricuspid valve abnormalities, and LVOT obstruction. It also reliably delineates coronary artery anatomy. Echocardiographic analysis of the IVS position or LV geometry is also used to noninvasively assess the LV to RV pressure ratio and IV mass in neonates with D-TGA and IVS who are being evaluated as candidates for an ASO.

In institutions with high-level echocardiography, a comprehensive cardiac catheterization is no longer routinely performed in neonates with D-TGA. A limited catheterization may be performed in conjunction with a balloon atrial septostomy. In the rare instance where coronary anatomy cannot be clearly delineated by echocardiography, coronary angiography may be indicated. During catheterization of infants

with PAH, a trial of ventilation at an fraction of inspired oxygen (FIO_2) of 1.0 may be used to determine whether PVR is fixed or remains responsive to oxygen-induced pulmonary vasodilation.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

A.11. What preoperative interventions can help stabilize a patient with D-TGA?

Intact Ventricular Septum

Most neonates with D-TGA and IVS will be hypoxemic (arterial saturation ≤60%) within the first day of life. A proportion of these patients will have severely reduced effective pulmonary and systemic blood flow resulting in a PaO_2 less than 20 mmHg, hypercarbia, and an evolving metabolic acidosis secondary to poor tissue oxygen delivery. Prostaglandin E_1 (0.01 to 0.05 μg/kg/min) is administered to dilate and maintain the patency of the ductus arteriosus. This will be effective in increasing effective pulmonary and systemic blood flow and in improving PaO_2 and tissue oxygen delivery *if* (1) PVR is less than SVR and (2) there is a nonrestrictive or minimally restrictive atrial septal communication. Prostaglandin E_1 infusion is associated with apnea, pyrexia, fluid retention, and platelet dysfunction.

An emergent balloon atrial septostomy is performed in the catheterization laboratory utilizing angiography or in the ICU utilizing echocardiography if prostaglandin E_1 does not improve tissue oxygen delivery. This increases the amount of intercirculatory mixing at the atrial level. Recall that for a given amount of intercirculatory mixing and total systemic blood flow, an increase in pulmonary venous or systemic venous saturation will result in an increase in arterial saturation. Pulmonary venous saturation will be increased by tracheal intubation and

mechanical ventilation with oxygen. This will also reduce ventilation/perfusion ($\dot{V}/\dot{Q}$) mismatch and reduce PVR through induction of a respiratory alkalosis. Sedation and muscle relaxation reduce oxygen consumption, thereby increasing mixed venous oxygen saturation and arterial saturation.

In some centers, all neonates stabilized on prostaglandin E_1 have a balloon atrial septostomy to enlarge the atrial septal communication so that prostaglandin E_1 can be stopped and surgery scheduled on a semi-elective basis.

In rare instances, the combination of prostaglandin E_1, an atrial septostomy, and mechanical ventilation with sedation/muscle relaxation will be ineffective. In this circumstance, extracorporeal membrane oxygenation (either venoarterial or venovenous) support to improve tissue oxygenation and to reverse end-organ insult and lactic acidosis before surgery is an alternative approach to emergent surgery in a critically ill neonate.

Ventricular Septal Defect

Infants in this subset are mildly cyanotic with symptoms of CHF. Pulmonary blood flow is elevated, and there is extensive intercirculatory mixing. Reducing PVR to further augment pulmonary blood flow and intercirculatory mixing will not greatly influence the systemic oxygenation. Reducing PVR in these patients may increase the recirculated volume in the pulmonary circuit by increasing the compliance of the pulmonary circulation. Maintaining systemic blood flow will then necessitate an increase in cardiac output from a heart that is already volume overloaded. These patients are usually stable enough not to require immediate surgical or catheterization laboratory intervention. An ASO needs to be performed before intractable CHF or advanced PAH develops.

Ventricular Septal Defect and Left Ventricular Outflow Tract Obstruction

The degree of cyanosis in these infants will depend on the degree of LVOT obstruction. LVOT obstruction not only reduces pulmonary blood flow and intercirculatory mixing but also protects the pulmonary vasculature from increased pressures and volumes that accelerate the development of PAH. Efforts to increase pulmonary blood flow by decreasing PVR are less effective when LVOT obstruction is severe. These infants will be severely cyanotic and will develop erythrocytosis and may require a palliative aortopulmonary shunt to increase pulmonary blood flow prior to definitive repair. The Rastelli, LeCompte, and Nikaidoh procedures are performed for D-TGA with LVOT obstruction.

Pulmonary Artery Hypertension

The goal of diagnosis and treatment of infants with D-TGA is to intervene surgically before the development of PAH. As PAH progresses, the child becomes progressively cyanotic and polycythemic. Efforts to reduce PVR will increase pulmonary blood flow and intercirculatory mixing in infants where PVR is not fixed. Infants with advanced PAH (PVR >10 Wood units; histologic grade 4) are generally candidates only for palliative therapy. In particular, closure of a VSD in the presence of advanced pulmonary hypertension carries a high mortality rate owing to the afterload mismatch and the resultant pulmonary ventricular (LV) dysfunction. These patients are candidates for a palliative intra-atrial physiologic repair (Mustard or Senning procedure) without closure or with fenestrated closure (4- to 5-mm hole in the center of the VSD patch) of the VSD.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

A.12. What are the surgical options for repair? Why is one chosen over the others?

Arterial Anatomic Repair: Arterial Switch (Jatene) Operation

The ASO anatomically corrects the discordant VA connections and is the procedure of choice for patients with D-TGA. Following repair, the RV is connected to the PA and the LV to the aorta. Clinical success with the ASO, summarized in **Figure 39.4**, was achieved in 1975. In order for the ASO to be successful, the original pulmonary ventricle (LV) must have sufficient mass to be capable of functioning, as the systemic ventricle following the switch. Patient selection and the timing of the surgical procedure are important variables in determining the success of this procedure. The ASO was originally described in patients with D-TGA and a large VSD or a large PDA. In these patients, the pulmonary ventricle (LV) remains exposed to systemic pressures, and the LV mass remains sufficient to support the systemic circulation. For this subset of patients, the ASO is generally performed within the first 2 to 3 months of life before intractable CHF or irreversible PAH develops.

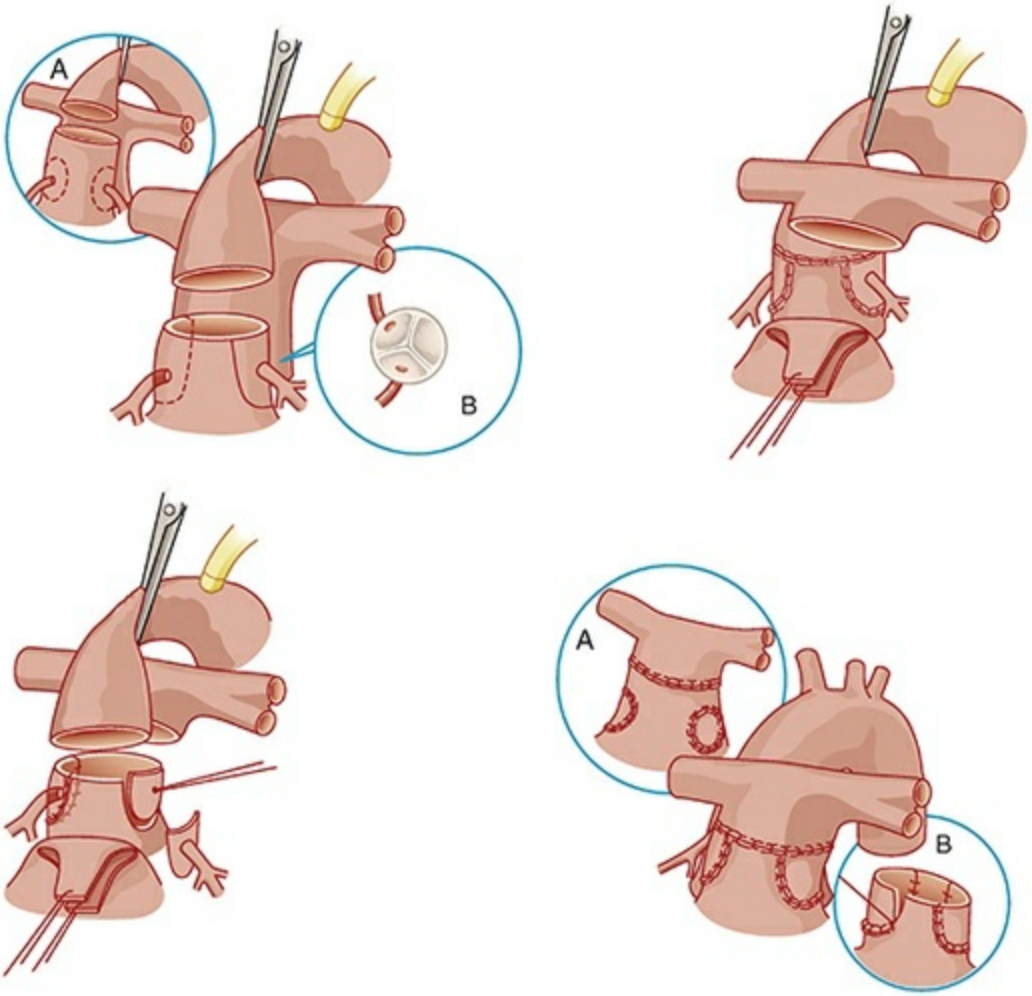

FIGURE 39.4. Details of the arterial switch procedure. Upper left. Aorta is transected and left and right main coronary arteries are excised using either button of aortic wall **(A)** or segment of aortic wall **(B)** extending from rim of aorta. **Lower left.** Equivalent segment of pulmonary arterial wall is excised, and coronary arteries are sutured to PA. **Upper right.** Distal PA is brought anterior to ascending aorta (LeCompte maneuver), and proximal PA is anastomosed to distal aorta. **Lower right.** Sites of coronary explantation are repaired using either patch of prosthetic material **(A)** or segment of pericardium **(B)**. Finally, proximal aorta is sutured to distal PA. (*Adapted from Castaneda AR, Norwood WI, Jonas RA, et al. Transposition of the great arteries and intact ventricular septum: anatomical repair in the neonate*. Ann Thorac Surg. *1984;38[5]:438–443. Copyright © 1984 The Society of Thoracic Surgeons. With permission.*)

Patients with D-TGA and IVS have a progressive reduction in LV mass over the first 3 or 4 weeks of life as the physiologic pulmonary hypertension present at birth resolves. Adequate mass to support the systemic circulation reliably exists in these patients only for the first 3 or 4 weeks of life, so a primary ASO

must be performed in this period. Most are performed in the first few days of life. Historically, favorable candidates for a primary ASO in the neonatal period were identified by cardiac catheterization with an LV to RV pressure ratio of at least 0.6. Currently, two-dimensional echocardiography is used to noninvasively assess the LV to RV pressure ratio. Three types of ventricular septal geometry have been described. Patients in whom the ventricular septum bulges to the left (type 3), indicating a low pressure in the pulmonary ventricle (LV), are not candidates for a neonatal ASO. Patients with septal bulging to the right (type 1), indicating a high pressure in the pulmonary ventricle (LV), and those patients with an intermediate septal position (type 2) are considered good candidates. Most neonates with D-TGA and IVS who are suitable candidates for an ASO have type 2 septal geometry.

The staged ASO for D-TGA with IVS is used for those neonates in whom surgery cannot be performed in the first month of life secondary to events such as prematurity, sepsis, low birth weight (<1.0 kg), or late referral. The first step of a staged procedure retrains the LV to accept the systemic workload and usually involves the creation of a nonrestrictive atrial septum (if it does not already exist), placement of a PA band, and creation of an aortopulmonary shunt with entry to the PA distal to the band. The PA band must be tight enough to increase pressure in the pulmonary ventricle (LV) to approximately one-half to two-thirds of that in the systemic ventricle (RV). This will increase the afterload sufficiently to stimulate an increase in LV mass. In the past, the PA band was left on for 3 to 6 months, after which the PA was debanded, the shunt taken down, and an ASO was performed. Currently, a rapid two-stage repair is favored where the ASO is performed as early as 1 week after preparatory PA banding, often during the same hospitalization. This approach is possible because the LV

mass usually doubles after 1 week of PA banding. Establishing the appropriate tightness of the band can be challenging, and the PA band as well as the systemic to PA shunt can distort the PA making the ASO difficult. Intraoperative echocardiography is useful in guiding placement of the PA band. The band is tightened enough to flatten the IVS by shifting it toward the RV.

Jonas RA, Giglia TM, Sanders SP, et al. Rapid, two-stage arterial switch for transposition of the great arteries and intact ventricular septum beyond the neonatal period. *Circulation*. 1989; 80 (3, pt 1):I203–I208.

Intra-atrial Physiologic Repairs: Mustard and Senning Procedures

The Mustard and the Senning procedures are atrial switch procedures that surgically create discordant AV connections so that there is a physiologic correction of the VA discordance. Systemic venous blood is routed to the anatomic LV and the PA, whereas pulmonary venous blood is routed to the anatomic RV and the aorta. This is not an anatomic correction because the RV becomes the systemic ventricle. These atrial switch procedures are primarily of historic interest, as the ASO is nearly universally performed for D-TGA.

Vejlstrup N, Sørensen K, Mattsson E, et al. Long-term outcome of Mustard/Senning correction for transposition of the great arteries in Sweden and Denmark. *Circulation*. 2015;132:633–638.

Rastelli, LeCompte, and Nikaidoh Procedures

These procedures are used to correct D-TGA with VSD and LVOT (subpulmonic and/or pulmonic) obstruction. Performance of an ASO under these circumstances would leave the infant with residual neoaortic or subneoaortic (LVOT) obstruction. In the Rastelli procedure, the subpulmonic LVOT obstruction is resected and the LVOT is baffled to the aorta with the patch used to close the VSD. An RV-PA conduit is created. The LeCompte procedure involves resecting the LV outlet septum,

closing the VSD to route the LV blood to the aorta, and bringing the PAs anteriorly to be reanastomosed to the RV. The Nikaidoh procedure is an aortic translocation procedure where the aortic root and coronary arteries are resected and reanastomosed to the RV after the outlet septum has been resected and the RVOT is reconstructed with a pericardial patch or homograft.

Bautisa-Hernandez V, Marx GR, Bacha EA, et al. Aortic root translocation plus arterial switch for transposition of great arteries with left ventricular outflow tract obstruction: intermediate-term results. *J Am Coll Cardiol*. 2007;49:485–490.

Honjo O, Kotani Y, Bharucha T, et al. Anatomical factors determining surgical decision-making in patients with transposition of the great arteries with left ventricular outflow tract obstruction. *Eur J Cardiothorac Surg*. 2013;44:1085–1094.

Martins P, Castela E. Transposition of the great arteries. *Orphanet J Rare Dis*. 2008;3:27.

B. Preoperative Evaluation and Preparation

B.1. What information is important to prepare for this case?

The preoperative evaluation should begin with a careful history and physical examination. Gestational age, birth complications, family history, and any other medical problems should be noted. A comprehensive airway evaluation should be performed and any previously used endotracheal tube sizes and leak pressure should be noted. Arterial and intravenous access should be assessed. A type and cross must be sent to the blood bank to ensure adequate red blood cells and blood component therapies are available in the operating room.

The preoperative ECG, chest radiograph, and echocardiograms should be reviewed. Particular attention should be paid to septal geometry, biventricular function, coronary anatomy, and adequacy of mixing at the atrial septal and ductal

levels. The duct may remain patent even if prostaglandin E_1 has been discontinued.

Laboratory data should include a complete blood count, electrolytes, platelet count, arterial blood gas, calcium, blood urea nitrogen, creatinine, liver function tests, and blood glucose. Given that this infant presented with severe hypoxemia, end-organ dysfunction must be ruled out. The liver function tests and creatinine should be normal; if they are elevated, consideration should be given to further medical optimization. A head ultrasonographic examination should be performed to rule out intraventricular hemorrhage.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

B.2. What are the anesthetic goals before cardiopulmonary bypass (CPB)?

- Maintain HR, contractility, and preload to maintain cardiac output; decreases in cardiac output decrease systemic venous saturation with a resultant fall in arterial saturation.
- Maintain ductal patency with prostaglandin E_1 (0.01 to 0.05 μg/kg/min) in ductal-dependent patients.
- Avoid increases in PVR relative to SVR. Increases in PVR will decrease pulmonary blood flow and reduce intercirculatory mixing. In patients with PAH, ventilatory interventions should be used to reduce PVR. In patients with LVOT obstruction that is not severe, ventilatory interventions to reduce PVR will increase pulmonary blood flow and intercirculatory mixing.
- Reductions in SVR relative to PVR should be avoided. Reducing SVR increases recirculation of systemic venous blood and decreases arterial saturation.
- In patients with D-TGA and VSD with symptoms of CHF,

ventilatory interventions to reduce PVR are not warranted because they will produce small improvements in arterial saturation at the expense of a reduction in systemic perfusion.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

B.3. What is the plan for glucose management in this patient?

Maintenance for caloric requirements in the awake neonate/infant are 100 kcal/kg/day or 4 kcal/kg/hr. This caloric requirement can be met with glucose 25 g/kg/day or 1 g/kg/hr. From a practical point of view, this glucose requirement can be met with 10% dextrose (100 mg per mL) run at the maintenance volume replacement rate of 4 mL/kg/hr. Ten percent dextrose run at half this rate (2 mL/kg/hr) is usually sufficient to meet the caloric requirements of an anesthetized infant while avoiding both the hyperglycemia and hypoglycemia that can be detrimental to neurologic outcome particularly following DHCA. Dextrose infusions should be discontinued before commencement of CPB because the associated neuroendocrine response to CPB generally produces mild hyperglycemia. Some infants receive nutritional support as part of medical stabilization before surgery. High-calorie total parenteral nutrition and intralipid therapy should be discontinued and replaced with a 10% dextrose infusion several hours before transport to the operating room. Continued administration of these high-calorie infusions makes intraoperative serum glucose management problematic. In these patients, higher dextrose infusion rates may be necessary pre-CPB to avoid rebound hypoglycemia.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and*

Children. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

C. Intraoperative Management

C.1. How would you monitor this infant?

Preinduction monitoring should include noninvasive blood pressure, ECG, and pulse oximetry. Pulse oximeter probes should be placed on the right upper and left upper or lower extremities to measure preductal and postductal oxygen saturations, respectively. An intraarterial catheter is placed for invasive blood pressure monitoring and a double-lumen central venous line is usually placed for monitoring and drug administration. A nasopharyngeal temperature probe is important to estimate brain temperature, and a rectal or bladder temperature probe is important to measure core body temperature. Infants transferred from the ICU will have an umbilical artery or femoral artery catheter in place. A bladder catheter to measure urine output should be placed. A TEE probe can be inserted if the patient is large enough, otherwise a transthoracic echocardiogram is performed after endotracheal intubation and stabilization. In reality, a pulse oximeter and an ECG may be all that is practical in the early stages of induction. The other monitors are then quickly added as induction progresses. An epicardial echocardiogram is usually performed after the repair to assess the coronary artery anastomoses and intracardiac repairs if a TEE probe was not placed.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

C.2. What would be the best method of induction for this patient?

An IV induction is indicated for this patient. Infants born with

D-TGA are stabilized in an ICU so peripheral or central IV access and possibly invasive arterial monitoring would have been established. Anesthesia is generally induced and maintained with a synthetic opioid, such as fentanyl or sufentanil. In a high-dose opioid technique, the opioid is the primary anesthetic. Twenty-five to 100 μg per kg fentanyl or 2.5 to 10 μg per kg sufentanil is usually required for the entire case. Inhalational agents or benzodiazepines supplement opioids in a low or moderate opioid technique, so only 5 to 25 μg per kg fentanyl or 0.5 to 2.5 μg per kg sufentanil is usually required for the case. The high-dose opioid technique is particularly useful in neonates and infants, since opioids provide hemodynamic stability, do not depress the myocardium, and blunt reactive pulmonary hypertension.

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C.3. Is CPB in infants and children different from adults?

The major differences between adult and pediatric CPB are summarized in **Table 39.2**.

TABLE 39.2 Major Differences between Adult and Pediatric Cardiopulmonary Bypass

Parameter	Adult	Pediatrics
Hypothermic temperature	Rarely below 25°C–32°C	Commonly 15°C–20°C
Use of total circulatory arrest	Rare	Common
Pump prime		
Dilution effects on blood volume	25%–33%	200%–300%
Additional additives in pediatric primes		Blood, albumin
Perfusion pressures	50–80 mmHg (Some centers accept 30 mmHg.)	20–50 mmHg
Influence of pH management strategy	Minimal at moderate hypothermia	Marked at deep hypothermia
	30–45 mmHg	20–80 mmHg

Measured $PaCO_2$ differences		
Glucose regulation		
Hypoglycemia	Rare—requires significant hepatic injury	Common—reduced hepatic glycogen stores
Hyperglycemia	Frequent—generally easily controlled with insulin	Less common—rebound hypoglycemia may occur

Flows of 2.0 to 2.5 L/min/m^2 are commonly used for infants, children, and adults during mild to moderate systemic hypothermia. Flow rates (expressed in mL/kg/min) will be substantially higher in the neonate than in the adult because of age-related differences in surface area to weight ratios. The recommended full flow rates for pediatric CPB are summarized in **Table 39.3**.

TABLE 39.3 Recommended Full Flow Rates for Pediatric Cardiopulmonary Bypass

Patient Weight (kg)	Full CPB Flow Rates (mL/kg/min)
<3	150–200
3–10	125–175
10–15	120–150
15–30	100–120
30–50	75–100
>50	50–75

CPB, cardiopulmonary bypass.

The vast majority of operative procedures in children require the use of either total CPB or DHCA. Arterial and venous cannulation can be particularly challenging in neonates and infants. Venous cannulation for DHCA is usually accomplished with a single large venous cannula in the RA. Once cooling is complete, CPB flow rates are reduced to zero and the venous cannula is removed to allow for maximum surgical exposure. In cases requiring total CPB, the superior and inferior cavae and other sources of systemic venous return are cannulated and surgical tourniquets or tapes are passed around the external

circumference of the vessels. When these tapes are tightened around the cannulae, the right heart can be isolated completely and opened without entrainment of air into the venous circuit or obscuration of the surgical field by venous blood. At least one tape must be left untightened during delivery of antegrade cardioplegia to allow egress of cardioplegia solution from the coronary sinus without distention of the RA. The superior vena cava (SVC) is larger than the inferior vena cava (IVC) in neonates and infants, so the larger venous cannula is usually placed in the SVC. The opposite is true in older children where two-thirds of systemic venous return is from the IVC.

Aortic cannulation in children may be complicated by a hypoplastic ascending aorta or aortic arch, as in patients with hypoplastic left heart syndrome. In these cases, systemic circulation is ductal dependent, so it may be necessary to establish systemic perfusion through the ductus arteriosus by cannulating the PA. If the aortic arch is interrupted, cannulation of the aorta proximal and distal to the interruption is necessary. In infants and children, the arterial cannula is large relative to the size of the aorta, so constant vigilance is necessary to avoid complete or partial obstruction of the aorta by the cannula. Signs of this include dampening of the arterial pressure tracing, distension of the systemic ventricle, and an increase in the aortic line pressure during placement or manipulation of the aortic cannula. The surgeon must reposition the line to ensure adequate perfusion. Some centers utilize near-infrared spectroscopy and transcranial Doppler ultrasonographic technology as adjunctive methods to assess cerebral blood flow during CPB.

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Gravlee GP, Davis RF, Hammon JW, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA:

Wolters Kluwer; 2015:655–695.

C.4. What is modified ultrafiltration (MUF)?

Ultrafiltration removes excess fluid from blood by hydrostatic pressure across a semipermeable membrane. The devices are the same, as those used in hemodialysis, but no dialysate is used. When used in conjunction with CPB, they are commonly called hemoconcentrators because they produce an increase in hematocrit by removing excess fluid. These devices consist of a core of microporous hollow fibers made of polysulfone, polyamide, or polyacrylonitrile material arranged in a bundle. The pore size is generally 0.30 to 0.40 μm. Blood inflow must be from the arterial side of the CPB circuit because of the pressure drop across the device. Outflow is diverted to the cardiotomy reservoir or venous reservoir. The ultrafiltrate composition is similar to a glomerular filtrate. It is collected in a container connected to a vacuum source and discarded.

The rate at which ultrafiltrate is produced is dependent on the transmembrane pressure (TMP) gradient. TMP is determined by the arterial inlet pressure (P_a), the venous outlet pressure (P_v), the absolute value of applied suction at the outlet (P_n), the oncotic pressure at the inlet (P_i), and the oncotic pressure at the outlet (P_o):

$$\text{TMP} = \frac{P_a + P_v}{2} + P_n - \frac{P_i + P_o}{2}$$

P_n is increased by adjusting the regulated vacuum source connected to the outlet of the device. TMP should not exceed 500 mmHg.

MUF is a technique used to ultrafiltrate blood after weaning from CPB while maintaining the integrity of the bypass circuit. MUF may be performed using either an arteriovenous or venovenous system. In the arteriovenous system, blood flows

from the aortic cannula through a separate circuit and roller pump to the inflow of the hemoconcentrator before returning to the RA. Blood volume is kept constant as ultrafiltrate is lost by replacing the ultrafiltrate volume with blood from the venous reservoir of the CPB circuit, which also passes through the hemoconcentrator circuit before returning to the RA. In this way, the patient's blood as well as the CPB circuit blood is hemoconcentrated and the CPB circuit remains primed. In the venovenous system, blood passes from the IVC cannula through a separate circuit and roller pump to the inflow of the hemoconcentrator before returning to the patient through the SVC cannula. Blood volume is also kept constant in this system by replacing ultrafiltrate volume with blood from the CPB circuit, which also passes through the ultrafiltrator before returning to the patient. The end point for termination of MUF following CPB varies from institution to institution, with institutions terminating MUF after a set time interval (15 to 20 minutes), a set hematocrit (40%), or a set volume removed (750 mL per m^2). Heparin anticoagulation must be maintained during MUF, with protamine reversal of heparin initiated after termination of MUF.

Neonates and infants are the patients who most benefit from MUF because the volume of the CPB circuit is large relative to their blood volume. Hemoconcentration increases the hematocrit and concentration of coagulation factors and reduces total body water. MUF may be an effective method of attenuating the deleterious consequences of using large asanguinous primes, particularly in neonates and infants. In studies comparing MUF to no ultrafiltration, a large asanguinous pump prime was usually defined as a 400 to 900 mL prime with packed red blood cells added to reach a hematocrit of 15% to 20%.

Continuous ultrafiltration is a similar MUF except it can occur only during CPB and only when there is sufficient volume

in the CPB circuit. MUF and continuous ultrafiltration are indistinguishable in their effect on hematocrit, mean arterial pressure, HR, and LV shortening fraction when equal volumes of fluid are removed.

Matte GS. *Perfusion for Congenital Heart Surgery: Notes on Cardiopulmonary Bypass for a Complex Patient Population*. Hoboken, NJ: Wiley-Blackwell; 2015:33–65.

Whiting D, Yuki K, DiNardo JA. Cardiopulmonary bypass in the pediatric population. *Best Pract Res Clin Anaesthesiol*. 2015;29(2):241–256.

Williams GD, Ramamoorthy C, Chu L, et al. Modified and conventional ultrafiltration during pediatric cardiac surgery: clinical outcomes compared. *J Thorac Cardiovasc Surg*. 2006;132(6):1291–1298.

C.5. Briefly describe the surgical techniques of the Mustard/Senning, ASO, and Rastelli procedures.

Intra-atrial Physiologic Repairs: Mustard and Senning Procedures

The Mustard and Senning procedure are atrial switch procedures where the interatrial septum is excised and a baffle is used to redirect pulmonary and systemic venous blood. In the Mustard procedure, the baffle is made of native pericardium or synthetic material. The Senning procedure uses autologous tissue from the right atrial wall and interatrial septum. In both procedures, the pulmonary blood flows over the baffle and is directed across the tricuspid valve into the RV and aorta, and the systemic venous blood flows on the underside of the baffle and is directed across the mitral valve into the LV and out the PA. This results in a physiologic but not anatomic correction of D-TGA because the morphologic RV becomes the systemic ventricle. These procedures are performed with total hypothermic CPB, bicaval cannulation, aortic cross-clamping during cardioplegic arrest, and sometimes LFCPB.

Arterial Anatomic Repair: Arterial Switch (Jatene)

Operation

In the ASO, the great arteries are switched so that VA concordance is restored. First, the PA and the aorta are transected distal to their respective valve and then the coronary arteries are explanted from the ascending aorta with 3 to 4 mm of surrounding tissue and reimplanted into the proximal PA (neoaorta). The explant sites are repaired either with pericardium or synthetic material. The distal PA is brought anterior to the aorta (LeCompte maneuver) to be reanastomosed to the old proximal aorta (right ventricular outflow) and the distal aorta reanastomosed to the old proximal PA (left ventricular outflow). The ASO is a complete anatomic and physiologic repair of D-TGA. The ASO is done using total hypothermic CPB with aortic cross-clamping and cardioplegic arrest. Intervals of LFCPB are customarily used, and a short interval of DHCA may be employed to close the atrial septum or VSD if a single venous cannula rather than bicaval venous cannulation is used. Closure of a VSD is preferentially done with a transatrial approach through the tricuspid valve to avoid a ventriculotomy that could contribute to postoperative RV dysfunction.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

Jatene AD, Fontes VF, Paulista PP, et al. Anatomic correction of transposition of the great vessels. *J Thorac Cardiovasc Surg*. 1976;72:364–370.

Rastelli Procedure

The Rastelli procedure is a physiologic repair for D-TGA with VSD and subpulmonic stenosis, where the LV and aorta are brought into continuity with a patch tunnel that also closes the VSD. The PA must be transected and ligated and the RV and proximal PA are brought into continuity with a valved conduit

or homograft. The VSD may have to be enlarged in some cases to prevent subaortic stenosis. The patch tunnel that connects the LV to the aorta bypasses subpulmonic and pulmonic stenosis. This procedure is performed under similar conditions as the ASO, with total hypothermic CPB, bicaval cannulation, aortic cross-clamping during cardioplegic arrest, and intervals of LFCPB.

Historically, most of these patients had a palliative systemic to PA shunt placed in the newborn period and then returned for the Rastelli procedure and takedown of the shunt at 2 to 3 years of age. The delay was felt necessary to avoid performing a right ventriculotomy in infants with immature myocardium and limited contractile elements and to allow adequate growth of the RV and PAs to permit placement of an RV to PA conduit. In the current era, with improvements in myocardial protection, CPB technology, and surgical technique, this procedure can be performed as a primary procedure in the neonatal period.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

Jatene AD, Fontes VF, Paulista PP, et al. Anatomic correction of transposition of the great vessels. *J Thorac Cardiovasc Surg*. 1976;72:364–370.

C.6. What is hypothermia, and how is it classified? What is low-flow cardiopulmonary bypass (LFCPB)? What is deep hypothermic circulatory arrest (DHCA)?

The levels of systemic hypothermia employed during CPB are generally defined as follows: mild (35°C [95.0°F] to 32°C [89.6°F]), moderate (31°C [87.8°F] to 26°C [78.8°F]), deep (25°C [77°F] to 20°C [68°F]), and profound (<20°C [68°F]). It is not uncommon for temperatures less than 20°C (68°F) used in conjunction with pediatric cardiac surgery to be called deep hypothermia. LFCPB in neonates/infants conducted in

conjunction with temperatures of 18°C (64.4°F) to 25°C (77°F) is generally defined as flow rates 50 to 70 mL/kg/min or approximately 1.0 to 1.5 L/min/m^2.

Profound hypothermic circulatory arrest, commonly referred to as DHCA, is conducted at temperatures of 18°C (64.4°F) to 20°C (68°F) and allows cessation of CPB, venous and arterial cannula removal, and exsanguination of the patient into the venous reservoir of the CPB circuit. This technique used to improve exposure of intracardiac defects and to facilitate aortic arch reconstruction in infants and children. There has been substantial refinement of the technique of DHCA since its successful inception in the 1970s. In the current era, DHCA is used selectively and for short intervals. It is utilized primarily for the aortic arch reconstruction component of the Norwood procedure, repair of interrupted aortic arch, neonatal repair of total anomalous pulmonary venous connection, and complicated intracardiac repairs such as complete AV canal defects in small (<2.0 kg) neonates and infants.

Matte GS. *Perfusion for Congenital Heart Surgery: Notes on Cardiopulmonary Bypass for a Complex Patient Population*. Hoboken, NJ: Wiley-Blackwell; 2015:33–65.

Matte GS, DiNardo JA. Pediatric cardiopulmonary bypass. In: Gravlee GP, Davis RF, Hammon JW, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2015:655–695.

Whiting D, Yuki K, DiNardo JA. Cardiopulmonary bypass in the pediatric population. *Best Pract Res Clin Anaesthesiol*. 2015;29(2):241–256.

C.7. Why is hypothermia beneficial to the brain during LFCPB and DHCA?

Hypothermia is arguably the most important component of LFCPB and DHCA. The hypothermia-induced reduction in cerebral metabolic rate for oxygen ($CMRO_2$) slows the rate of depletion of high-energy phosphates and the development of

intracellular acidosis and delays or prevents the neuronal energy failure that leads to terminal membrane depolarization and subsequent neuronal injury or death during an ischemic episode.

Q_{10} defines the ratio of organ oxygen consumption at a defined temperature to the oxygen consumption at a temperature 10°C (18°F) lower. The cerebral Q_{10} is approximately 3.65 in children and 2.3 in adults. The cerebral metabolic rate will still be approximately 10% to 15% of its normothermic baseline at 15°C (59°F). If it is assumed that 3 to 5 minutes of cerebral ischemia can be tolerated at 37°C (98.6°F) and the Q_{10} is 3.0, 9 to 15 minutes of ischemia can be tolerated at 27°C (80.6°F) and 27 to 45 minutes can be tolerated at 17°C (62.6°F).

In addition to reducing $CMRO_2$, hypothermia also serves to ameliorate some of the sequelae of neuronal ischemia when instituted before the ischemia insult. Specifically, hypothermia markedly reduces release of the excitatory neurotransmitters glutamate, aspartate, and glycine that accompany cerebral ischemia and subsequent reperfusion. In energy-deprived cells, glutamate in particular is neurotoxic in part due to the role it plays in inducing massive calcium influx through *N*-methyl-D-aspartic acid receptors. Hypothermia also blunts the inhibitory effect of hypoxia on nitroxidergic (postganglionic parasympathetic nerve where nitric oxide is the neurotransmitter)-induced cerebral vasodilation. In addition, there is evidence that hypothermia may attenuate neutrophil migration into ischemic tissue.

Matte GS, DiNardo JA. Pediatric cardiopulmonary bypass. In: Gravlee GP, Davis RF, Hammon JW, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2015:655–695.

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C.8. Explain the difference between *α*-stat and pH-stat blood gas management.

pH-stat and *α*-stat are acid–base management strategies that address the temperature-induced differences in blood pH, oxygen solubility, and CO_2 solubility. These management strategies directly influence blood flow to the brain and other organs during hypothermic CPB or DHCA. The difference between these two strategies becomes marked because patient temperature progressively decreases below 37°C (98.6°F) but is not clinically relevant until patient temperature is less than 30°C (86°F). At normothermia (37°C [98.6°F]), there is no difference between pH-stat and *α*-stat management.

Although pH-stat and *α*-stat acid–base management are commonly mentioned in association with temperature-corrected and temperature-uncorrected interpretation of blood gases, these are entirely different concepts. The method of blood gas interpretation (corrected or uncorrected) does not dictate the method of acid–base management (pH-stat or *α*-stat). *α*-Stat or pH-stat management is possible with use of both temperature-corrected and temperature-uncorrected blood gases.

When a blood gas sample is drawn from a hypothermic patient at 25°C (77°F) and sent to the blood gas laboratory, the sample is warmed to 37°C (98.6°F) before measurement. The values obtained at 37°C (98.6°F) are called the temperature-uncorrected values. These values are converted to temperature-corrected values using a nomogram. The nomogram accounts for temperature-induced changes in pH, oxygen solubility, and CO_2 solubility in a closed-blood system. When blood in a closed system is cooled to a lower temperature, the electrochemically neutral pH is higher and the associated P_{CO_2} is lower than in a closed blood system at 37°C (98.6°F). Therefore, electrochemical neutrality is maintained by keeping pH alkalotic

in temperature-corrected blood gases and normal in temperature-uncorrected gases. This is known as *α-stat regulation*. For practical purposes, it is easier to use uncorrected gases and keep pH and P_{CO_2} in the range considered normal at 37°C (98.6°F). It has been demonstrated clinically that cerebral blood flow and oxygen consumption are appropriately coupled when *α*-stat regulation is used. Deep hypothermia in the presence of *α*-stat regulation produces loss of cerebral autoregulation such that cerebral blood flow varies directly with arterial pressure.

pH-stat regulation refers to maintaining pH and P_{CO_2} at normal values for blood at 37°C (98.6°F) regardless of actual blood temperature. With this strategy, a blood sample will have a normal pH and P_{CO_2} when temperature-corrected gases are used, and acidotic pH and P_{CO_2} values when temperature-uncorrected gases are used. For practical purposes, pH-stat is maintained by adding CO_2 to the ventilating gas during hypothermic CPB to increase P_{CO_2} and decrease the pH. In contrast to *α*-stat regulation, in which total CO_2 content is kept constant, pH-stat regulation results in an increase in total CO_2 content. The cerebral vasculature maintains vasomotor responses to varying P_{CO_2} during hypothermic CPB. This response is maintained during both moderate and deep hypothermia despite the fact that deep hypothermia induces loss of cerebral blood flow autoregulation. It has been demonstrated clinically that when pH-stat regulation is used with moderate hypothermic CPB, there is uncoupling of cerebral blood flow and metabolism and loss of cerebral autoregulation. As a result, cerebral blood flow varies linearly with arterial blood pressure, and cerebral hyperperfusion exists with cerebral blood flow far in excess of that dictated by cerebral metabolic rate. This hyperperfusion state is the result of (1) reduced cerebral oxygen consumption induced by hypothermia and (2) cerebral

vasodilation resulting from a disproportionately high P_{CO_2} for the degree of hypothermia present. The potential danger of the hyperperfused state is that it may result in increased delivery of microemboli into the cerebral circulation.

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Matte GS, DiNardo JA. Pediatric cardiopulmonary bypass. In: Gravlee GP, Davis RF, Hammon JW, et al, eds. *Cardiopulmonary Bypass and Mechanical Support: Principles and Practice*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2015:655–695.

C.9. What are the immediate post-CPB issues following ASO?

Hemorrhage from the extensive suture lines can require emergent surgical repair on CPB or can be caused by post-CPB coagulopathy. Temporarily reducing arterial blood pressure with vasodilating agents can be helpful. Aggressive blood component therapy is often required and may require 1 to 2 units of platelets (0.25 to 0.5 units per kg) to obtain a therapeutic platelet count increase in neonates. Because platelets are suspended in fresh frozen plasma, a platelet transfusion of this size usually results in a fresh frozen plasma transfusion of 10 to 15 mL per kg. Cryoprecipitate transfusion is sometimes necessary to restore fibrin levels to presurgical levels. Point of care assessment and characterization of coagulopathy using thromboelastography or rotational thromboelastometry may be helpful.

Myocardial ischemia following reimplantation of the coronary arteries is a potential problem following the ASO. Epicardial or transesophageal echocardiography is helpful to assess the patency of the reimplanted coronary arteries and to prevent coronary artery air emboli by ensuring adequate removal of air from the LA and LV before termination of CPB. Maintenance of high perfusion pressures on CPB after aortic

cross-clamp removal will facilitate the distal migration of air emboli. In other instances, kinking of the reimplanted artery or compromise of the implanted coronary ostia may require immediate surgical intervention. Pharmacologic intervention with traditional therapies to improve the balance of myocardial oxygen demand and delivery such as nitroglycerin and β-blockade are never a long-term alternative to prompt surgical revision of the appropriate anastomosis.

Despite comprehensive preoperative evaluation, the LV of patients undergoing an ASO may be marginal in its ability to support the systemic circulation in the post-CPB period. This may occur as the result of myocardial ischemia, inadequate LV mass, poor protection of the LV during aortic cross-clamping, or a combination of these variables. Echocardiography is useful in identifying and continuously evaluating both global and regional LV systolic dysfunction. It also detects mitral regurgitation, which may occur secondary to papillary muscle dysfunction or to dilation of the mitral valve annulus. Inotropic support of the LV and afterload reduction may be necessary to terminate CPB.

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D. Postoperative Management

D.1. How is myocardial ischemia addressed in the intensive care unit (ICU) following the ASO?

Myocardial ischemia in the ICU following an ASO is usually heralded by ST-segment/T-wave changes or the development of atrial or ventricular arrhythmias. Myocardial ischemia should be considered to be mechanical in nature until proved otherwise.

Thrombin soaked absorbable gelatin pads are sometimes used for hemostasis around the coronary anastomoses and can compress the coronary ostia, as can adjacent thrombi. Surgical reexploration is indicated and likely to be immediately therapeutic.

LV dilation can initiate and exacerbate myocardial ischemia in patients who have undergone an ASO. Myocardial ischemia, afterload mismatch, or overzealous volume infusion can result in LV distension and LA hypertension. This is more likely if there is mitral insufficiency from either papillary muscle dysfunction or dilation of the mitral valve annulus. LV distention may result in stretching or kinking of the coronary reanastomosis sites causing a cycle of worsening myocardial ischemia and LV dilation. LA hypertension produces elevations in PA pressure and distention of the PA and can compress or place tension on the coronary ostia because the LeCompte maneuver brings the distal PA anterior to the ascending aorta. The resulting myocardial ischemia produces further LV dilation, progressive elevations in LA and PA pressures, and continuing compromise of coronary blood flow. Attempts to induce coronary vasodilation with nitroglycerin are unlikely to be beneficial in this setting, although the reduction in preload and afterload may be beneficial. Afterload reduction with nitroprusside or milrinone also might be helpful.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

D.2. What immediate postoperative problems would be anticipated following the Rastelli procedure?

Right (pulmonary) ventricular dysfunction related to the ventriculotomy used to close the VSD and create the new pulmonary outflow tract can occur, as can heart block given the

proximity of the VSD to the intraventricular conduction pathways. A residual VSD following repair is always possible, as is LV outflow tract obstruction around the tunnel used to create LV and aortic continuity.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

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D.3. What intermediate and long-term surgical problems are seen after ASO?

Supravalvar pulmonary stenosis is probably the most common complication of ASO. This stenosis is usually caused by retraction of the tissue used to repair the PA in the area of the explanted coronaries, but in most patients is not extensive enough to result in valvular pulmonary stenosis. Series with long-term follow-up (15 years) confirms that the incidence of supravalvar stenosis severe enough to require reoperation (generally a gradient >50 to 60 mmHg) is approximately 4% to 8%.

The second most common complication of the ASO is aortic insufficiency and occurs in approximately 10% to 15% of patients at long-term follow-up, with the majority (96%) graded as trivial or mild. This is a rare source of morbidity or indication for reoperation following the ASO.

Early concerns of the long-term patency and growth potential of the reimplanted coronary arteries following the ASO have not materialized on a large scale.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

Villafañe J, Lantin-Hermoso MR, Bhatt AB, et al. D-transposition of the great

arteries: the current era of the arterial switch operation. *J Am Coll Cardiol*. 2014;64:498–511.

D.4. What are the long-term outcomes after ASO?

Actuarial survival in experienced centers at 1 year is 90% for patients with D-TGA and IVS and 83% for patients with D-TGA and VSD. A review of 470 patients from one institution experienced in the ASO revealed a 1-year survival rate of 92% and an 8-year survival rate of 91% for patients with both D-TGA and IVS and D-TGA and VSD. A similar review of 1,200 patients from another experienced institution revealed a 1- and 15-year survival rate of 92% for patients with D-TGA and IVS, and 1- and 15-year survival of 81% and 80% for D-TGA and VSD, respectively. A recent multi-institution review of 631 patients with D-TGA and 167 patients with D-TGA and VSD revealed similar initial and long-term (15 years) outcomes. Freedom from adverse cardiovascular events has recently been shown to be 93% at 25 years.

Ninety to 97% of patients with D-TGA have normal-sized, patent coronary arteries as assessed by coronary angiography. A recent study of a large cohort demonstrated that survival without coronary events (death from myocardial infarction, sudden death, and reoperation for coronary stenosis) is 92.7% at 1 year and 88.2% at 15 years. The incidence of coronary events is bimodal with a high early and low late event rate. Eighty-nine percent of all coronary events occurred in the first 3 months after ASO. The event rate did not increase again until 6 years after ASO. Abnormal coronary, specifically a single coronary artery origin or two coronaries originating close to each other at a facing commissure were risk factors for a coronary event.

One of the potential advantages of the ASO over the atrial switch procedure is the use of the native LV as the systemic ventricle. Long-term follow-up indicates that patients who have undergone an ASO have higher systemic ventricular ejection

fractions than do patients who have undergone atrial switch procedures. In fact, patients who had D-TGA and IVS repaired in infancy and patients who had D-TGA and VSD repaired later have LV end-diastolic dimensions and contractile indices similar to normal patients. Myocardial contractility in patients having undergone a rapid or traditional two-stage arterial switch is mildly depressed as compared to patients having undergone a primary arterial switch. No progression of this ventricular dysfunction has been noted at either intermediate or long-term follow-up.

DiNardo JA, Shukla AC, McGowan FX. Anesthesia for congenital heart surgery. In: Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:633–698.

Khairy P, Clair M, Fernandes SM, et al. Cardiovascular outcomes after the arterial switch operation for D-transposition of the great arteries. *Circulation*. 2013;127:331–339.

Villafañe J, Lantin-Hermoso MR, Bhatt AB, et al. D-transposition of the great arteries: the current era of the arterial switch operation. *J Am Coll Cardiol*. 2014;64:498–511.

D.5. What are the long-term outcomes after Rastelli repair for patients with D-TGA with left ventricular outflow tract (LVOT) obstruction?

Outcome following the Rastelli procedure for TGV with VSD and LVOT obstruction is good, with a near 100% early survival rate. A recent series reports survival to be 93% at 5, 10, and 20 years. The need for reintervention (either surgical or catheterization) increases over time. Intervention to relieve right ventricular outflow tract (RVOT) (RV to PA conduit) obstruction accounts for 75% of all interventions, with pacemaker insertion and relief of LVOT obstruction (aortic outflow) accounting for most of the remaining interventions. In an effort to reduce the need to intervene again for LVOT obstruction associated with the Rastelli procedure, some

institutions are making greater use of the LeCompte and Nikaidoh procedures.

Brown JW, Ruzmetov M, Huynh D, et al. Rastelli operation for transposition of the great arteries with ventricular septal defect and pulmonary stenosis. *Ann Thorac Surg*. 2011;91:188–194.

Emani SM, Beroukhim R, Zurakowski D, et al. Outcomes after anatomic repair for d-transposition of the great arteries with left ventricular outflow tract obstruction. *Circulation*. 2009;120:S53–S58.

Hazekamp MG, Gomez AA, Koolbergen DR, et al. Surgery for transposition of the great arteries, ventricular septal defect and left ventricular outflow tract obstruction: European Congenital Heart Surgeons Association multicentre study. *Eur J Cardiothorac Surg*. 2010;38:699–706.

D.6. What is long-term neurologic outcome like after ASO?

The best assessment of neurologic outcome following ASO is data from the Boston Circulatory Arrest Trial. In this trial, 171 infants undergoing ASO for D-TGA with IVS or VSD were randomized to strategy of either DHCA or LFCPB using α-stat pH management. Infants in the DHCA group underwent an average of 52 minutes of DHCA, whereas those in the LFCPB group underwent 14 minutes of DHCA.

Children in this cohort had overall physical and psychosocial health status similar to the general population. However, at age 8 years, parents of children in both groups reported more problems with attention, learning, speech, and the frequency of developmental delay than parents of children in a normative sample. There was no association between physical and psychosocial scores and the presence or absence of a VSD or the use of LFCPB versus DHCA. Neurodevelopmental outcome in this cohort was generally not adversely affected unless the duration of DHCA exceeded 41 minutes. Beyond 41 minutes, there was a nonlinear (steadily worsening) outcome with increasing duration of DHCA.

Eight-year and 16-year data from the trial also demonstrated that neurologic status, IQ, academic achievement, memory, problem solving, and visual–motor integration did not differ between the DHCA and LFCPB groups. Nonetheless, DHCA was associated with greater functional deficiencies in motor function, visual–motor tracking, phonic awareness and speech apraxia, whereas patients in the LFCPB exhibited more impulsive behavior and worse behavior in school as rated by teachers.

Marelli A, Miller SP, Marino BS, et al. Brain in congenital heart disease across the lifespan: the cumulative burden of injury. *Circulation*. 2016;133:1951–1962.

Mebius MJ, Kooi EMW, Bilardo CM, et al. Brain injury and neurodevelopmental outcome in congenital heart disease: a systematic review. *Pediatrics*. 2017;140:e20164055.

40 Pyloric Stenosis

Aarti Sharma and Vinod Malhotra

A 3-week-old first-born male infant had projectile vomiting, which contained the ingested formula but no bile. His body weight was 2.5 kg; serum electrolytes: K^+, 2.2 mEq per L; Cl^-, 86 mEq per L; and blood pH, 7.68. This infant was also noted to have a systolic murmur heard best at the second intercostal space along the left sternal border, which was assessed by a cardiologist and diagnosed as a ventricular septal defect (VSD).

A. Medical Disease and Differential Diagnosis

1. What is the diagnosis in this patient?
2. What is the differential diagnosis of pyloric stenosis?
3. What are the metabolic problems in this newborn secondary to his disease?
4. What are the adverse effects of metabolic alkalosis?
5. How would you treat this infant?
6. How would you determine fluid replacement in a newborn, and what fluids would you use?
7. How would you correct the metabolic alkalosis in this patient?
8. What causes a cardiac murmur?

B. Preoperative Evaluation and Preparation

1. How would you evaluate this patient preoperatively?
2. How would you evaluate a heart murmur?
3. How would you differentiate between functional versus organic murmur?
4. What are the types of VSD? What type of shunt do they cause?
5. What are the risks of surgery and anesthesia in a patient with VSD?
6. How would you prepare this patient rapidly for emergency surgery? Is surgical intervention an acute emergency in this case?
7. How would you prepare this patient for anesthesia?

C. Intraoperative Management

1. What induction–intubation sequence would you use?
2. What are the anatomic characteristics of the airway in the newborn and how do they differ from those in the adult?
3. How do you determine the size of an endotracheal tube in a pediatric patient?
4. What anesthesia system would you use and why?
5. What are the advantages and the disadvantages of commonly employed nonrebreathing systems?
6. How would you monitor this patient intraoperatively?
7. How does the pulse oximeter function?
8. What factors affect the measurement of oxygen saturation by the pulse oximeter?

D. Postoperative Management

1. What are the complications that can occur in the postanesthesia recovery period?
2. How would you treat postextubation “croup” in this infant?

A. Medical Disease and Differential Diagnosis

A.1. What is the diagnosis in this patient?

The most likely diagnosis in this patient is pyloric stenosis. The factors that favor the diagnosis are as follows:

- Age—3 weeks (average age at onset; range 5 days to 5 months)
- Boy child (boy-to-girl ratio = 4:1)
- Projectile vomiting (characteristic)
- Contents—ingested formula, no bile

The resultant biochemical abnormality in this patient is a hypokalemic, hypochloremic, metabolic alkalosis.

Pyloric stenosis occurs in 3 of 1,000 infants born in the United States; its incidence may be increasing. It is more common in Whites of Northern European ancestry, less common in Blacks, and rare in Asians. Reduced nitric oxide in pyloric tissue may contribute to the pathogenesis of pyloric stenosis.

Kliegman RM, St. Geme JW, Blum NJ, et al, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:1945–1949.

A.2. What is the differential diagnosis of pyloric stenosis?

Pyloric stenosis can be distinguished from other congenital anomalies that cause obstruction of the alimentary tract in the newborn. These other anomalies include chalasia of the esophagus, hiatus hernia, duodenal atresia, jejunal atresia, ileal atresia, pancreatic annulus, malrotation of the gut, intra-abdominal hernias, and Meckel diverticulum. Pathognomonic features of pyloric stenosis include absence of bile staining of the vomitus and visible gastric peristaltic waves on abdominal examination along with the palpable pyloric mass. The diagnosis is commonly made clinically. An “olive” is sometimes palpated in the epigastrium just to the right of the midline. The diagnosis can be confirmed by abdominal ultrasound. Occasionally, an upper gastrointestinal (GI) series with barium is necessary.

Kliegman RM, St. Geme JW, Blum NJ, et al, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:1945–1949.

A.3. What are the metabolic problems in this newborn secondary to his disease?

Metabolic changes occur secondary to protracted vomiting and characteristically include a hypokalemic, hypochloremic alkalosis, as evident in this infant. Hyponatremia, although present, may not be manifested in serum value determinations because of severe dehydration. Compensatory respiratory acidosis is a frequent finding; it results from hypoventilation that may be marked and associated with periods of apnea. In severe dehydration leading to circulatory shock, the lack of adequate perfusion coupled with impaired renal and hepatic function may produce an entirely different picture of metabolic acidosis with hyperventilation, resulting in respiratory alkalosis. Therefore, depending on the severity and duration of vomiting and the type of fluid replenishment, one can encounter wide variations in arterial blood gas and electrolyte determinations. However, the most frequent findings are hypokalemia, hyponatremia, hypochloremia, and primary metabolic alkalosis with secondary respiratory acidosis. The renal response to vomiting is twofold. Initially, serum pH is maintained by the excretion of alkaline urine with sodium and potassium loss. Then, after the depletion of these electrolytes, the kidneys secrete acidic urine (paradoxic acidosis), which exacerbates the metabolic alkalosis. These findings are summarized in **Table 40.1**.

TABLE 40.1 Metabolic Findings in the Newborn Secondary to Pyloric Stenosis

Severity of Dehydration	Arterial Blood Gases				Serum Electrolytes			
	pH	P_{CO_2}	C_{O_2}	P_{O_2}	NA	K	CL	HCO_3
Mild	↑	↑	↑	↔	↓↔	↓	↓↓	↑
Moderate	↑↑	↑↑	↑↑	↔	↓	↓↓	↓↓↓	↑↑
Severe	↓↓	↓	↓↓	↓	↓	↓↓	↓↓↓	↓↓

↔, no change; ↑/↓, slight change; ↑↑/↓↓, moderate change; ↑↑↑/↓↓↓, marked change.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:789–815.

Kliegman RM, St. Geme JW, Blum NJ, et al, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:1945–1949.

A.4. What are the adverse effects of metabolic alkalosis?

- An increase in pH results in shifting of the oxygen-dissociation curve to the left, thereby binding more oxygen to the hemoglobin and unloading less oxygen at the tissue level. This phenomenon assumes even more importance in newborns because at 3 weeks, they still have up to 70% fetal hemoglobin with an already low value of P50 (i.e., 20 to 22 mmHg).
- Respiratory compensation is affected by hypoventilation with increased potential for atelectasis as well as periods of apnea.
- Decrease in ionized calcium
- Increased potential for seizures

Kliegman RM, St. Geme JW, Blum NJ, et al, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:1945–1949.

A.5. How would you treat this infant?

Medical management of this infant with pyloric stenosis is acutely urgent. The principles of management can be grouped under the following three categories: supportive therapy to stabilize the patient, diagnostic tests to confirm the diagnosis and monitor therapy, and surgery as the corrective therapy.

Supportive Therapy

- Circulatory support
- Correction of electrolyte imbalance
- Prevention of aspiration

Fluids

The infant with pyloric stenosis is hypovolemic and dehydrated secondary to persistent vomiting. Dehydration severity can vary

from mild hypovolemia to circulatory shock. The following parameters are good indicators of dehydration severity:

- Physical appearance—skin turgor, parched mucous membranes, sunken fontanels, sunken eyeballs
- Blood pressure—decreased
- Pulse—increased
- Urine output—decreased
- Weight (birth and present) and weight loss

Quantitative assessment of these parameters gives a fair estimate of the amount of total body fluid depletion. A wide-bore intravenous (IV) cannula should be placed and an infusion started immediately to correct the deficits and provide maintenance fluids.

Electrolytes

The patient is alkalotic, hypokalemic, hypochloremic, and hyponatremic and must be provided with necessary ions to replenish the deficit. Albumin or Ringer's lactate may be used to treat the shock first. Next, the deficit should be corrected, 0.45% to 0.9% saline in 5% to 10% dextrose. Potassium (usually 40 mEq per L) must be added to this to correct hypokalemia and aid in the correction of alkalosis. However, potassium infusion should be withheld until satisfactory renal function is established. Fluid therapy should be continued until the infant is rehydrated and serum bicarbonate concentration is less than 30 mEq per dL, which implies that the alkalosis has been corrected.

Prevention of Aspiration

A nasogastric tube should be inserted to thoroughly empty the stomach, and the upper airway reflexes should be preserved.

Diagnostic Tests

- To assess the severity of fluid and electrolyte derangement and to monitor therapy, the following should be evaluated:

complete blood count, serum electrolytes, blood gases, blood urea nitrogen (BUN), electrocardiogram (ECG) (for marked hypokalemia).

- To confirm the diagnosis: barium swallow, ultrasound imaging

Surgery

Pyloromyotomy is the definitive treatment for these infants. Ramstedt pyloromyotomy through a right upper quadrant transverse incision has been the traditional treatment for hypertrophic pyloric stenosis. Recently, laparoscopic and circumumbilical approaches have been introduced as alternative methods to improve cosmesis, but concerns about greater operative times, costs, and complications remain. Surgery should be carried out early but only after the patient has been stabilized satisfactorily.

Coran AG, Caldamone A, Adzick NS, et al. *Pediatric Surgery*. 7th ed. Philadelphia, PA: Elsevier Saunders; 2012:1021–1028.

Kliegman RM, St. Geme JW, Blum NJ, et al, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:1945–1949.

A.6. How would you determine fluid replacement in a newborn, and what fluids would you use?

The general principles of fluid therapy are based on fluid maintenance, correction of deficits, and replacement of losses.

Maintenance Fluids

In the newborn, maintenance fluids are as follows:

- First 48 hours of life—75 mL/kg/day or 3 mL/kg/hr
- 2 days to 1 month—150 mL/kg/day or 6 mL/kg/hr
- 1 month onward (up to 10 kg)—100 mL/kg/day or 4 mL/kg/hr

Estimation of the degree of dehydration in a newborn is shown in **Table 40.2**.

TABLE 40.2 Estimation of the Degree of Dehydration in a Newborn

	Mild	Moderate	Severe
Percentage fluid loss	5	10	15–20
Skin turgor	Poor	Very poor	Parched
Mucous membrane and tongue	Dry	Dry	Parched
Fontanel and eyes	Normal	Sunken fontanel	Sunken eyes
Urine	Concentrated oliguria	Oliguria	Oliguria, anuria
Pulse	Normal	Tachycardia	Marked tachycardia
Blood pressure	Normal	Hypotension	Marked hypotension, shock

The maintenance fluids take into account the fluid losses occurring normally through the kidney, bowel, skin, and lungs. At birth, the kidney is still undergoing maturation, and what may be called "a glomerular imbalance" exists. What it implies is that some mature glomeruli may be connected to the immature tubules and vice versa. Hence, the kidney is functionally limited at birth but undergoes rapid maturation during the first week of life.

Electrolytes

The newborn is an obligate sodium loser as well as a poor tolerator of excessive sodium overload. The maintenance electrolytes are as follows:

- Sodium—3 to 5 mEq/kg/day
- Potassium—2 to 3 mEq/kg/day
- Chloride—1 to 3 mEq/kg/day

Correction of Deficits

Deficits take into account the previous unreplaced losses because of a period of no intake by mouth and dehydration resulting from increased losses (e.g., from vomiting, diarrhea, and increased body temperature). The amount of deficit can be assessed by physical examination (**Table 40.2**), body weight loss, and hematocrit.

Replacement of Losses

Replacing losses covers ongoing abnormal losses not covered by maintenance fluids. Intraoperatively, it covers evaporative losses from the operative site, third spacing, and losses from the lungs if dry gases are used in nonrebreathing circuits (**Table 40.3**).

TABLE 40.3 Fluid Requirement to Replace Intraoperative Fluid Losses (Except Blood Loss) in the Newborn

	Fluid Replacement (mL/kg/hr)
Minor surgery (e.g., herniorrhaphy)	1–3
Moderate surgery (e.g., pyloromyotomy)	3–5
Major surgery (e.g., intestinal)	5–7
Respiratory water loss due to dry gases	2

The younger and more physically immature the patient, the higher the skin permeability, the ratio of body surface area to weight, and the metabolic demand. In addition, the use of radiant warmers and phototherapy increases insensible water loss.

Gropper MA, Eriksson LI, Fleisher LA, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2420–2458.

A.7. How would you correct the metabolic alkalosis in this patient?

To correct the metabolic alkalosis in this patient, the underlying electrolyte derangements (hyponatremia, hypokalemia, and hypochloremia) must be corrected. We correct the deficits by using calculated volumes of 5% dextrose in normal saline or Ringer's lactate solution, which helps to restore sodium and chloride mainly. Dextrose, 5%, with one-fourth strength normal saline may be used to provide maintenance fluids. Once renal function is established, potassium supplements are added to the infusion. Depending on the deficit, this therapy can require

anywhere from 12 to 72 hours. In severely alkalotic patients, HCl (hydrochloric acid) and NH_4Cl (ammonium chloride) have been used to correct the derangement. However, we have rarely found it necessary.

Barash PG, Cahalan MD, Cullen MD, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:385–386, 1213, 1407–1408.

A.8. What causes a cardiac murmur?

Cardiac murmurs are caused by turbulent blood flow across cardiac valves or septal defects and are audible sound waves in the range of 20 to 2,000 Hz. Most murmurs in pediatric patients are normal or innocent, occurring in almost 50% of all school-aged children but must be distinguished from those murmurs associated with significant structural heart disease. Auscultation is critically important in diagnosing these murmurs; however, echocardiography remains the gold standard.

Allen HD, Shaddy RE, Penny DJ, et al, eds. *Moss and Adams' Heart Disease in Infants, Children, and Adolescents: Including the Fetus and Young Adult*. 9th ed. Philadelphia, PA: Wolters Kluwer; 2016:255–257.

B. Preoperative Evaluation and Preparation

B.1. How would you evaluate this patient preoperatively?

The following information is necessary in evaluating this patient:

History

Onset of illness, frequency and amount of vomiting, last feeding, diarrhea, urine output, activity of the newborn (active or lethargic), and birth weight

Physical Examination

Present body weight (to determine the weight loss), temperature, signs of dehydration (skin turgor, mucous membranes, fontanels,

eyeballs, blood pressure, pulse, color, and volume of urine), muscle tone, and level of consciousness

Laboratory Findings

Complete blood count, electrolytes, BUN and blood sugar, urinalysis, and arterial blood gases

Based on the data available, we can determine the fluid and electrolyte status of the patient and correct these accordingly to stabilize the patient for surgery and anesthesia.

B.2. How would you evaluate a heart murmur?

Heart murmurs can be innocent or organic. By definition, innocent murmurs occur in the absence of structural or physiologic cardiac disease. The clinical diagnosis of a normal or innocent murmur should occur in the setting of an otherwise normal history, physical examination, and appearance. The presence of a family history of hypertrophic cardiomyopathy; congenital cardiac disease; or unexplained infant, childhood, or early adult death is particularly worrisome. The perinatal history of prematurity, maternal diabetes, drug or toxin ingestion, fetal distress, or clearly definable chromosomal disorders has particular cardiorespiratory relevance. The initial approach to the evaluation of the cardiovascular system should include an assessment of the cardiorespiratory system functionality as a pump and delivery system. An index of exercise or play capacity should be sought as a component of assessing growth and development. We would ask about exercise tolerance, shortness of breath, cyanotic episodes, growth (because congestive heart failure may manifest as failure to thrive), and symptoms of congestive heart failure.

Allen HD, Shaddy RE, Penny DJ, et al, eds. *Moss and Adams' Heart Disease in Infants, Children, and Adolescents: Including the Fetus and Young Adult*. 9th ed. Philadelphia, PA: Wolters Kluwer; 2016:255–257.

B.3. How would you differentiate between functional versus organic murmur?

Normal murmurs of childhood are composed of five systolic and two continuous types but never solely diastolic (**Table 40.4**). A functional murmur is usually soft, 1/6 or 2/6, and never associated with palpable thrill. Pathologic murmurs are usually louder, 3/6 or greater, and are associated with other cardiovascular pathologic features.

TABLE 40.4 Innocent Murmurs of Childhood

Systolic Murmurs	Continuous Murmurs
Vibratory Still murmur	Venous hum
Pulmonary flow murmur	Mammary arterial souffle
Peripheral pulmonary artery stenosis murmur	
Supraclavicular systolic murmur	
Aortic systolic murmur	

Park MK. *Park's Pediatric Cardiology for Practitioners*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2014:36–39.

B.4. What are the types of VSD? What type of shunt do they cause?

One common classification of VSD is based on anatomic location.

- Type I defects, or supracristal defects (5% of all VSDs), are outflow defects located above the crista supraventricularis just under the annulus of aorta.
- Type II defects, or infracristal defects (80% of all VSDs), are lower in membranous septum beneath the crista supraventricularis.
- Type III defects, or canal type (11% incidence), are inlet VSDs that accompany complete atrioventricular (AV) canal defects. They result from failure of the endocardial cushions to fuse.

- Type IV, or muscular, defects (2% to 7% incidence) probably result from excessive resorption of septal tissue during the muscular septal formation. They may be located anywhere in the muscular septum and may be multiple (also known as the Swiss cheese defect).

VSD is left-to-right shunt. Pathophysiologic effects of VSD include left-to-right shunting, pulmonary hypertension, and heart failure resulting from volume overload.

Allen HD, Shaddy RE, Penny DJ, et al, eds. *Moss and Adams' Heart Disease in Infants, Children, and Adolescents: Including the Fetus and Young Adult*. 9th ed. Philadelphia, PA: Wolters Kluwer; 2016:784–792.

B.5. What are the risks of surgery and anesthesia in a patient with VSD?

Infective endocarditis is a complication of most congenital cardiac anomalies, so the patient requires antibiotic prophylaxis. There is also risk of increasing the flow in the shunt or reversing the flow in the shunt, resulting from decreases in pulmonary vascular resistance causing hypoxemia and congestive heart failure or acute and persistent increases in systemic vascular resistance. Right ventricular infundibular hypertrophy may be present in the patients with a VSD. Normally, this is a beneficial change because it increases the resistance to right ventricular ejection, leading to decrease in magnitude of the left-to-right shunt. Nevertheless, perioperative events that exaggerate this obstruction to right ventricular outflow, such as increased myocardial contractility or hypovolemia, must be minimized. Therefore, these patients are often anesthetized with a volatile anesthetic. In addition, intravascular fluid volume should be maintained by prompt replacement of blood loss. During the anesthetic, a normal end-tidal carbon dioxide (CO_2) should be maintained and routine air bubble precautions should be taken.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2017:130–133, 541–542.

B.6. How would you prepare this patient rapidly for emergency surgery? Is surgical intervention an acute emergency in this case?

Hypertrophic pyloric stenosis is a medical emergency and not a surgical emergency. Therefore, no newborn should be subjected to the additional hazards of anesthesia and surgery until stabilized medically.

Kliegman RM, St. Geme JW, Blum NJ, et al, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:1945–1949.

B.7. How would you prepare this patient for anesthesia?

Fluid and electrolyte replacement should be accomplished satisfactorily—this may take anywhere from 12 to 72 hours depending on the patient's status. The next step is to empty the stomach through a wide-bore nasogastric tube, lavaging out the gastric contents and any leftover barium. Alternatively, an oral-gastric approach allows for passage of a tube with wider lumen that ensures better stomach emptying. Premedication is usually atropine (0.01 to 0.02 mg per kg) IV or intramuscular if the patient does not have IV line.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:789–815.

C. Intraoperative Management

C.1. What induction–intubation sequence would you use?

These children should arrive to the operating room with an IV access. Standard monitors are placed. The stomach is emptied by inserting an orogastric tube (atropine may be used as premedication) to reduce the chance of regurgitation during

induction. Because the stomach may not be completely emptied, a rapid sequence induction and intubation with cricoid pressure is highly recommended to minimize the risk of aspiration. Awake intubation may be accomplished in skillful hands in a lethargic neonate or in a critically sick infant. In most cases, however, neonates presenting for this procedure are fit and do not require awake intubation, which can be more traumatic.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:795–797.

Jöhr M. Anesthesia for the child with full stomach. *Curr Opin Anaesthesiol*. 2007;20(3):201–203.

C.2. What are the anatomic characteristics of the airway in the newborn and how do they differ from those in the adult?

The special characteristics of the upper airway in the newborn are as follows:

- Nasopharynx—narrow nasal passages, obligate nasal breathers
- Oropharynx—large tongue, long and pendulous epiglottis
- Larynx—the distinctive features shown in **Table 40.5**

TABLE 40.5 Comparative Anatomy of the Larynx and Trachea in the Newborn and the Adult

Anatomic Features	Newborn	Adult
Size	4 cm	10–13 cm
Shape	Funnel	Cylindrical
Position of the glottis	C3–C4	C6
Narrowest point	1 cm below vocal cords	At vocal cords
Vocal cords	Slanting anteriorly	Transverse or slightly Slanting posteriorly
Mucous membrane	Loose (swells easily)	More firmly bound

It is apparent, therefore, that the newborn who has low

respiratory reserve can develop airway obstruction easily. The infant may present problems during intubation and tolerate airway trauma poorly.

Comparative anatomy of the larynx and trachea in the newborn and the adult is shown in **Table 40.5**.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:349–370.

C.3. How do you determine the size of an endotracheal tube in a pediatric patient?

The two parameters of endotracheal tube sizes are the tube length and diameter, depending on the age of the child, as shown in **Table 40.6**. However, these are approximate sizes and one must have one size bigger and one size smaller tube available when selecting any size tube. A simple way to remember these numbers is to know the sizes at newborn, 6 months, and 1 year. Between 2 and 12 years, the following guide may be used:

- Tube length from tip to incisor teeth (cm) = 11 + age in years
- Tube internal diameter (mm) = 4 + age / 4
- French size (French) = 18 + age
- External circumference (French) = ID (mm) × 4 + 2

TABLE 40.6 Endotracheal Tube Size for Pediatric Patient

Age	Length	Internal Diameter (mm)	French Sizes
Newborn	10	3.0	14
6 months	12	3.5	16
1 year	14	4.0	18
2 years	15	4.5	20
4 years	16	5.0	22
6 years	17	5.5	24
8 years	18	6.0	26
10 years	19	6.5	28
12 years	20	7.0	30

(French size means external circumference in millimeters, which equals π times external diameter; $\pi = 3.1416$.)

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:349–370.

C.4. What anesthesia system would you use and why?

We employ the circle system with a light circuit. The circle system is more advantageous because it maintains heat and humidification better and offers the freedom of choosing varying gas flows. The controversy about the increased resistance in the adult system is discounted by the fact that the respiration is assisted or controlled intraoperatively. Newer anesthesia machines use valves with much less resistance than older models. Dead space in these systems is no more than that of the Mapleson circuits.

Dorsch JA, Dorsch SE. *Understanding Anesthesia Equipment*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:209–218.

C.5. What are the advantages and the disadvantages of commonly employed nonrebreathing systems?

Commonly used nonrebreathing systems include Bain Breathing circuit (Mapleson D system) and Jackson-Rees modification of Ayre T-piece. They offer the following advantages and disadvantages:

Advantages

- Minimal dead space
- No valves, low resistance
- Lightweight
- Reservoir bag to assist ventilation
- Good appreciation of patient's respiratory exchange

Disadvantages

- High flow of fresh gases required
- Low flows may allow rebreathing of gases without CO_2

absorption.

- Loss of heat and humidity because of high flow of cold, dry gases (Bain circuit allows some heating of inspired gases by surrounding fresh gas flow tubing with expired gas tubing.)
- Scavenging problems of waste gases

Dorsch JA, Dorsch SE. *Understanding Anesthesia Equipment*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:191–208.

C.6. How would you monitor this patient intraoperatively?

Monitoring should include blood pressure, ECG, rectal temperature, precordial stethoscope, pulse oximeter, and an end-tidal CO_2 monitor.

C.7. How does the pulse oximeter function?

Commonly used pulse oximeters combine the scientific principles of spectrophotometric oximetry and plethysmography. Light of two wavelengths, 660 nm (red) and 920 nm (infrared), is emitted by a pair of light-emitting diodes (LED) and is passed through the tissue being measured to a photodetector. Because the saturated hemoglobin absorbs more blue light than unsaturated hemoglobin, the absorption of light for each color is an indication of the ratio of oxygen saturated blood to unsaturated blood. The pulsating vascular bed, by expanding and relaxing, creates a change in light-path length that modifies the amount of light detected. The microprocessor-controlled circuitry in the unit senses the pulsatile waveform, which is solely produced by the arterial blood, thereby allowing measurement of pulse rate and arterial saturation. The oximeter is reliably accurate in 60% to 100% saturation range.

Ehrenwerth J, Eisenkraft JB, Berry JM, eds. *Anesthesia Equipment: Principles and Applications*. 2nd ed. New York: Elsevier; 2013:256–270.

Kim SH, Lilot M, Murphy LS, et al. Accuracy of continuous noninvasive

hemoglobin monitoring: a systematic review and meta-analysis. *Anesth Analg*. 2014;119:332–346.

Saraswat A, Simionato L, Dawson JA, et al. Determining the best method of Nellcor pulse oximeter sensor application in neonates. *Acta Paediatr*. 2012;101(5):484–487.

C.8. What factors affect the measurement of oxygen saturation by the pulse oximeter?

Dysfunctional hemoglobin, such as carboxyhemoglobin, sulfhemoglobin, and methemoglobin, can affect the accuracy of the oximeter. Intravascular dyes, such as indocyanine green and methylene blue, can also interfere with the accuracy of the instrument. Skin color, tissue thickness, venous blood, light intensity, and ambient light do not affect the accuracy of the instrument because they do not pulse.

Ehrenwerth J, Eisenkraft JB, Berry JM, eds. *Anesthesia Equipment: Principles and Applications*. 2nd ed. New York: Elsevier; 2013:256–270.

D. Postoperative Management

D.1. What are the complications that can occur in the postanesthesia recovery period?

The patient should be carefully observed for signs of respiratory depression and periods of apnea secondary to the combination of metabolic alkalosis, general anesthesia, and decreased body temperature. However, these infants do not appear to be at increased risk of postoperative apnea. Hypoventilation predisposes to atelectasis. These patients should be awake and responsive to avoid aspiration. Severe hypoglycemia resulting from depletion of liver glycogen stores has been reported 2 to 3 hours after surgery. Postextubation “croup” is a potentially dangerous complication in this age group.

Davis PJ, Cladis FP, eds. *Smith’s Anesthesia for Infants and Children*. 9th ed.

Philadelphia, PA: Elsevier; 2017:789–816.

D.2. How would you treat postextubation "croup" in this infant?

Treatment of the potentially catastrophic postextubation laryngeal edema should be immediate, vigorous, and carried out under direct observation of the anesthesiologists. It consists of the following:

- Increasing inspired oxygen concentration (50% to 60%)
- Humidification of inspired gases
- Adequate hydration using parenteral fluids
- Light sedation to calm the patient and allow for cooperation in therapy
- Avoidance of any significant respiratory depression
- Epinephrine through handheld nebulizer and mask, 50 μg/kg/min of active isomer
- Racemic epinephrine (2.25%) 0.05 mL per kg diluted in 5-mL saline solution delivered in 10 minutes

Treatment should be given over 10 minutes and may be repeated every 30 minutes, as necessary. Rebound phenomenon may be expected approximately 2 hours after cessation of this therapy.

- Steroids—dexamethasone, 0.5 to 1 mg per kg IV
- Reintubation—if signs of deterioration or hypoxia appear
- Tracheostomy, if necessary—rarely, subglottic edema may be so rapid and so severe that tracheostomy is the only choice

The age group most likely to manifest this complication is 1 to 4 years. Infants younger than 1 year are at most risk, mainly because of the size of their airway. Fortunately, an infant of this age is most amenable to early and vigorous intervention and should always be treated as an emergency requiring the continued presence of and evaluation by a physician who is adept at securing an airway for the child.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:789–816.

41 Inflammatory Airway Disease in Childhood: Laryngotracheobronchitis

Miles Dinner and Anthony Longhini

A 3-year-old boy was brought to the emergency room because of respiratory distress. He was noted to have stridor with substernal retractions and excessive drooling. He complained of a sore throat and had a fever of 39.5°C (103.1°F).

A. Medical Disease and Differential Diagnosis

1. What portion of the airway is affected in the croup syndrome and why?
2. What is stridor?
3. How does stridor correlate with anatomic location?
4. Define croup. What is the clinical presentation of laryngotracheitis?
5. What is the differential diagnosis of acute upper airway obstruction in children?
6. What is bacterial tracheitis?
7. What congenital problems can mimic features of croup?
8. How is the severity of croup assessed?
9. What is the medical management of croup? Does this have

implications for the anesthesiologist?

10. What is epiglottitis? What are its common causes? What is the incidence?
11. What are the clinical manifestations of epiglottitis?
12. How is the diagnosis of epiglottitis made?
13. What is postextubation croup? How is it managed?
14. What are the nonacute causes of partial airway obstruction in children?

B. Preoperative Evaluation and Preparation

1. Is intubation always required in children with epiglottitis?
2. Why is general anesthesia administered to a child with epiglottitis?
3. How would you prepare the patient for anesthesia?

C. Intraoperative Management

1. How is the airway of the child with epiglottitis best secured?
2. How would you induce anesthesia?
3. Should a child with epiglottitis undergo a rapid sequence induction?
4. Is awake intubation a practical alternative to secure the patient's airway?
5. What would you do if the airway cannot be secured with intubation?
6. Should this patient have a nasotracheal or orotracheal tube placed?
7. Shortly after intubation, frothy secretions were obtained on suctioning the endotracheal tube. What is the reason for this? How can this be treated?

D. Postoperative Management

1. How long should this patient remain intubated? What criteria determine extubation time?
2. How would you make this patient comfortable during the

course of intubation?

3. What outcome can one expect for the child with acute epiglottitis?

A. Medical Disease and Differential Diagnosis

A.1. What portion of the airway is affected in the croup syndrome and why?

The subglottis is typically involved in infants and children presenting with croup. The subglottis is defined as the segment of the upper airway directly below the vocal cords fusing with the upper trachea. It contains pseudostratified columnar respiratory epithelium, which is loosely adherent and prone to swelling. Because this segment is fully cartilagenized in childhood, it lacks the ability to expand and thus can produce early symptoms due to even small degrees of inflammation.

Coté CJ, Lerman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:754–789.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2551.

Sobol SE, Zapata S. Epiglottitis and croup. *Otolaryngol Clin North Am*. 2008;41:551–566.

A.2. What is stridor?

Stridor is the high-pitched adventitious sound produced in the respiratory cycle by the turbulent flow of respiratory gases through a segmental narrowing in the airway. It can be biphasic, inspiratory, or expiratory, depending on the anatomic location.

Coté CJ, Lerman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:754–789.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2551.

A.3. How does stridor correlate with anatomic location?

Inspiratory stridor is characteristic of laryngeal or supraglottic obstruction. Conditions such as laryngeal papillomatosis, laryngeal web, laryngomalacia, and vocal cord paresis produce inspiratory stridor. Expiratory stridor is usually typical of intrathoracic processes such as extrinsic tracheal compression by a vascular ring or mass, tracheomalacia, or bronchotracheitis. Biphasic stridor is indicative of lesions or infections involving both the larynx and subglottis, such as the croup syndrome, subglottic stenosis, or intralaryngeal masses.

Coté CJ, Lerman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:754–789.

A.4. Define croup. What is the clinical presentation of laryngotracheitis?

Croup is the constellation of inspiratory stridor, barking cough, and possible respiratory distress due to subglottic mucosal edema. The majority of croup cases is infectious and is termed laryngotracheobronchitis for the structures involved. Spasmodic croup is considered an allergic reaction to viral antigens. Patients with spasmodic croup are afebrile, lack severe laryngeal inflammation, and are typically managed as outpatients with supportive care. Infectious croup is caused by a number of viruses, including human rhinovirus; *Haemophilus parainfluenzae* virus types 1, 2, and 3; respiratory syncytial virus; influenza virus; or human corona virus. It commonly affects children between 6 months and 3 years of age, with a median age of 18 months. Most cases of infectious croup occur during the colder months, and there is a 1:1 male-to-female prevalence. It manifests subacutely as an exacerbation of cold symptoms with low fever, barking cough, noisy breathing, and hoarseness. Exudative inflammation of the upper airway may cause dyspnea and in extreme cases can lead to exhaustion and frank hypoxia. In most cases, it is self-limited and benign.

Coté CJ, Lerman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:754–789.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2551.

Johnson DW. Croup. *BMJ Clin Evid*. 2014;2014:0321.

Miller EK, Gebretsadik T, Carroll KN, et al. Viral etiologies of infant bronchiolitis, croup and upper respiratory illness during 4 consecutive years. *Pediatr Infect Dis J*. 2013;32:950–955.

Rosychuk RJ, Klassen TP, Metes D, et al. Croup presentations to emergency departments in Alberta, Canada: a large population study. *Pediatr Pulmonol*. 2010;45:83–91.

van der Hoek L, Sure K, Ihorst G, et al. Human coronavirus NL63 infection is associated with croup. *Adv Exp Med Biol*. 2006;581:485–491.

A.5. What is the differential diagnosis of acute upper airway obstruction in children?

A full differential for this condition involves a host of infectious causes. Among the most important are bacterial tracheitis, diphtheria, retropharyngeal abscess, peritonsillar abscess, measles, and Epstein-Barr viral infection. Other causes to be considered are thermal burns, foreign body aspiration, laryngeal fractures, angioneurotic edema, vocal cord paralysis, and uvulitis.

Coté CJ, Lerman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:754–789.

Mandal A, Kabra SK, Lodha R. Upper airway obstruction in children. *Indian J Pediatr*. 2015;82(8):737–744.

Wald EL. Croup: common syndromes and therapy. *Pediatr Ann*. 2010;39:15–21.

A.6. What is bacterial tracheitis?

Bacterial tracheitis is a severe and potentially fatal disease of an infectious nature occurring as a consequence of infection with *Staphylococcus aureus*, various streptococcal species, and *H. influenzae*. It occurs in colder weather in young children as a secondary complication of viral laryngotracheitis. Although

presenting with the same symptoms as epiglottitis, it tends not to evolve as rapidly and generally does not have odynophagia and drooling, two characteristic signs of epiglottitis. Most of these children require intubation for thick and difficult-to-clear secretions, and during endoscopy, subglottic edema with mucosal ulceration is seen.

Mandal A, Kabra SK, Lodha R. Upper airway obstruction in children. *Indian J Pediatr*. 2015;82(8):737–744.

Wald EL. Croup: common syndromes and therapy. *Pediatr Ann*. 2010;39:15–21.

A.7. What congenital problems can mimic features of croup?

A host of anatomic problems can share similar signs and symptoms with the infectious agents causing airway compromise. These are distinguished from croup by the absence of fever and the chronicity of the illness. Vocal cord paralysis, vascular anomalies, laryngeal webs, laryngomalacia, subglottic masses (hemangiomas), and stenosis can all cause airway compromise.

Johnson DW. Croup. *BMJ Clin Evid*. 2014;2014:0321.

Wald EL. Croup: common syndromes and therapy. *Pediatr Ann*. 2010;39:15–21.

A.8. How is the severity of croup assessed?

The following parameters are evaluated in assessing severity of the illness: (1) Work of breathing: Is there tachypnea and/or retractions? (2) Chest wall motion: Is the tidal volume adequate with inspiration? (3) Overall appearance: Is the child cyanotic, obtunded, or comfortable? (4) Vocal quality: Is there stridor, diminished voice, or cry? Severe croup unresponsive to the medical therapy may require tracheal intubation. Once the diagnosis of croup has been established, the child is given a

croup score, which helps determine therapy (**Table 41.1**).

TABLE 41.1 The Westley Croup Score

	0	1	2	3	4	5
Cyanosis	None	—	—	—	With agitation	At rest
Level of consciousness	Normal, including sleep	—	—	—	—	Disoriented
Stridor	None	With agitation	At rest	—	—	—
Air entry	Normal	Decreased	Markedly decreased	—	—	—
Retractions	None	Mild	Moderate	Severe	—	—

Mild croup has a score <2, moderate is between 3 and 7, and severe has a score >8.

Charles R, Fadden M, Brook J. Acute epiglottitis. *BMJ*. 2013;347:f5235.

Coté CJ, Lerman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:754–789.

Johnson DW. Croup. *BMJ Clin Evid*. 2014;2014:0321.

A.9. What is the medical management of croup? Does this have implications for the anesthesiologist?

Most cases of croup resolve with minimal intervention and less than 10% of patients require hospitalization. Mild croup is treated with inspired gas humidification, hydration, and oxygen to improve the attendant hypoxemia. Steroids and racemic epinephrine are the prime modalities of therapy.

If the patient has moderate retractions and appears dyspneic, 0.5 mL of a 2.25% racemic epinephrine solution in 2.5 mL of normal saline can be administered via nebulizer every 1 to 2 hours. Airway resistance can be high with the reactive transudation and intraluminal narrowing. By vasoconstricting the arterioles of the mucosal vasculature, racemic epinephrine relieves edema. Racemic epinephrine is a 1:1 mixture of the levo (L) and dextro (D) isomers to limit cardiac stimulation because only the L form is an active component. Patients often improve

markedly within 30 minutes, but edema may recur due to epinephrine's brief duration of action. Racemic epinephrine should be avoided in children with glaucoma and ventricular outflow obstruction.

Dexamethasone and budesonide when given early in viral croup can be beneficial in reducing inflammation and alleviating symptoms. This takes time to work, however, requiring hours for effective onset. The pediatric dose of dexamethasone is 0.5 to 1 mg per kg orally or intramuscularly. Clinical evaluation of topical steroids such as budesonide has shown effective improvement, especially with laryngeal edema. Nebulized budesonide has been shown to be as effective as dexamethasone in treatment. The role of heliox (helium–oxygen mixture) has yet to be defined but may be helpful in severe croup.

Bjornson C, Russell K, Vandermeer B, et al. Nebulized epinephrine for croup in children. *Cochrane Database Syst Rev*. 2013;(10):CD006619.

Eboriadov M, Chryssanthopoulou D, Stamodis P, et al. The effectiveness of local corticosteroid therapy in the management of mild to moderate croup. *Minerva Pediatr*. 2010;62:23–28.

Kliegman RM, St. Geme JW, Blum NJ, et al, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:2202–2206.

Terregino CA, Nairn SJ, Chansky ME, et al. The effect of heliox on croup: a pilot study. *Acad Emerg Med*. 1998;5:1130–1133.

Zalzal GH. Stridor and airway compromise. *Pediatr Clin North Am*. 1989;36(6):1389–1402.

A.10. What is epiglottitis? What are its common causes? What is the incidence?

Epiglottitis is an inflammation of the epiglottis usually secondary to an infectious process. It can involve other supraglottic structures such as the arytenoid, false cords, and posterior tongue leading to obstruction of the airway. Progression of swelling can rapidly lead to complete airway occlusion and death. **Table 41.2** contrasts epiglottitis with

croup. Epiglottitis is most often bacterial in origin. The causative agent used to be *H. influenzae* type B. The *H. influenzae* type B vaccine has resulted in a remarkable decline in incidence, although epiglottis may still occur in vaccinated individuals. *Streptococcus pneumoniae* also has been infrequently associated with epiglottitis, and recently, group A *β*-hemolytic streptococci cases have been on the increase. Burn injury, neoplastic infiltration, caustic ingestion, lymphoproliferative disease, and angioneurotic edema are other causes. The incidence has declined to 1.8 per 10,000 admissions at The Children's Hospital of Philadelphia after the *H. influenzae* type B vaccine. In one study, five cases of epiglottitis occurred among children who had been immunized.

TABLE 41.2 Characteristics of Croup and Epiglottitis

	Croup	Epiglottitis
Etiology	Parainfluenza virus	*Haemophilus influenzae*
Age	4 months to 2 years	2–5 years
Onset	Subacute exacerbation of preexistent URI	Acute
Temperature	Low-grade fever	High fever
Course	Usually mild, stridor may worsen at night	Rapid progress of symptoms
Symptoms	Barky cough, stridor	Dysphagia, sore throat Dysphonia, respiratory distress

URI, upper respiratory infection.

A recent retrospective review reaffirms that epiglottitis remains a significant problem in the United States, with nearly 4,000 admissions in 2006. The demographics of the disease have shifted away from that of predominantly pediatric nature to one of adulthood. Surprisingly, the mean age in the study period from 1998 to 2006 was 45 years old, and the mortality was 36%.

D'Agostino J. Pediatric airway nightmares. *Emerg Med Clin North Am*. 2010;28:119–126.

Shah RK, Roberson DW, Jones DT. Epiglottitis in the *Hemophilus influenzae* type B vaccine era: changing trends. *Laryngoscope*. 2004;114:557–560.

Shah RK, Stocks C. Epiglottitis in the United States: national trends, variances, prognosis, and management. *Laryngoscope*. 2010;120:1256–1262.

A.11. What are the clinical manifestations of epiglottitis?

This illness presents acutely in the otherwise healthy child between 2 and 5 years of age with a fever as high as 40°C. Within a few hours, the epiglottic inflammation progresses, and the child becomes dyspneic. The child sits forward to use the accessory muscles of respiration and complains of a fullness and pain in the throat. Speech sounds are muffled, known as a "hot potato voice." Salivation often is characteristic and swallowing is difficult. The child appears anxious and concentrates only on breathing. The barking cough of croup usually is absent. The older child will assume a tripod posture with the neck extended to maximize air entry. As the child fatigues, cyanosis leading to complete asphyxia may ensue without intervention. Inspiratory effort is maximal with severe airway compromise, and thoracoabdominal asynchrony, otherwise known as paradoxical breathing, may be observed in the supine position; the abdomen protrudes and the chest wall retracts due to upper airway obstruction. Negative pressure pulmonary edema can occur. Chest auscultation may reveal decreased breath sounds.

Coté CJ, Lerman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:754–789.

Kliegman RM, St. Geme JW, Blum NJ, et al, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:583–601.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2420–2458.

A.12. How is the diagnosis of epiglottitis made?

Acute epiglottitis is a dire emergency, and any child whose clinical presentation warrants the diagnosis of epiglottitis must be evaluated promptly in a hospital.

Although epiglottitis and croup have similar features, the presence of drooling and absence of coughing are sensitive and specific signs of epiglottitis, whereas the absence of drooling and the presence of coughing are sensitive and specific signs of croup.

Pharyngoscopy to visualize an inflamed epiglottis should not be attempted in an office setting because this can stimulate upper airway reflexes and lead to increasing dyspnea. All medical centers should have in place a management protocol that standardizes the approach to this rapidly progressive and fatal disease and that involves a team of physicians and nurses from the specialties of pediatrics, otolaryngology, and anesthesiology. A logical approach is as follows:

- The child is kept calm with a parent in attendance at all times. Supplementary oxygen, maintenance of a sitting position, and reassurance are essential.
- If the patient clinically conforms to a classical presentation of epiglottitis, the operating room is alerted and the child is taken there immediately for intubation.
- With other diagnostic considerations, such as a foreign body in the upper airway, retropharyngeal abscess, congenital anomalies, and croup, the child may be escorted to radiology. The time taken for the x-ray examination obviously should be avoided in the critically ill child. A physician skilled in airway management should accompany the child with all necessary resuscitation equipment available.
- The classic thumb sign on a lateral x-ray film is an aptly named shape seen with epiglottic enlargement. However, the absence of this sign does not eliminate the diagnosis of epiglottitis. Croup is distinguished by the steeple sign representing a uniform narrowing of the subglottic airway by inflammation. Recently, magnetic resonance imaging has demonstrated the standard measurements for the

hypopharyngeal space in various age groups, and it has correlated this measurement with the change produced by epiglottic inflammation. This may be a useful tool in the future to assess the severity of airway involvement.

- Laboratory evidence is nonspecific, although a high white count with bands and polymorphonuclear leukocytes is more suggestive of epiglottitis than of croup.
- Fiberoptic pharyngoscopy can be most effective if performed gently by a skilled examiner; it immediately confirms or eliminates the diagnosis. Do not perform a laryngoscopy if anxiety is increased by the procedure and hence exacerbates airway obstruction.

Kliegman RM, St. Geme JW, Blum NJ, et al, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:1732–1734.

Shorten GD, Opie NJ, Graziotti P, et al. Assessment of upper airway anatomy in awake, sedated and anaesthetized patients using magnetic resonance imaging. *Anaesth Intensive Care*. 1994;22:165–169.

Tibballs J, Watson T. Symptoms and signs differentiating croup and epiglottitis. *J Paediatr Child Health*. 2011;47:77–82.

A.13. What is postextubation croup? How is it managed?

Anesthesiologists are often in the position of treating patients with postextubation airway edema, which resembles croup in its symptomatology.

Pediatric patients undergoing general endotracheal anesthesia may mimic many of the physical signs of the croup syndrome following extubation. The tracheal and subglottic mucosa have become irritated by the plastic tube, which initiates an inflammatory response, causing airway luminal narrowing. Because airway resistance is inversely proportional to the fourth power of the tracheal radius (with turbulent flow, this increases to the fifth power), the pediatric airway is especially compromised by edema. Halving the lumen will increase laminar airflow resistance 16 times.

Postextubation croup may manifest more frequently in a patient who has received large quantities of fluid or transfusions; maintained unusual or strained lateral head positioning; has a history of smoke inhalation, restrictive congenital anomalies such as a tracheoesophageal fistula, or acquired subglottic stenosis secondary to prolonged intubation as a neonate; has a coexistent upper respiratory infection, especially bronchitis; or has a cuffed or uncuffed endotracheal tube with a high (>25 cm H_2O) leak pressure. The air leak test, which gauges the pressure needed to generate an audible leak in the presence of an endotracheal tube, may be predictive of postextubation stridor in children over 7 years of age. Ensuring an adequate air leak may decrease the risk of postextubation croup.

Management involves reducing airway constriction by administering nebulized racemic epinephrine, steroids, and humidification of inspired gases. On occasion, reintubating with a soft endotracheal tube one-half to one size smaller than previously used is necessary until the inflammation subsides. Note that topical lidocaine ointment can have vasodilatory actions and should not be used in patients with postextubation croup.

Coté CJ, Lerman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:754–789.

Lukkassen IM, Hassing MB, Markhorst DG. Dexamethasone reduces reintubation rate due to post extubation stridor in a high-risk paediatric population. *Acta Paediatr*. 2006;95(1):74–76.

Mhanna MJ, Zamel YB, Tichy CM, et al. The air leak test around the endotracheal tube as a predictor of post extubation stridor is age dependent in children. *Crit Care Med*. 2002;30(12):2639–2643.

Suominen P, Taivainen T, Tuominen N, et al. Optimally fitted tracheal tubes decrease the probability of postextubation adverse events in children undergoing general anesthesia. *Paediatr Anaesth*. 2006;16(6):641–647.

A.14. What are the nonacute causes of partial airway

obstruction in children?

Several congenital anomalies are associated with respiratory difficulties. These can be subdivided into intrinsic and extrinsic pathologies as follows.

Extrinsic Pathologies

- Cystic hygroma—a proliferation or expansion of lymphatic channels, usually in the cervical region, that can compress the airway and lead to enlargement of the tongue
- Vascular anomalies—abnormalities of the aortic arch usually caused by aberrant vessels lead to compression of the airway. This is often position-dependent and may be responsible for coughing and wheezing when the patient is supine.
- Neoplastic compression of the trachea by lymphoma, hemangioma, neurofibromatosis, rhabdomyosarcoma, and other neural tumors in the mediastinum may occur and enlarge or compress airway structures.

Intrinsic Pathologies

- Subglottic stenosis—especially as acquired in previously intubated neonates. This form of airway narrowing occurs below the vocal cords, and it can lead to marked airway obstruction with respiratory infections. The congenital form may not be appreciated until an upper respiratory infection is present, when stridor may occur.
- Vocal cord paralysis—considered the second most common laryngeal anomaly in children; it is associated with the Arnold-Chiari malformation.
- Laryngeal structural anomalies—webs, laryngoceles, and cysts

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Shaw KN, Bachur RG, eds. *Fleisher & Ludwig's Textbook of Pediatric Emergency Medicine*. 7th ed. Philadelphia, PA: Wolters Kluwer; 2016:1420–1422.

B. Preoperative Evaluation and Preparation

B.1. Is intubation always required in children with epiglottitis?

Adult patients often can be managed under very vigilant observation provided that there is no impending obstructive danger. However, contemporary practice warrants the establishing of an airway with an endotracheal tube in the vast majority of infants and children. Nasotracheal intubation is most often used for ease of maintaining the child's comfort and safety. Endoscopic evaluation using appropriate fiberoptic airway endoscopy is a major advance in the management of epiglottitis.

Acevedo JL, Lander L, Choi S, et al. Airway management in pediatric epiglottis: a national perspective. *Otolaryngol Head Neck Surg*. 2009;140:548–551.

Coté CJ, Lerman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:754–789.

Damm M, Eckel HE, Jungehülsing M, et al. Airway endoscopy in the interdisciplinary management of acute epiglottitis. *Int J Pediatr Otorhinolaryngol*. 1996;38:41–51.

Shaw KN, Bachur RG, eds. *Fleisher & Ludwig's Textbook of Pediatric Emergency Medicine*. 7th ed. Philadelphia, PA: Wolters Kluwer; 2016:1421–1422.

B.2. Why is general anesthesia administered to a child with epiglottitis?

General anesthesia facilitates several activities. It gives the examiner a thorough look at the supraglottic area, which would be impossible and dangerous in the awake child. In addition, endotracheal intubation can be accomplished under controlled, relaxed conditions without trauma and laryngospasm. Intubation can be difficult because of the swelling and deformation of the paraepiglottic tissues. Clinicians who have no experience with

this unusual appearance will find it easier to visualize landmarks and secure the airway when the patient is in a surgical plane of anesthesia.

Coté CJ, Lerman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:754–789.

Jenkins IA, Saunders M. Infections of the airway. *Paediatric Anaesth*. 2009;19:118–130.

B.3. How would you prepare the patient for anesthesia?

Expedience is crucial. Once the diagnosis is made and the operating room alerted, the child is transported accompanied by parents and a physician with airway supportive equipment. An intravenous line can be placed more easily under anesthesia without upsetting the child. Anything that causes the child to cry will potentially worsen the obstruction and interfere with breathing. The child should, therefore, be kept calm and reassured. Nasal prong or face tent oxygen should be provided, and portable pulse oximetry should be used.

Airway equipment including a suitable mask and endotracheal tubes up to two sizes smaller than normally expected should be available. Lidocaine, succinylcholine, atropine, and ketamine in appropriate dilutions should be ready. A cricothyrotomy tray should be available as a precaution.

The parent should accompany the child into the operating room. Before induction, the parent is instructed on his or her role in comforting the child, encouraging complicity with mask breathing, and gently holding the child when the inhalation induction commences. When parents can provide their assistance in an emotionally controlled, supportive way, a smooth, safe anesthetic induction via mask can be well facilitated.

Coté CJ, Lerman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:754–789.

Tan GM. New way to mask induce a child. *Paediatric Anesth*. 2002;12:742–743.

C. Intraoperative Management

C.1. How is the airway of the child with epiglottitis best secured?

There is little debate over the safety and efficacy of endotracheal intubation provided that supportive staff is readily available. The endotracheal tube should be sized down 0.5 or 1.0 mm due to the inherent swelling and to protect against postextubation complications. Thick, copious secretions must be cleared frequently to prevent obstruction, and the child must be sedated to tolerate the endotracheal tube and to keep it secure in place.

Charles R, Fadden M, Brook J. Acute epiglottitis. *BMJ*. 2013;347:f5235.

Coté CJ, Lerman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:754–789.

Shaw KN, Bachur RG, eds. *Fleisher & Ludwig's Textbook of Pediatric Emergency Medicine*. 7th ed. Philadelphia, PA: Wolters Kluwer; 2016:1421–1422.

C.2. How would you induce anesthesia?

Verbal assurance is given continually. The child is seated on the parent's lap in the operating room and is oxygenated. Sevoflurane is a good choice of induction agent because it is less pungent and irritant than desflurane and is usually well tolerated. The inhalation drug should be initiated in low concentration and slowly increased as tolerated. As the child gets sleepy, he or she is placed in the supine position. The patient may undergo a brief period of excitement during which care is taken not to be overzealous with ventilation. Spontaneous, unassisted ventilation should continue as an intravenous line is placed. Glycopyrrolate 0.01 mg per kg is given intravenously as an antisialagogue. A crystalloid fluid bolus of 20 to 40 mL per kg

should be administered to treat dehydration. Ventilation may be assisted but not controlled. End-tidal gas is monitored continuously, and the airway is adjusted to provide maximal tidal exchange. Sevoflurane concentration is increased as tolerated to 8%, provided cardiovascular stability is maintained, to achieve an adequate depth of anesthesia. Airway obstruction will decrease ventilation and anesthetic uptake, requiring a longer induction time.

When the patient is in a deep plane of anesthesia (remember that the minimal alveolar concentration of sevoflurane in children is higher than in adults), a careful laryngoscopy is carried out. Paralysis is unnecessary in this deep plane of anesthesia. However, if several attempts are required with the possibility of the patient becoming light and reactive, a small dose of a neuromuscular blocker (e.g., rocuronium 0.4 mg per kg) will serve to maintain stable intubating conditions. This should be given only after it has been shown that the patient can be ventilated with a bag and mask.

Coté CJ, Lerman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:754–789.

Spalding MB, Ala-Kokko TI. The use of inhaled sevoflurane for endotracheal intubation in epiglottitis. *Anesthesiology*. 1998;89:1025–1026.

C.3. Should a child with epiglottitis undergo a rapid sequence induction?

In a child with a full stomach, a mask induction leaves the airway unprotected from aspiration of gastric contents. However, a rapid sequence induction may predispose the patient to severe hypoxia and hypoventilation should the clinician not be able to intubate expediently. Because the supraglottic landmarks are distorted by erythema and edema, recognition of the glottic inlet is obscured. In the spontaneously breathing patient, small air movements and the resultant secretional

bubbling may highlight the glottic opening. In addition, paralysis in no way assures ventilatability.

If the patient must be manually ventilated, it is possible to meet with complete obstruction secondary to invagination of the swollen supraglottic tissues into the laryngeal introitus. In such a case, positive end-expiratory pressure or the jaw-thrust maneuver may fail to correct the airway obstruction.

Should the child be too agitated to cooperate with an inhalational induction, an intramuscular dose of ketamine (2 to 3 mg per kg) will accomplish sedation and preserve ventilation. However, it may accentuate airway reflexes, and the clinician should be wary of laryngospasm. Videolaryngoscopy is the optimal choice whenever available.

Coté CJ, Lerman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:754–789.

Nagler J, Bachur RG. Advanced airway management. *Curr Opin Pediatr*. 2009;21(3):299–305.

Shaw KN, Bachur RG, eds. *Fleisher & Ludwig's Textbook of Pediatric Emergency Medicine*. 7th ed. Philadelphia, PA: Wolters Kluwer; 2016:1421–1422.

C.4. Is awake intubation a practical alternative to secure the patient's airway?

Awake intubation in these children is not generally recommended even though some authors have suggested awake intubation with topical anesthesia in the past. Risks of difficult visualization, agitation, trauma, worsening of epiglottic edema, and compromised ventilation far outweigh the benefits. Unless one has acquired great skill at awake pediatric intubation in the child with a normal airway, this technique should be avoided in these patients. In the adult, the awake GlideScope intubation has been reported with success.

Sinofsky AH, Milo SP, Scher C. The awake Glidescope intubation: an

additional alternative to the difficult intubation. *Middle East J Anesthesiol*. 2010;20:743–746.

C.5. What would you do if the airway cannot be secured with intubation?

Preemptive preparation is critical, and an otorhinolaryngologist should be present. In the event that the airway is lost, percutaneous transtracheal ventilation can be performed. This involves inserting a needle through the cricothyroid membrane as follows. Localize the cricothyroid membrane and topically cleanse the area with antiseptic. Anesthetize the skin with lidocaine (if time permits) and then insert a 16-gauge catheter (attached to needle) in the midline in the inferior portion of the cricothyroid membrane and directed caudally. Attach a 3-mL syringe to the needle barrel applying negative pressure. If the syringe contains a few milliliters of saline, air bubbles will be apparent when the trachea is entered. Following entry, advance the catheter into the trachea. Depending on the hub size, a 3.0-mm or 3.5-mm endotracheal tube adapter can be inserted into the catheter to interface with an Ambu bag. Alternatively, a 6.5- or 7.0-mm endotracheal tube adapter can be inserted into a 3-mL syringe without the plunger to interface with an Ambu bag or anesthesia circuit (**Fig. 41.1**). Jet ventilation can also be applied with high-pressure tubing keeping careful observation of respiratory dynamics and saturation. A tracheotomy in skilled hands also can be performed.

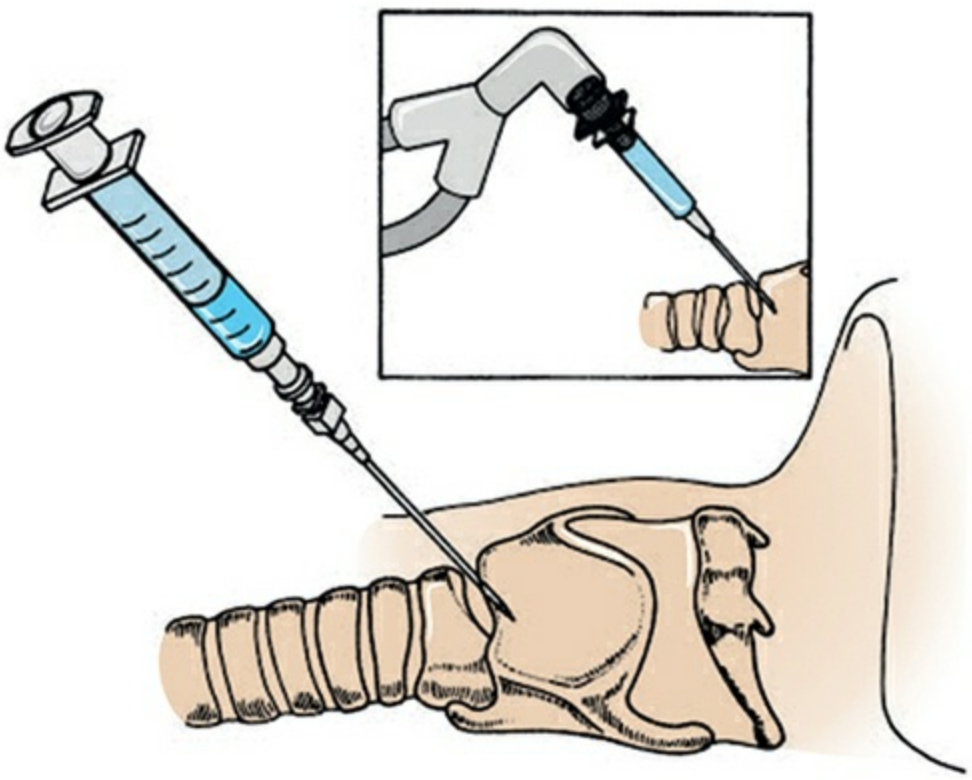

FIGURE 41.1. An emergency cricothyrotomy may be performed by passing a 14-gauge intravenous catheter through the cricothyroid membrane into the trachea. A 3-mL syringe with the plunger removed will accept a 15-mm endotracheal tube adapter that allows attachment of an oxygen-delivery system. (*Reprinted with permission from Barash PG, Cullen BF, Stoelting RK, eds*. Clinical Anesthesia. *4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001:1035–1041.*)

Delaney WA, Kaiser RE Jr. Percutaneous transtracheal jet ventilation made easy. *Anesthesiology*. 1991;74:952.

Deutsch ES. Tracheotomy: pediatric considerations. *Respir Care*. 2010;55:1082–1090.

C.6. Should this patient have a nasotracheal or orotracheal tube placed?

The patient will better tolerate a nasal endotracheal tube for prolonged intubation. Oropharyngeal toilet will also be easier. However, because the intubation can be difficult with epiglottitis and may predispose the patient to the problems listed in section C.4, the orotracheal route is easier and safer. Once the airway is secured orally, a nasotracheal tube can be inserted with laryngoscopic guidance.

C.7. Shortly after intubation, frothy secretions were obtained on suctioning the endotracheal tube. What is the reason for this? How can this be treated?

Davis et al. describe 7% of these patients as having pulmonary edema after intubation. This phenomenon relates to the transudation into the alveoli during periods of increased transpulmonary pressure. This occurs especially during obstructed inspiration. If the obstruction is complete, it is referred to as the "Müller" maneuver. The high negative pressures are buffered by the decreased venous return during exhalation. However, relief of the airway obstruction facilitates the extravasation of fluid for an increased venous return.

Treatment of this negative pressure pulmonary edema requires positive end-expiratory pressure. Diuretics and fluid restriction are not required because this condition generally is self-correcting. This can be administered by nasal bilevel means, mask continuous pressure, or intubation.

Davis HW, Gartner JC, Galvis AG, et al. Acute upper airway obstruction: croup and epiglottitis. *Pediatr Clin North Am*. 1981;28:859–880.

Silva PS, Monteiro Neto H, Andrade MM, et al. Negative-pressure pulmonary edema: a rare complication of upper airway obstruction in children. *Pediatr Emerg Care*. 2005;21:751–754.

D. Postoperative Management

D.1. How long should this patient remain intubated? What criteria determine extubation time?

Earlier studies have shown a mean intubation duration of 36 hours in 23 patients with a range of 19 to 67 hours. These patients were treated with ampicillin or chloramphenicol, and the epiglottis was visualized before extubation. The current antibiotic regimen is cefazolin 75 to 100 mg/kg/day in three

divided doses or clindamycin 30 to 40 mg/kg/day in three divided doses with the addition of a third-generation cephalosporin such as cefotaxime or ceftriaxone.

Criteria for extubation include an increased air leak around the endotracheal tube as well as decreased erythema and edema. Vernon and Sarnaik, however, feel that instrumentation and examination of the child is unnecessary and extubation at 36 to 48 hours can be accomplished easily in all patients. Hopkins recommended that the flexible fiberoptic laryngoscope be used to visualize the epiglottis and determine extubation time.

Charles R, Fadden M, Brook J. Acute epiglottitis. *BMJ*. 2013;347:f5235.

Coté CJ, Lerman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:754–789.

Damm M, Eckel HE, Jungehülsing M, et al. Airway endoscopy in the interdisciplinary management of acute epiglottitis. *Int J Pediatr Otorhinolaryngol*. 1996;38:41–51.

Hopkins RL. Extubation in epiglottitis. *Anesth Analg*. 1984;63:468.

Vernon DD, Sarnaik AP. Extubation in epiglottitis. *Anesth Analg*. 1984;63:469–470.

D.2. How would you make this patient comfortable during the course of intubation?

The child must be kept sedated to minimize movement, to prevent inadvertent extubation, and to provide anxiolysis. There are several options. Midazolam (0.075 mg per kg) as a starting dose titrated upward to effect followed by a continuous infusion of 0.04 to 0.1 mg/kg/hr will be effective, often in combination with a fentanyl infusion of 1 to 3 μg/kg/hr. Alternatively, a short infusion of propofol can be given, taking care to monitor for propofol-related infusion syndrome. Dexmedetomidine is also a useful adjunct. A bilateral superior laryngeal nerve block in experienced hands may allow for better endotracheal tube toleration.

Appropriate respiratory care, humidification, suctioning, and

secretion mobilization also should be provided.

Charles R, Fadden M, Brook J. Acute epiglottitis. *BMJ*. 2013;347:f5235.

Coté CJ, Lerman J, Anderson BJ, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:754–789.

D.3. What outcome can one expect for the child with acute epiglottitis?

Residual airway problems are unusual in the vast majority of children. Most children who are diagnosed in time and intubated go on to a full recovery without sequelae. Complications are related to securing the airway and include associated pneumonia, respiratory failure, hypoxia, cardiac arrest, and death.

Charles R, Fadden M, Brook J. Acute epiglottitis. *BMJ*. 2013;347:f5235.

Kliegman RM, St. Geme JW, Blum NJ, et al, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:2202–2206.

42 Cleft Palate

Aarti Sharma

A 3-month-old male infant was scheduled for repair of a cleft lip and a cleft palate. According to his pediatrician, the infant was born at full term and had no other medical problems.

A. Medical Disease and Differential Diagnosis

1. Describe the anatomic concept of a cleft palate and a cleft lip.
2. What is the cause of a cleft lip or a cleft palate?
3. What is the incidence of a cleft lip and a cleft palate?
4. Discuss the pathophysiology of a cleft lip and palate in the neonate and the older child (e.g., age >5 years).
5. What other conditions are associated with a cleft lip and a cleft palate?
6. What is Pierre Robin syndrome?
7. What is Treacher Collins syndrome?
8. What kind of specialized team care would these patients need?
9. Discuss indications and timing of closure of cleft lip and palate.
10. What is velopharyngeal incompetence, and how can it be diagnosed?
11. What is the relation of tonsillectomy and adenoidectomy to velopharyngeal incompetence?

B. Preoperative Evaluation and Preparation

1. What information do you need before closure of a cleft lip and palate?
2. What preoperative orders are needed?

C. Intraoperative Management

1. What monitors will you need for cheiloplasty and palatoplasty?
2. Discuss the induction and the anesthetic management for cleft lip and palate.
3. What positioning is recommended for cleft palate repair surgery?
4. What are the reported complications of this type of surgery and anesthesia?
5. Briefly describe the surgical techniques used to repair cleft defects.
6. How does a pharyngeal flap affect anesthetic management or any subsequent anesthetic administered to this patient?
7. What is an Abbe flap? What are its anesthetic implications?
8. What is the crucial problem of anesthesia for cleft palate? What are the unique considerations of this surgical repair?
9. What is laryngospasm? How would you make a diagnosis of laryngospasm?
10. How would you manage the patient with laryngospasm?

D. Postoperative Management

1. What complications of cleft lip and cleft palate surgery may be seen in the recovery room?
2. How do you protect the airway postoperatively?
3. How would you control postoperative pain in patients following a cleft lip and cleft palate repair?

A. Medical Disease and Differential Diagnosis

A.1. Describe the anatomic concept of a cleft palate and a cleft lip.

Congenital clefts of upper lip occur because of failure of fusion of the maxillary, medial, and lateral nasal processes. They vary from a notch in the upper lip to a cleft through the lip and the floor of the nose involving the alveolar ridge, or they may present as a complete cleft of the lip and the palate.

The cleft palate is divided into prepalatal and postpalatal clefts. The incisive foramen marks the boundary between the two. They have different embryologic development. A prepalatal cleft involves the anterior palate, alveolus, lip, nostril floor, and ala nasi. Postpalatal clefts may extend anywhere from soft and hard palate to the incisive foramen. The third type is a submucosal cleft in which a bone defect exists without a mucosal defect. The most common cleft of the palate is a left complete cleft of the prepalatal and palatal structures. The second most common is a midline cleft of the entire soft palate and part of the hard palate without a cleft in the prepalatal area. Various degrees of the cleft palate and lip are shown in **Figure 42.1**.

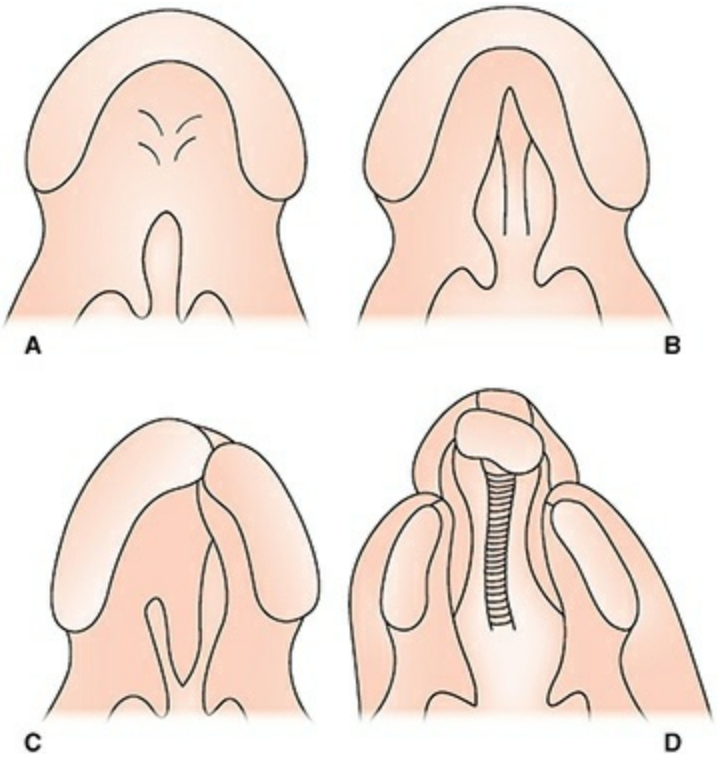

FIGURE 42.1. Various degrees of cleft palate and lip. A. Cleft of the soft palate only. **B.** Cleft of the soft and hard palate as far forward as the incisive foramen. **C.** Complete unilateral alveolar cleft, usually involving the lip. **D.** Complete bilateral alveolar cleft, usually associated with bilateral clefts of the lip. (*Modified from McCarthy JG, ed.* Cleft Lip and Palate and Craniofacial Abnormalities. *Philadelphia, PA: WB Saunders; 1990.* Plastic Surgery; *vol 4. Copyright © 1990 Elsevier. With permission.*)

Chung KC, ed. *Grabb and Smith's Plastic Surgery*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2019:225–237.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. Chichester, United Kingdom: Wiley-Blackwell; 2012:832–844.

A.2. What is the cause of a cleft lip or a cleft palate?

Major components of the face develop between 4 and 7 weeks of fetal life. There are three mesodermal islands, one central and two lateral. Prepalatal clefts are caused by the failure of these mesodermal elements to develop and fuse. Palatal clefts are caused when the palatal ridges fail to migrate medially, contact, and fuse (**Fig. 42.1**).

Chung KC, ed. *Grabb and Smith's Plastic Surgery*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2019:225–237.

A.3. What is the incidence of a cleft lip and a cleft palate?

A cleft lip and cleft palate may occur together or separately. A cleft lip with or without a cleft palate is more common in boys, whereas an isolated cleft palate is more common in girls. The overall prevalence of a cleft lip with or without a cleft palate is 9.92 per 10,000. The prevalence of a cleft lip is 3.28 per 10,000 and that of a cleft lip and palate is 6.64 per 10,000. There were 5,918 cases (76.8%) that were isolated clefts, 1,224 (15.9%) had malformations in other systems, and 562 (7.3%) occurred as part of recognized syndromes. Cases with greater dysmorphologic severity of cleft lip with or without cleft palate were more likely to include malformations of other systems.

The highest incidence of cleft lip and cleft palate occurs among Asians (1.61:1,000 births), whereas the lowest incidence is in African Americans (0.3:1,000 births). The incidence in Whites is intermediate (0.9:1,000 births).

IPDTOC Working Group. Prevalence at birth of cleft lip with or without cleft palate: data from the International Perinatal Database of Typical Oral Clefts (IPDTOC). *Cleft Palate Craniofac J*. 2011;48(1):66–81.

Samanich J. Cleft palate. *Pediatr Rev*. 2009;30(6):230–232.

A.4. Discuss the pathophysiology of a cleft lip and palate in the neonate and the older child (e.g., age >5 years).

A cleft palate is responsible for some major physiologic disorders. The pharynx communicates more extensively with the nasal fossae and the oral cavity. The complex mechanisms of swallowing, breathing, hearing (through the eustachian tube), and speech are, therefore, impaired.

The presence of a cleft lip and palate in a neonate results in feeding difficulties. The neonate cannot suck because the cleft makes the creation of a negative pressure difficult. Breastfeeding is improbable, and bottle-feeding is difficult.

Essentially, all children with a cleft palate have middle ear

disease because abnormal anatomy of the nasopharynx adversely affects eustachian tube function. Chronic middle ear effusions produce varying degrees of conductive hearing loss. Nasal septation between food and air is absent, creating a nonphysiologic mixing chamber in the nasopharynx. Not infrequently, this is associated with chronic rhinorrhea that must be distinguished preoperatively from infection.

Secondary defects of tooth development, growth of the ala nasi, and velopharyngeal function (contact between the soft palate and the posterior pharynx for speech and swallowing) can also occur.

Psychological problems may be considerable as this youngster approaches school age and peer association. The speech of these children is typically nasal with an inability to produce the so-called plosive (*p*/*k*/*d*/*t*) and fricative (*s*/*f*) sounds.

Kosowski TR, Weathers WM, Wolfswinkel EM, et al. Cleft palate. *Semin Plast Surg*. 2012;26(4):164–169.

A.5. What other conditions are associated with a cleft lip and a cleft palate?

Associated anomalies occur 30 times more frequently in the patient with isolated cleft palate than in the noncleft population.

The most common non–syndrome-related abnormalities are umbilical hernias, clubfoot, and limb and ear deformities.

The most common syndromes associated with a cleft lip and a cleft palate are the following:

- Velocardiofacial (Shprintzen) syndrome
- Van der Woude syndrome
- Stickler syndrome
- Pierre Robin syndrome
- Fetal alcohol syndrome
- Goldenhar syndrome (facioauriculovertebral syndrome or hemifacial microsomia)

- Treacher Collins syndrome
- Nager syndrome
- Down syndrome

Calzolari E, Pierini A, Astolfi G, et al. Associated anomalies in multi-malformed infants with cleft lip and palate: an epidemiologic study of nearly 6 million births in 23 EUROCAT registries. *Am J Med Genet A*. 2007;143A:528–537.

A.6. What is Pierre Robin syndrome?

This syndrome is characterized by retrognathia or micrognathia, glossoptosis, and airway obstruction. For facial cleft surgeons, Pierre Robin syndrome is defined by a triad of clinical criteria:

- Retrognathia
- Severe respiratory and/or digestive disorders in early infancy
- Cleft palate

An incomplete cleft of the palate is associated with the syndrome in approximately 50% of these patients. In patients with micrognathia (small jaw) or retrognathia, the chin is posteriorly displaced causing the tongue to fall backward toward the posterior pharyngeal wall. This results in obstruction of the airway on inspiration. Crying or straining by these children can often keep the airway open. However, when the child relaxes or sleeps, airway obstruction occurs. Because of these respiratory problems, feeding may become very difficult. This can lead to a sequence of events: glossoptosis, airway obstruction, crying or straining with increased energy expenditure, and decreased oral intake. This vicious cycle of events if untreated can led to exhaustion, cardiac failure, and ultimately death.

Jones KL, Jones MC, del Campo M, eds. *Smith's Recognizable Patterns of Human Malformation*. 7th ed. Philadelphia, PA: WB Saunders; 2013:314.

A.7. What is Treacher Collins syndrome?

It is a highly complex disease process consisting of the following:

- Hypoplastic cheeks, zygomatic arches, and mandible
- Microtia with possible hearing loss
- High-arched or cleft palate
- Macrostomia (abnormally large mouth)
- Antimongoloid slant to the eyes
- Colobomas (notching of the outer portion of the lower eyelid)
- Increased anterior facial height
- Malocclusion (anterior open bite)
- Small oral cavity and airway with normal-sized tongue
- Pointed nasal prominence

Jones KL, Jones MC, del Campo M, eds. *Smith's Recognizable Patterns of Human Malformation*. 7th ed. Philadelphia, PA: WB Saunders; 2013:334–335.

A.8. What kind of specialized team care would these patients need?

These patients need a pediatrician to maintain their overall health and a surgeon and an anesthesiologist to accomplish the various surgeries. They need a speech therapist to prevent or overcome the speech deficiencies and an orthodontist for early orthodontic intervention to develop and maintain a relatively normal bite and dentition. The care team should also include a geneticist, pediatric dentist, prosthodontist, psychologist, medical social worker, and public health nurse.

Kliegman RM, St. Geme JW III, Blum NJ, et al, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:1915–1917.

A.9. Discuss indications and timing of closure of cleft lip and palate.

Functional goals of cleft palate surgery are normal speech, hearing, and maxillofacial growth. It is thought that speech and hearing are improved by early cleft palate repair (before 24 months of age) and that the delayed closure (after 4 years) is associated with less retardation of midfacial growth. There is no

consensus in the exact timing of lip and palate closure. These variations likely reflect the anatomic situation in different patients as well as the personal preferences of the surgeon. An early two-stage palate repair is advocated in management of these patients. The recommended sequence involves closure of the soft palate at 3 to 6 months of age with secondary closure of the residual hard palate at 15 to 18 months of age. This sequence takes advantage of the early physiology and growth that occurs in the soft palate, which is vital in the development of speech. Furthermore, it avoids the potential pitfalls of the growth disturbance related to early periosteal undermining of palatal and vomerine tissue. This repair sequence also provides total palatal closure before speech evolves. If soft palate is repaired at the time of lip repair, an additional anesthetic is avoided.

Thiele OC, Kreppel M, Dunsche A, et al. Current concepts in cleft care: a multicenter analysis. *J Craniomaxillofac Surg*. 2018;46(4):705–708.

A.10. What is velopharyngeal incompetence, and how can it be diagnosed?

Velopharyngeal incompetence is the inability of the soft palate to fulfill its role in closing the nasopharynx, which seriously affects phonation.

To produce plosive sounds, *p*/*k*/*t*/*d*, or the sibilants, *s*/*sh*, the soft palate must touch the posterior pharyngeal wall to close the nose. Failure of closure results in the typical hypernasal speech. The most common cause of this is the cleft palate, but patients with congenitally short palates and no cleft can also have this typical speech pattern. Treatment consists of surgical lengthening of the palate by the pushback operation with or without pharyngeal flap. The diagnosis of velopharyngeal incompetence can be suggested by the child's speech. More objective diagnosis can be obtained by direct vision of the soft palate while the child is pronouncing certain keywords (*kah*,

kah), by the fogging of the hand mirror placed under the nose during speech, and from cinefluorographic x-ray films.

In patients with velopharyngeal incompetence, videofluoroscopy and nasopharyngoscopy can provide information that will help select the appropriate procedure, either pharyngoplasty or posterior pharyngeal flap.

Dudas JR, Deleyiannis FW, Ford MD, et al. Diagnosis and treatment of velopharyngeal insufficiency: clinical utility of speech evaluation and videofluoroscopy. *Ann Plast Surg*. 2006;56(5):511–517.

A.11. What is the relation of tonsillectomy and adenoidectomy to velopharyngeal incompetence?

There is often a considerable mass of tonsillar and adenoidal tissue at the age when surgery is usually performed, and, in addition to the latent danger of infection, the flap used in pharyngoplasty creates an obstruction that seriously complicates their subsequent removal. Furthermore, bulky tonsils may hinder retrodisplacement of the soft palate or block the airflow by obstructing the cavum, which has already been reduced in volume by the retrodisplacement and the presence of the flap. It is, therefore, preferable to remove the tonsils and adenoids a few months before pharyngoplasty. The parents may wonder why this decision has been made because they have been repeatedly told that the adenoids should not be removed in the case of cleft palate because this might create or aggravate velar insufficiency. However, once velar inadequacy is confirmed, the parents are in a position to understand that these precautions are no longer justified and that the adenoids can represent a source of problems if not treated with radical measures. During tonsillectomy, it is important to leave the tonsillar pillars absolutely intact because their muscle structure has a vital physiologic role.

Milczuk HA. Effects of oropharyngeal surgery on velopharyngeal

competence. *Curr Opin Otolaryngol Head Neck Surg*. 2012;20(6):522–526.

B. Preoperative Evaluation and Preparation

B.1. What information do you need before closure of a cleft lip and palate?

Preoperative anesthetic evaluation is invaluable and includes the history and physical examination and suitable laboratory data. It gives a picture of the patient's general health. Hemoglobin level, which is often low in very young infants, should be obtained. If Treacher Collins or Pierre Robin syndrome is suspected, an x-ray film of the mandible may be helpful. Examination of the mouth may indicate potential intubation problems. The examination also offers a good opportunity to assess the family environment because parental cooperation is essential for proper postoperative care.

Most surgeons repair a cleft lip when the baby is 6 to 10 weeks old and repair a cleft palate at 6 to 12 months of age. The exact age of repair will depend on the size and health of the child and the surgeon's preference.

Because periosteoplasty and lip adhesions are carried out as soon as the segments are in alignment and the surgery is less extensive, the rule of 10 can be used with moderate license:

- *Weight*—approximately 10 lb
- *Hemoglobin*—10 g per dL or more
- *White blood cell count*—less than 10,000 per μL
- *Age*—can be less than 10 weeks

Of the rule of 10 metrics, only weight below 10 lb (4.5 kg) was identified as an independent predictor of overall complications in cleft patients. Preoperative screening is essential in cleft patients because underlying cardiac abnormalities dramatically increase the risk of perioperative morbidity.

With open cleft palate, however, it is common to have crusting and a low-grade infection of the nasopharynx because of food and fluid regurgitation through the cleft. It is nearly impossible to eliminate this completely. Unless an acute inflammatory process is present, this does not lead to complications.

Chow I, Purnell CA, Hanwright PJ, et al. Evaluating the rule of 10s in cleft lip repair: do data support dogma? *Plast Reconstr Surg*. 2016;138(3):670–679.

Chung KC, ed. *Grabb and Smith's Plastic Surgery*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2019:225–237.

B.2. What preoperative orders are needed?

Preoperative fasting has been a prerequisite for elective surgery. An issue of particular importance to the pediatric patient is the wonderful change that has taken place regarding preoperative fasting. Recent work has shown that prolonged fasting does not reduce the risk of aspiration pneumonitis during anesthesia. This has led to reduction in the fasting times. Reduced fasting increases patient comfort and may decrease the potential for intraoperative hypoglycemia. Fasting guidelines for infants and children are shown in **Table 42.1**.

TABLE 42.1 Minimum Fasting Period (Hours) for Pediatric Patients

	Clear Fluids	Breast Milk	Formula or Cow's Milk	Solids
Children	2	—	6	6
3–12 months	2	4	6	6
<3 months	2	4	4	6

Because multiple operations may be required, the emotional trauma of each hospital experience must be minimized. The most common premedication used at Weill Cornell Medical Center in pediatric patients is oral midazolam. The dose ranges from 0.25 to 0.5 mg per kg orally. Children younger than 8

months rarely require premedication. Children with anticipated difficulty in airway management and those with a propensity toward airway obstruction are better off without premedication.

Special orders include antibiotics if the infant or child has associated congenital heart disease and the typing and crossmatching of a unit of blood for palatal surgery.

Coté CJ. Preparation, premedication and induction of anesthesia in children. In: *ASA Annual Meeting Refresher Course Lectures*. Park Ridge, IL: American Society of Anesthesiologists; 2001:243.

C. Intraoperative Management

C.1. What monitors will you need for cheiloplasty and palatoplasty?

Heart rate, respiration, blood pressure, temperature, and oxygen saturation are monitored at all times. An electrocardiogram provides visual and audible evidence of the electrical activity of the heart. A precordial stethoscope monitors both heart and respiratory sounds. It is particularly important in this patient because once the surgery has begun, the anesthesiologist no longer has easy direct access to the airway. The use of pulse oximetry and an end-tidal carbon dioxide (CO_2) monitor is indispensable. Temperature should be monitored per rectum or axilla. A warming blanket should be used in these patients to avoid hypothermia. Blood loss determination should be made by a calibrated catchment trap in the suction line and by weighing sponges. Blood loss rarely exceeds 10% of circulating blood volume; however, properly crossmatched and screened blood should be available but used only if absolutely necessary.

C.2. Discuss the induction and the anesthetic management for cleft lip and palate.

After suitable monitors are attached, the anesthetic is induced

with oxygen, nitrous oxide, and either sevoflurane or halothane. Because the cardiac depressant effects of sevoflurane are less pronounced than those of halothane, we prefer to use sevoflurane for induction. In addition, the myocardium is more sensitive to exogenous epinephrine when halothane is used. The recommended maximal dose of lidocaine for palate or lip surgery is 5 mg per kg and of epinephrine is 10 μg per kg. This epinephrine dose is for hypocarbic or normocarbic patients.

Once the patient is asleep, an intravenous line is established and appropriate intravenous fluids are started. Intubation can be facilitated with a nondepolarizing muscle relaxant. Muscle relaxants should be withheld if any possibility of difficulty in intubation exists.

Laryngoscopy in patient with a cleft lip is generally straightforward, but the cleft palate has the capability to trap and immobilize a straight blade. Should this occur, the anesthesiologist must first recognize the problem and then consider inserting a gauze pack or a dental roll into the cleft before laryngoscopy.

To achieve a cosmetic repair, symmetry is essential, so the endotracheal tube should exit the mouth in the midline without facial distortion from either the tube or the securing tape. Some surgeons prefer to suture the tube to the lower gum.

An orogastric tube should be passed to empty the stomach of gas and secretions, and it should be removed before preparation of the surgical field.

A pharyngeal pack of moistened ribbon gauze is inserted for cleft lip repairs; as for a cleft palate repair, the surgeon inserts the gag before insertion of the pharyngeal pack. Following the gag and pack insertion, ventilation should be reassessed because tube compression may have occurred. To avoid eye injury, an ocular lubricant is placed in the eyes, and the upper eyelids are splinted shut with tape.

During the surgery, it is necessary to have good communication and cooperation between the surgeon and the anesthesiologist because the surgeon's tools and hands and the anesthesiologist's endotracheal tube and apparatus all occupy the same very small space.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. Chichester, United Kingdom: Wiley-Blackwell; 2012:832–834.

C.3. What positioning is recommended for cleft palate repair surgery?

Correct positioning of the child is important for the plastic surgeon, who sits at the head of the operating table. Head extension must be maximal for cleft palate surgery. The entire body is raised with a thick foam mat or folded blanket, allowing the head to drop back hyperextended into a stockinette head support. Not only does this position provide good exposure, but it also allows blood to flow away from larynx and toward the nasopharynx allowing it to be removed by suction.

C.4. What are the reported complications of this type of surgery and anesthesia?

Anesthetic complications include obstruction of the endotracheal tube, inadvertent extubation during the procedure, and cardiac arrest. Postanesthetic complications include airway obstruction, bleeding with or without aspiration, and pneumonia. Complications not related to anesthetic management are wound healing, diarrhea, and otitis media. The mortality rate has been reported to be less than 0.5%.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. Chichester, United Kingdom: Wiley-Blackwell; 2012:832–834.

C.5. Briefly describe the surgical techniques used to repair cleft defects.

The Furlow procedure is the most common technique for cleft palate closure. It involves opposing Z-plasties of the mucosa and the musculature of the soft palate. The goal is to separate the nonfunctioning attachments from the posterior border of the hard palate and to displace the mucosa and the musculature posteriorly.

Other basic surgical techniques include the von Langenbeck technique, Schweckendiek technique, two-flap technique, and three-flap/V-Y technique.

Although most of the repairs do not involve repairing the muscular sling, doing so allows better palatal and eustachian tube function.

A surgical robot may offer enhanced precision, visualization, and access and the potential to improve outcomes in cleft palate surgery in future.

Sadove AM, van Aalst JA, Culp JA. Cleft palate repair: art and issues. *Clin Plast Surg*. 2004;31(2):231–241.

C.6. How does a pharyngeal flap affect anesthetic management or any subsequent anesthetic administered to this patient?

The presence of this flap prohibits nasoendotracheal intubation and makes many nasal techniques difficult (e.g., insertion of nasogastric tube). The degree of obstruction is related to the width of the flap. Traumatic rupture of this flap secondary to attempted nasotracheal intubation could produce bleeding, aspiration, and laryngospasm.

Traumatic rupture of soft palate can occur from placement of laryngeal mask airway.

Knowledge of prior surgery is essential to good anesthetic management. Following the pushback and pharyngeal flap operation (pharyngoplasty), significant airway obstruction has been noted in the early postoperative period. Sleeping pulse

oximetry has demonstrated obstruction and desaturation in the first 48 to 72 hours.

Dearlove O, Perkins RJ, Briggs G. Anaesthesia after cleft palate repair. *Anaesthesia*. 2004;59(10):1032.

Somerville NS, Fenlon S, Boorman J, et al. Disruption of cleft palate repair following the use of the laryngeal mask airway. *Anaesthesia*. 2004;59(4):401–403.

C.7. What is an Abbe flap? What are its anesthetic implications?

An Abbe flap is a full-thickness pedicle flap taken from the lower lip and swung on its own artery to a position in the upper lip to replace a tissue deficit resulting from any cause, such as surgical excision of malignancy or loss of tissue in a bilateral cleft lip. The lips must remain closed until the flap "takes," and then it can be detached from its blood supply. Usually, this operation is performed in children of an older age under local anesthesia, but it occasionally requires general anesthesia if the patient is young. All the problems of a closed mouth, such as the possibility of vomiting and aspiration, are encountered in addition to those associated with preservation of the flap.

Koshy JC, Ellsworth WA, Sharabi SE, et al. Bilateral cleft lip revisions: the Abbe flap. *Plast Reconstr Surg*. 2010;126(1):221–227.

C.8. What is the crucial problem of anesthesia for cleft palate? What are the unique considerations of this surgical repair?

The establishment, maintenance, and protection of the airway are the crucial problems of anesthesia for palate surgery. Failure to establish, maintain, and protect the airway results in tachypnea, CO_2 retention, hypoxemia, increased bleeding, hypovolemia, arrhythmia, cardiac arrest, and death. The major cause of cardiac arrest in infants and children is hypoxia.

Positioning of the patient is usually supine with table rotated 90 to 180 degrees with a preformed oral RAE (Ring-Adair-Elwyn) or reinforced endotracheal tube extending down the midline of the jaw taped to the chin. The mouth gag that is used for surgical exposure may be released intermittently to allow reperfusion of tongue. However, each manipulation may affect the endotracheal tube. Blood that collects in the oropharynx should be carefully suctioned at the end of the procedure without disrupting the suture line. Residual blood and secretions in the oropharyngeal cavity may irritate the larynx and cause laryngospasm.

Jaffe RA, Schmiesing CA, Golianu B, eds. *Anesthesiologist's Manual of Surgical Procedures*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2014:1460–1462.

C.9. What is laryngospasm? How would you make a diagnosis of laryngospasm?

This is defined as glottic closure resulting from a reflex constriction of the laryngeal muscles. It is much more common in pediatric than adult anesthesia. The incidence is twice that of adults in older children and three times that of adults in younger children. Airway complications are further increased in children with upper respiratory tract infections. In the pediatric patient, the oxygen consumption is greater, so the consequences of laryngospasm in children are more serious. The oxygen consumption is highest in the youngest patients.

Laryngospasm seems to occur during anesthesia for two reasons: first, a lack of inhibition of glottic reflexes because of central nervous system depression, and second, an increased number of stimuli−such as manipulation of the airway, secretions or blood irritating the cords, and stimulation of visceral nerve endings at an inadequate depth of anesthesia.

Bingham R, Lloyd-Thomas A, Sury M, eds. *Hatch & Sumner's Textbook of*

Paediatric Anaesthesia. 3rd ed. London: Hodder Arnold; 2008:288–289.

C.10. How would you manage the patient with laryngospasm?

Laryngospasm may be partial or complete. Partial spasm will be diagnosed by a characteristic stridorous noise and a mismatch between the patient's respiratory effort and the disappointingly small movements of the reservoir bag. Methods of overcoming laryngospasm include applying positive pressure to the airway, deepening anesthesia, and administering muscle relaxants or a bolus of propofol. Recently, it was found that a bolus of propofol works extremely quickly, without the side effects of succinylcholine. The exact mechanism of action of propofol is not clear, but it could be due to increasing the depth of anesthesia or direct effect on the glottis. When there is complete laryngospasm, there will be silence with regard to air movement. The application of positive pressure may not be helpful in these circumstances and indeed may make the situation worse by forcing the false cords against the tightly closed true cords. It is much better to relax the cords before the hypoxia is severe. Succinylcholine can be given intramuscular or intravenous.

Bingham R, Lloyd-Thomas A, Sury M, eds. *Hatch & Sumner's Textbook of Paediatric Anaesthesia*. 3rd ed. London: Hodder Arnold; 2008:288–289.

D. Postoperative Management

D.1. What complications of cleft lip and cleft palate surgery may be seen in the recovery room?

Complications include airway obstruction, bleeding, neurosensory disturbance, and hypothermia. Airway obstruction is the result of closure of the cleft structures plus some edema secondary to trauma. In the case of a pushback procedure with or without a pharyngeal flap, the obstruction is due to the new

posterior position of the palate and the pharyngeal flap. Combination of a closed palate, a small mandible pushing the tongue into a small pharynx, edema, blood, and the residual effects of anesthesia make postextubation airway obstruction more likely. There could also be swelling of the tongue due to mouth gag placement during surgery. The anesthesiologist must be aware of the potential problems such as subglottic edema, flap edema, increased oral secretions, posterior displacement of tongue, mucosal swelling of hypopharynx, and an overlooked throat pack.

Blood loss is not an anesthetic complication, but its replacement is an anesthesiologist's responsibility, as is prevention of aspiration.

Patients may experience paresthesia in the cheek after surgery, very rarely the sensory disturbance may be permanent.

Hypothermia delays emergence and produces metabolic acidosis and respiratory and myocardial depression. The most important problem for the anesthesiologist is maintenance of airway.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:817–843.

Neligan PC, Rodriguez ED, Losee JE, et al, eds. Cleft and craniofacial orthognathic surgery. In: *Craniofacial, Head and Neck Surgery and Pediatric Plastic Surgery*. 4th ed. London: Elsevier; 2018:660–677. *Plastic Surgery*; vol 3.

D.2. How do you protect the airway postoperatively?

Following palatoplasty, the pharynx and nasopharynx are suctioned before extubation. Some anesthesiologists advocate that this be done with the aid of a laryngoscope to ensure removal of any mucus, blood, or clots. If suctioning is done before removing the Dingman gag, the laryngoscope may not be necessary. The infant should be as awake as possible. A long traction suture is placed through the tongue and tied loosely.

Traction on the suture stimulates respiration and clears the airway. Neither an oral nor a nasal airway should be inserted unless absolutely necessary; either one could disrupt the sutures and undo all the surgical work. The traction suture is removed when the infant leaves the recovery room.

Following palate surgery, the infant is placed in prone or lateral position with the head dependent, turned to the side, and hyperextended. This position can be achieved with a jack placed under the foot of the crib or by placing a bulky bath blanket under the hips of the infant. Any blood or mucus will accumulate in the dependent cheek or roll out of the mouth.

Following cleft lip surgery, a Logan bow is frequently used to take the tension off the newly sutured lip. The infant can still be placed in the lateral position. Elbow restraints are essential, and they are placed on the infant or the child before leaving the operating room. A high-humidity atmosphere is recommended postoperatively to reduce the incidence of tracheitis, but others have failed to show any correlation between the use of humidity and the incidence of tracheitis.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:817–843.

D.3. How would you control postoperative pain in patients following a cleft lip and cleft palate repair?

In patients with cleft lip or cleft palate repair, the continuum of pain management continues through to the recovery room, the pediatric intensive care unit, or to an inpatient bed. No child should be discharged from recovery room with uncontrolled pain. Cleft palate repair is associated with the risk of postoperative airway obstruction, which may be increased with administration of opioids. Nerve blocks may be used to improve pain relief, to decrease perioperative consumption of opioids, and to favor early feeding resumption after repair.

Infraorbital nerve block can be used for pain control after cleft lip repair. Nasopalatine and palatine nerve block will provide palatal hard and soft tissue anesthesia. Recently, bilateral maxillary nerve blocks using a suprazygomatic approach have been used for effective pain relief.

Opioid analgesics that can be used postoperatively are shown in **Table 42.2**.

TABLE 42.2 Opioid Analgesics for Pediatric Patients

Drugs	Dosage	Form
Fentanyl	1 μg/kg	IV
Morphine	0.05–0.1 mg/kg	IV
Meperidine	1 mg/kg	IV
Oxycodone	0.15 mg/kg	PO: 5-mg tablets; syrup 5 mg/mL

IV, intravenous; PO, by mouth.

Nonopioid analgesics that can be used postoperatively are shown in **Table 42.3**.

TABLE 42.3 Nonopioid Analgesics for Pediatric Patients

Drug	Dosage	Forms Available
Acetaminophen (Tylenol)	10–15 mg/kg PO maximum 2,600 mg/day	Tablets: 80 mg Syrup: 325 mg/5 mL Suppositories: 120 mg, 325 mg, 650 mg
Ibuprofen (Motrin)	10–20 mg/kg PO q6h	Tablets: 300 mg, 400 mg Syrup: 100 mg/5 mL
Ketorolac (Toradol)	0.5 mg/kg IV to load (maximum dose 30 mg) 0.5 mg/kg q8h intramuscularly or intravenously (limit use to 48 hr)	Parenteral form used intramuscularly/intravenously

IV, intravenous; PO, by mouth.

Lonnqvist PA, Morton NS. Paediatric day-case anaesthesia and pain control. *Curr Opin Anaesthesiol*. 2006;19:617–621.

Mesnil M, Dadure C, Captier G, et al. A new approach for peri-operative analgesia of cleft palate repair in infants: the bilateral suprazygomatic maxillary nerve block. *Paediatr Anaesth*. 2010;20(4):343–349.

43 Congenital Heart Disease with a Cervical Mass in Infancy

Miles Dinner and Elizabeth Q. Starker

A 1-week-old male infant was diagnosed shortly after birth with an interrupted aortic arch (IAA). The workup revealed the child to have a 22q11 deletion syndrome (formerly known as *DiGeorge syndrome*). An enlarging cervical mass was noted, and the child was brought to the operating room for exploration.

A. Medical Disease and Differential Diagnosis

1. What is 22q11 deletion syndrome?
2. What are the associated cardiovascular defects in 22q11 deletion syndrome?
3. What are the metabolic and endocrine abnormalities in patients with 22q11 deletion syndrome and the attendant manifestations?
4. What are the immunologic findings in 22q11 deletion syndrome?
5. What is the differential diagnosis of cervical masses in infancy?
6. What is a cystic hygroma? What are the complications? What

is the treatment?

7. What is the IAA anomaly?
8. What is the pathophysiology of the IAA syndrome?
9. How is ductal patency maintained?
10. What are the side effects of prostaglandin infusion?
11. What is the hyperoxia test?

B. Preoperative Evaluation and Preparation

1. What preoperative studies should be obtained to evaluate the neck mass?
2. How would you categorize the difficult airway in children?
3. What features of the difficult airway can be noted on physical examination?
4. How would you preoperatively optimize the ability to secure the airway in the operating room?
5. What laboratory studies are necessary before surgery?
6. What are the causes of heart failure (HF) in the infant? How would you assess this infant in your preoperative evaluation for signs of HF?
7. How would you optimize the preoperative treatment of HF?
8. How would you premedicate this infant?
9. When is premedication useful in infants and children?
10. Before the planned surgery, the infant is scheduled for a magnetic resonance imaging (MRI) scan. You are asked to ensure that the baby remains immobile for 20 minutes to perform the scan adequately. How would you accomplish this?

C. Intraoperative Management

1. What anesthesia equipment, circuit, and monitors would you use?
2. Describe techniques other than direct laryngoscopy that would be useful for securing the airway in this baby.
3. How would you monitor blood loss in this patient?
4. What anesthetic technique should be used in a patient who

may experience severe loss of blood intraoperatively?

5. How would you induce and maintain anesthesia in this neonate?
6. Intraoperatively, the surgeon must dissect the tumor in the anterior mediastinum and needs to have a quiet surgical field. How would you accomplish this in the infant?

D. Postoperative Management

1. How would you manage this patient postoperatively?

A. Medical Disease and Differential Diagnosis

A.1. What is 22q11 deletion syndrome?

The 22q11 deletion syndrome is one of the most common multiple anomaly syndromes in humans and has historically been referred to as velocardiofacial syndrome, DiGeorge sequence, conotruncal anomalies face syndrome, CATCH 22, and Sedlackova syndrome—different names describing the same disorder. This syndrome has an expansive phenotype with more than 180 clinical features that can involve every organ and system. The syndrome is caused by a microdeletion of chromosome 22 at the q11.2 band. The syndrome has a prevalence of approximately 1 in 4,000 in the United States. The majority of patients have a constellation of abnormalities resulting from an embryogenic disruption in the formation of the third and fourth aortic arches. The common clinical features are hypocalcemia, immunodeficiency, dysmorphic facial features, palatal and velopharyngeal dysfunction, renal anomalies, and congenital heart disease (CHD). The DiGeorge variant is characterized by thymic and parathyroid aplasia and/or hypoplasia, cardiovascular defects, and dysmorphic facies. Depending on the extent of the thymic hypoplasia, clinical manifestations can range from frequent upper respiratory tract

infections to severe immunodeficiency that can only be corrected with T-cell–replete hematopoietic stem cell transplantation (HSCT) or thymus transplantation.

Jones JW, Tracy M, Perryman M, et al. Airway anomalies in patients with 22q11.2 deletion syndrome: a 5-year review. *Ann Otol Rhinol Laryngol*. 2018;127(6):384–389.

Kliegman RM, St. Geme JW, Blum NJ, et al, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:3646–3650.

Kuo CY, Signer R, Saitta SC. Immune and genetic features of chromosome 22q11.2 deletion (DiGeorge syndrome). *Curr Allergy Asthma Rep*. 2018;18(12):75.

Zucker EJ. Syndromes with aortic involvement: pictorial review. *Cardiovasc Diagn Ther*. 2018;8(suppl 1):S71–S81.

A.2. What are the associated cardiovascular defects in 22q11 deletion syndrome?

Congenital heart defects are found in 80% of patients with this syndrome. Most of these patients have conotruncal defects with additional anomalies of the aortic arch, pulmonary arteries, infundibular septum, and semilunar valves. The most common abnormalities include tetralogy of Fallot, pulmonary atresia with ventricular septal defect (VSD), truncus arteriosus, IAA, isolated anomalies of the aortic arch, and VSD. These defects arise during the crucial developmental stages of the truncoconal parts of the heart from the pharyngeal pouch derivatives. Echocardiography, computed tomography (CT), and cardiac MRIs are important in defining the cardiac and associated anatomy in detail. These modalities can provide an invaluable understanding of the anatomy required for presurgical planning.

Friedman, K. Preoperative physiology, imaging, and management of interrupted aortic arch. *Semin Cardiothorac Vasc Anesth*. 2018;22(3):265–269.

Jonas RA. Management of interrupted aortic arch. *Semin Thorac Cardiovasc Surg*. 2015;27:177–188.

Zucker EJ. Syndromes with aortic involvement: pictorial review. *Cardiovasc Diagn Ther*. 2018;8(suppl 1):S71–S81.

A.3. What are the metabolic and endocrine abnormalities in patients with 22q11 deletion syndrome and the attendant manifestations?

Because of errors of embryogenesis of the third and fourth pharyngeal arches, parathyroid hypoplasia and/or aplasia is common and results in hypocalcemia. This can be transient in neonates or may be permanent requiring calcium and vitamin D supplementation. Because hypocalcemia can be difficult to detect in the neonate, a high index of suspicion is necessary if a neonate exhibits irritability, jitteriness, twitching, seizure activity, failure to thrive, tachycardia, and hypotension. Stridor (which needs to be differentiated from laryngeal web, which is also prevalent in 22q11 deletion syndrome) and carpopedal spasm may also occur. It is important to remember that in patients with this syndrome, hypocalcemia may be precipitated by the stress of surgery and by increased needs during puberty or pregnancy. Chronic hypocalcemia may result in poor dentition that is prone to caries.

The prevalence of thyroid disease is significantly higher in the pediatric population with 22q11 deletion syndrome than in the general pediatric population. Some sources suggest that screening for thyroid disease should be added into the routine medical management of these children.

Levy-Shraga Y, Gothelf D, Goichberg Z, et al. Growth characteristics and endocrine abnormalities in 22q11.2 deletion syndrome. *Am J Med Genet A*. 2017;173(5):1301–1308.

Shugar AL, Shapiro JM, Cytrynbaum C, et al. An increased prevalence of thyroid disease in children with 22q11.2 deletion syndrome. *Am J Med Genet A*. 2015;167:1560–1564.

Sperling MA, ed. *Pediatric Endocrinology*. 4th ed. Philadelphia, PA: Elsevier Saunders; 2014:734–754.

A.4. What are the immunologic findings in 22q11 deletion syndrome?

Patients with this syndrome demonstrate marked variability in their immune system ranging from complete thymic aplasia to reduced T-cell counts and function. The majority of patients (approximately 75%) have a decrease in the total number of T cells, and approximately 1.5% of patients have complete thymic aplasia requiring transplant. Reduced levels of immunoglobulin A (IgA) and immunoglobulin M (IgM) also occur more frequently compared to the general population. Almost all patients have a tendency toward infection, particularly of the respiratory tract. As long as there is a working thymus, patients with 22q11 deletion syndrome can be immunized and generate a good antibody response because humoral immunity is usually intact. However, poor vaccine-specific antibody responses have been described. Neonatal diagnosis historically relied on fluorescence in situ hybridization (FISH) testing and phenotype recognition. However, T-cell receptor excision circles (TRECs) are now being included in the newborn screening panel for severe combined immunodeficiency (SCID). This allows for early identification of 22q11.2 deletion syndrome patients with severe T-cell lymphopenia. Autoimmune conditions are found in up to a third of patients, the most common being juvenile chronic arthritis, autoimmune thrombocytopenia, hemolytic anemia, Raynaud phenomena, and autoimmune thyroid disease.

Habel A, Herriot R, Kumararatne D, et al. Towards a safety net for management of 22q11.2 deletion syndrome: guidelines for our times. *Eur J Pediatr*. 2014;173:757–765.

Kuo CY, Signer R, Saitta SC. Immune and genetic features of chromosome 22q11.2 deletion (DiGeorge syndrome). *Curr Allergy Asthma Rep*. 2018;18(12):75.

A.5. What is the differential diagnosis of cervical masses

in infancy?

Neck masses can originate from a congenital anatomic anomaly, infection, or neoplasm. Congenital anomalies consist of branchial and thyroglossal duct cysts and failed thymic descents. In the embryo, branchial cysts arise from the thymic stalk or the pharyngeal pouch and may be present at birth or develop later. They lie beneath the sternocleidomastoid muscle and may bulge out from its anterior border. The branchial cysts can become infected and enlarge to the extent that they compress the airway or upper esophagus. Thyroglossal duct cysts are spherical, midline masses that may extend back to the base of the tongue and may represent all of the neonate's thyroid tissue. In the embryo, the thymus gland arises high in the neck and descends into the anterior mediastinum. If there is any interruption of this caudad movement, the thymus can appear as a soft, compressible mass anywhere along the anterior border of the sternocleidomastoid muscle.

Infectious masses can be due to tuberculosis, Kawasaki disease, Epstein-Barr viral infection, cellulitic facial infections (Ludwig angina), and subacute regional lymphadenitis (catscratch disease).

Neoplastic masses in the cervical region can be teratomas, hemangiomas, neurofibromas, lymphomas, goiters, or cystic hygromas. Teratomas are firm, midline masses arising adjacent to the thyroid isthmus. Hemangiomas may be extensive, consequently compressing vital structures. Neurofibromas may arise individually or as a consequence of neurofibromatosis (von Recklinghausen disease) and can be very large. Goiters are enlarged thyroid glands that may present a hypothyroid, hyperthyroid, or euthyroid state. Ultrasound, CT, and MRI are the imaging modalities used most often to determine the nature of a neonatal neck mass.

Long SS, Prober CG, Fischer M, eds. *Principles and Practice of Pediatric Infectious Diseases*. 5th ed. Philadelphia, PA: Saunders Elsevier; 2017:136–148.

Tranvinh E, Yeom KW, Iv M. Imaging neck masses in the neonate and young infant. *Semin Ultrasound CT MR*. 2015;36:120–137.

A.6. What is a cystic hygroma? What are the complications? What is the treatment?

Cystic hygroma is a developmental malformation of the lymphatic system found most often in the posterior triangle of the neck and axilla of children. They are divided into suprahyoid and subhyoid masses. They are compressible masses that are most often found in infants younger than 1 year and can intermittently enlarge. Suprahyoid masses can be extremely difficult to manage because of the associated obstructive symptoms, feeding difficulties, and potential for infection, which further can compromise airway patency. Surgical removal is the treatment of choice in these patients. Complete surgical removal of these masses is often impossible. Repeat debulking is sometimes the only treatment. The mortality of a prenatally diagnosed cystic hygroma remains high, due to other comorbidities and the risk of airway obstruction. Therefore, intubation of the neonate during delivery while maintaining uninterrupted maternal–fetal circulation until the airway is secured (ex utero intrapartum treatment [EXIT] procedure) has been performed to prevent the fatal consequences of immediate postnatal airway obstruction. Other treatment modalities include radiofrequency ablation, CO_2 laser, and percutaneous sclerotherapy. Bleomycin, doxycycline, or derivatives of *Streptococcus pyogenes* have been used as sclerosing agents with favorable results.

Damaskos C, Garmpis N, Manousi M, et al. Cystic hygroma of the neck: single center experience and literature review. *Eur Rev Med Pharmacol Sci*. 2017;21(21):4918–4923.

Laje,P, Tharakan SJ, Hedrick HL. Immediate operative management of the fetus with airway anomalies resulting from congenital malformations. *Semin Fetal Neonatal Med*. 2016;21(4):240–245.

Noia G, Maltese PE, Zampino G, et al. Cystic hygroma: a preliminary genetic study and a short review from the literature. *Lymphat Res Biol*. 2019;17(1):30–39.

Vijayasekaran S, Lioy J, Maschhoff K. Airway disorders of the fetus and neonate: an overview. *Semin Fetal Neonatal Med*. 2016;21:220–229.

A.7. What is the IAA anomaly?

An IAA anomaly is extremely rare and represents approximately 1% of CHD. In IAA, there is complete aorta atresia somewhere along its arch, which is usually associated with a VSD and other complex cardiovascular anomalies. This defect is categorized into three types depending on where the atresia occurs. Left untreated, it is uniformly lethal within 1 week of life, as a result of closure of the ductus arteriosus. In type A (30%), the aorta is interrupted between the left subclavian artery and the aortic isthmus. In type B (the most common, 65% to 70%), the interruption lies between the left common carotid and the left subclavian arteries. With type C (least common type, <1%), the arch is interrupted between the innominate and the left common carotid arteries. One in three patients with IAA has the 22q11.2 deletion, which is usually associated with a more proximal location of the arch interruption (type C or B).

Friedman, K. Preoperative physiology, imaging, and management of interrupted aortic arch. *Semin Cardiothorac Vasc Anesth*. 2018;22(3):265–269.

Jonas RA. Management of interrupted aortic arch. *Semin Thorac Cardiovasc Surg*. 2015;27:177–188.

Zucker EJ. Syndromes with aortic involvement: pictorial review. *Cardiovasc Diagn Ther*. 2018;8(suppl 1):S71–S81.

A.8. What is the pathophysiology of the IAA syndrome?

IAA is a neonatal medical emergency. It warrants immediate infusion of prostaglandin E_1 (PGE_1) to maintain ductal patency

as well as stabilization of coexisting HF. Due to the discontinuity between the descending aorta and the arch, blood flow to the descending aorta and its tributaries cannot occur unless the ductus arteriosus stays open. After medical stabilization, surgical correction should occur as soon as possible because of the risk of mortality in untreated IAA. The cause of death is usually a combination of greatly increased left-to-right shunt with increased pulmonary blood flow (which results in biventricular failure and pulmonary edema), ductal stenosis, the sequelae of renal failure, and metabolic acidosis. Pulse oximetry will reveal normal saturation in the right arm, with a decreased saturation in the lower extremities. If there is inadequate perfusion to the lower body because of ductal closure, death quickly ensues from the combination of increased left-to-right shunt with increased pulmonary blood flow via the VSD, biventricular congestive heart failure (CHF), pulmonary edema, renal insufficiency, severe metabolic acidosis, and shock. Symptoms of ductal closure include tachypnea, lethargy, and poor feeding. A transthoracic echocardiography is diagnostic. Cardiac CT, MRI, and catheterization are also utilized in the diagnosis of IAA.

Friedman, K. Preoperative physiology, imaging, and management of interrupted aortic arch. *Semin Cardiothorac Vasc Anesth*. 2018;22(3):265–269.

Jonas RA. Management of interrupted aortic arch. *Semin Thorac Cardiovasc Surg*. 2015;27:177–188.

Kliegman RM, St. Geme JW, Blum NJ, et al, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:2384–2393.

A.9. How is ductal patency maintained?

The ductus arteriosus is kept open by the infusion of PGE_1. Both PGE_1 and prostaglandin E_2 are produced endogenously in the ductus and are metabolized in the lungs. Among the endogenous

prostaglandins, prostaglandin E_2 is the most important. Postnatally, the levels fall dramatically secondary to increased metabolism resulting from the increase in pulmonary blood flow. A prostaglandin infusion will delay the natural closure of the ductus and improve systemic arterial perfusion and oxygenation. Less acidosis will also be seen in arterial blood gases compared to those obtained prior to PGE_1 infusion administration. In the case of an IAA, circulation to the lower body is completely dependent on the patency of the ductus; therefore, PGE_1 must be continuously infused to keep the infant alive. Of note, the PGE_1 infusion has a relatively long half-life; its inadvertent discontinuation will not acutely cause ductal closure, but it should be maintained until surgical repair is complete.

Burbano-Vera N, Zaleski KL, Latham GJ, et al. Perioperative and anesthetic considerations of interrupted aortic arch. *Semin Cardiothorac Vasc Anesth*. 2018;22(3):270–277.

Kliegman RM, St. Geme JW, Blum NJ, et al, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:2384–2393.

A.10. What are the side effects of prostaglandin infusion?

Prostaglandin has a wide array of side effects including fever, seizure-like activity, hypotension, flushing, and edema. Platelet aggregation may also be reduced, and apnea with associated bradycardia can occur. This is most often seen in neonates weighing less than 2 kg at birth and usually appears during the first hour of initiating the drug infusion. Therefore, respiratory status should be monitored throughout treatment with mechanical ventilation as a consideration. It is recommended that a prostaglandin infusion be continuously administrated via a separate intravenous line that can be monitored for any disruptions in flow.

Kliegman RM, St. Geme JW, Blum NJ, et al, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:2407–2420.

A.11. What is the hyperoxia test?

This test is performed to distinguish pulmonary causes from cardiac causes of cyanosis. To perform the test, the patient is first placed on 100% oxygen for 10 minutes. A preductal arterial blood gas is then taken from the patient's right arm. In patients with pulmonary disease, this supplemental oxygen significantly augments systemic oxygenation, which is not the case in cyanotic congenital heart defects. However, in some pulmonary conditions, the oxygen tension may not rise significantly. In these patients, a chest radiograph is invaluable for affirming pulmonary pathology. In some congenital heart lesions with mixing (i.e., truncus arteriosus), the supplemental oxygen decreases the pulmonary vascular resistance, which results in an increase in oxygen tension but is rarely greater than 150 mmHg.

Keane JF, Lock JE, Fyler DC, eds. *Nadas' Pediatric Cardiology*. 2nd ed. Philadelphia, PA: Saunders Elsevier; 2006:141–142.

B. Preoperative Evaluation and Preparation

B.1. What preoperative studies should be obtained to evaluate the neck mass?

Because cervical masses have a variable nature and the potential for airway compression, studies need to be done preoperatively. A flexible neonatal bronchoscopy can define any extrinsic compressive deformations of the airway. Ultrasound and MRI of the head and neck can define the nature of the cystic hygroma and elucidate the degree of airway compression. These cysts are known to invade the anterior mediastinum and can cause extrinsic distortion of the lower airway anywhere from the cricoid ring to the carina. Under sonographic guidance, cystic

fluid can be aspirated to reduce the size of the mass and potentially relieve compressive symptoms. Rarely, there may be invasion into the pericardium and displacement of the lung. If the mass is suprahyoid, radiologic studies will reveal the degree of laryngeal compression and retropharyngeal involvement, which are vital to know prior to intubation.

Tranvinh E, Yeom KW, Iv M. Imaging neck masses in the neonate and young infant. *Semin Ultrasound CT MR*. 2015;36:120–137.

Vijayasekaran S, Lioy J, Maschhoff K. Airway disorders of the fetus and neonate: an overview. *Semin Fetal Neonatal Med*. 2016;21:220–229.

B.2. How would you categorize the difficult airway in children?

Children with difficult airways can be grouped into four main groups. The first group includes children who have congenital anomalies affecting the airway such as vascular rings, laryngomalacia, micrognathia, or neurofibromatosis. The second group includes patients with an acutely acquired obstruction of the airway such as trauma or foreign body. The third group includes infectious etiologies such as retropharyngeal abscess, laryngotracheobronchitis, or peritonsillar abscess. The last group is composed of children without known congenital or anatomic abnormalities that have unanticipated difficulty with intubation secondary to glottic visualization problems on direct laryngoscopy.

Belanger J, Kossick M. Methods of identifying and managing the difficult airway in the pediatric population. *AANA J*. 2015;83(1):35–41.

Vijayasekaran S, Lioy J, Maschhoff K. Airway disorders of the fetus and neonate: an overview. *Semin Fetal Neonatal Med*. 2016;21:220–229.

B.3. What features of the difficult airway can be noted on physical examination?

Many anatomic abnormalities can be noted simply by

performing a thorough airway exam. Visual inspection of the size of the patient's mouth can alert the anesthesiologist to a constricted oral opening that may be seen in conditions, such as scleroderma, epidermolysis bullosa, or congenital microstomia, which could prevent insertion of the laryngoscope. Micrognathia or maxillary protrusion often accompanies an anterior larynx, making glottic visualization during direct laryngoscopy impossible. This is seen in children with craniofacial syndromes, such as Pierre Robin sequence, Treacher Collins syndrome, Apert syndrome, or Crouzon syndrome. Macroglossia as a consequence of certain metabolic storage diseases (i.e., Hurler syndrome, Hunter syndrome), cystic abnormalities, and/or hamartomatous tumors of the tongue (Goltz syndrome) can also make effective laryngoscopy impossible. Assessing the temporomandibular joint can reveal signs of ankylosis, which can occur in patients with juvenile rheumatoid arthritis and other autoimmune processes that may prevent adequate mouth opening. A narrow, high-arched palate may also suggest a difficult intubation. One should evaluate range of motion of the neck to reveal any decreased neck extension, which may accompany some neuromuscular disorders, arthritic conditions, trauma, Klippel-Feil syndrome, or Goldenhar syndrome. Lastly, one should attempt to palpate the patient's neck to access for tracheal deviation. A preoperative chest radiograph may better serve to note tracheal deviation as well as provide a baseline for the state of the lungs.

Belanger J, Kossick M. Methods of identifying and managing the difficult airway in the pediatric population. *AANA J*. 2015;83(1):35–41.

Shadfar S, Drake AF, Vaughn BV, et al. Pediatric airway abnormalities: evaluation and management. *Oral Maxillofac Surg Clin North Am*. 2012;24(3):325–336.

Wetmore RF, Muntz HR, McGill TJ. *Pediatric Otolaryngology: Principles and Practical Pathways*. 2nd ed. New York: Thieme Medical; 2012:501–512.

B.4. How would you preoperatively optimize the ability to secure the airway in the operating room?

Because there are inherent risks in inducing anesthesia and securing the airway in this neonate, one would prepare for a fiberoptic-guided intubation. The infant bronchoscope is so small in diameter that it does not allow the presence of a suction port, which can impair visualization if there are excessive secretions. An antisialagogue should be given at least 15 to 20 minutes before beginning the fiberoptic intubation to facilitate recognition of the anatomy. Glycopyrrolate (0.01 mg per kg intravenous and/or intramuscular [IM]) will limit secretions without causing the excessive tachycardia that may occur with atropine. In this neonate with cardiac compromise, any unnecessary stress on the heart should be avoided. In addition to the fiberoptic bronchoscope being available, an appropriate laryngeal mask airway (LMA) and equipment trays for an emergency cricothyrotomy should also be ready. Having a pediatric otolaryngologist present for the induction of anesthesia as well as a rigid infant bronchoscope with video imaging capability should also be strongly considered. The rigid bronchoscope cannot only facilitate visualization of the laryngeal inlet, but it can also provide a route to temporarily ventilate the patient and hold the endotracheal tube as an introducing stylet to facilitate intubation.

Apfelbaum JL, Hagberg CA, Caplan RA, et al. Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on Management of Difficult Airway. *Anesthesiology*. 2013;118(2):251–270.

Enterlein G, Byhahn C. Practice guidelines for management of difficult airway: update by the American Society of Anesthesiologists Task Force [in German]. *Anaesthesist*. 2013;62(10):832–835.

B.5. What laboratory studies are necessary before surgery?

Serum calcium should be measured because of the strong association of 22q11 deletion syndrome with hypocalcemia. Serum glucose and sodium levels should be reviewed, as the infant will have been started on total parenteral nutrition due to the inability of oral feeding due to dysphagia caused by the cystic hygroma. Because there is also the potential for severe metabolic acidosis secondary to inadequate perfusion of the lower body as a result of the IAA, serum pH and bicarbonate concentrations must be obtained. The $Paco_2$ level will indicate the baseline adequacy of ventilation in the face of a potentially obstructing mass, and the Pao_2 level will serve as a guide in assessing the neonate's degree of CHF, pulmonary insufficiency, and central shunting. Because the surgery can be extensive, with a significant loss of blood, a baseline complete blood count with hematocrit should be obtained. In addition, the prothrombin time and partial thromboplastin time should be obtained before surgery because of the possibility of baseline immaturity in coagulation factor production and the inherent bleeding potential from the large dissection that will be done.

B.6. What are the causes of heart failure (HF) in the infant? How would you assess this infant in your preoperative evaluation for signs of HF?

The causes of HF can be divided into five major areas:

- Cardiac rhythm disturbances (heart block and supraventricular tachycardia)
- Volume overload (anemia, sepsis, and VSD)
- Systolic ventricular dysfunction (myocarditis, malnutrition, and dilated cardiomyopathy)
- Pressure overload (aortic stenosis and coarctation)
- Diastolic ventricular dysfunction (pericardial tamponade and restrictive cardiomyopathy)

HF occurs either in response to an excessive volume or

pressure load or as a consequence of myocardial muscle impairment. Volume overload is due to factors causing a large increase in cardiac output (e.g., large VSD or ductus arteriosus). In these circumstances, there must be a sufficiently large left-to-right shunt to cause a severe strain on the heart. In the normal newborn, these lesions do not usually produce HF until 1 to 2 months of age because it takes longer than usual for the pulmonary vascular resistance to fall. The elevated pulmonary vascular resistance protects the left ventricle from the stress of overcirculation. This is not true in premature neonates who do not manifest the same degree of pulmonary arteriolar constriction; therefore, they are susceptible to large left-to-right shunts early and show HF more readily.

Regurgitant valvular lesions can also lead to HF. In complex CHD (i.e., truncus arteriosus or tricuspid atresia with transposition), the additional stress of hypoxemia or univentricular overload may herald the early onset of HF. Large arteriovenous malformations may also occur intracranially and cause HF. Excessive pressure loads are seen in obstruction to cardiac output from aortic stenosis, aortic coarctation, and aortic interruption.

In the immediate newborn period, right-sided HF is seen with greater frequency because of severe pulmonary hypertension. Pulmonary hypertension has many causes including intrinsic lung parenchymal insufficiency or pathology (i.e., diaphragmatic hernia, meconium aspiration, or hyaline membrane disease), chronic hypoxemia, hypervolemia, and polycythemia.

Primary myocardial failure is unusual and rare in the newborn. If it occurs, it is likely due to endocardial fibroelastosis and anomalous coronary circulation. Nonetheless, the myocardium in the infant is susceptible to depression from metabolic derangements such as hypoglycemia, hypocalcemia,

hypoxemia, and hypercarbia. Also, severe anemia with the associated decreases in systemic and myocardial oxygen supply forces an increase in myocardial work that can lead to HF.

Infants are different from adults in their manifestations of HF. Signs of cardiac dilation may be absent because of decreased systemic venous return from the elevated intrathoracic pressure as a consequence of coexisting lung disease in premature infants. Although immature, the carotid baroreceptors still initiate an increase in sympathetic outflow in response to reduced perfusion. The increased α-adrenergic stimulation impairs blood flow to the systemic arteriolar beds, resulting in cold, underperfused extremities, and diminished splanchnic perfusion. Fatigue, loss of appetite, and failure to thrive quickly follow. Tachycardia from β-adrenergic receptor stimulation occurs. Generalized sweating results from sympathetic cholinergic fiber stimulation. Extracellular water increases because of decreased renal excretion of sodium due to a decreased glomerular filtration rate; however, peripheral pitting edema is much less common in infants compared to older children and adults. The venous system in infants is extremely distensible, so much so that elevated right atrial pressures may not show jugular venous engorgement. The most prominent manifestation of HF in the infant is tachypnea. Because pulmonary venous pressure is elevated from left ventricular failure, the lung compliance decreases because of the augmented interstitial fluid. Breathing becomes rapid and shallow further increasing the body's oxygen requirement, which leads to a cyclic dependency to maintain both tachycardia and tachypnea. It is common to see subcostal retractions due to the increase in respiratory effort in infants with HF.

Infants have a greater lymphatic drainage capacity compared to adults and can clear interstitial accumulations more readily. Therefore, rales are less often appreciated in infants with HF, as

opposed to adults with HF. The bronchial mucosa may become swollen because of engorgement of the bronchial venous system resulting in narrowing of the airway lumen. This can produce an audible wheeze that is often seen in infantile HF. Lastly, hepatomegaly is a cardinal sign of right ventricular failure in infants.

Das BB. Current state of pediatric heart failure. *Children (Basel)*. 2018;5(7):88. doi:10.3390/children5070088.

Hinton RB, Ware SM. Heart failure in pediatric patients with congenital heart disease. *Circ Res*. 2017;120:978–994.

Kliegman RM, St. Geme JW, Blum NJ, et al, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:2476–2483.

B.7. How would you optimize the preoperative treatment of HF?

The typical manifestations of CHF in infants (i.e., tachycardia, tachypnea, subcostal retractions, and rhonchi) are also cardinal signs of pulmonary infection in this age group. They can be difficult to distinguish. Often, they coexist and treatment must address both conditions. In this patient, the structural abnormality of the IAA needs surgical correction; however, correction must be deferred until the neck mass is resected. In this infant, the CHF is caused by pressure overload from the IAA, and the hypocalcemia is due to parathyroid hormone insufficiency. Calcium must be normalized by intravenous infusion. If glucose is low, as would be expected in an infant who is unable to feed by mouth, has glycogen depletion from the stress of illness, has an immature liver that is unable to generate sufficient gluconeogenesis, and has an increased utilization from a baseline higher metabolic rate (compared to adults), a glucose source should be continuously supplemented by slow intravenous administration. Myocardial work is compromised by the presence of metabolic acidosis, which occurs as a

consequence of the increased lactic acid production during anaerobic metabolism resulting from lower body hypoperfusion. The pH should be normalized with sodium bicarbonate.

With the guidance of a pediatric cardiologist, myocardial function should be optimized with ace inhibitors, β-blockers, and digoxin in infants with HF. A catecholamine (e.g., dopamine or dobutamine) can be infused to boost contractility. Pulmonary symptoms should be treated with antibiotics and positive pressure ventilation (i.e., high-flow nasal cannula, nasal continuous positive airway pressure [CPAP]) with oxygen titrated to arterial blood gas measurements. Intubation and mechanical ventilation may be necessary in many infants with HF. Diuresis, with furosemide in conjunction with fluid restriction, will promote restoration of pulmonary compliance by decreasing lung water.

Das BB. Current state of pediatric heart failure. *Children (Basel)*. 2018;5(7):88. doi:10.3390/children5070088.

McMillan JA, Feigin RD, DeAngelis C, et al, eds. *Oski's Pediatrics: Principles & Practice*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:357.

B.8. How would you premedicate this infant?

Infants younger than 2 years do not routinely require preoperative anxiolytics or narcotics. An infant with a compromised airway and abnormal circulation cannot tolerate any degree of respiratory depression; therefore, no sedative premedication should be given at all. Because a fiberoptic intubation is planned, glycopyrrolate should be given preoperatively for its antisialagogue activity.

B.9. When is premedication useful in infants and children?

Patients with dynamically responsive cyanotic CHD (i.e., tetralogy of Fallot) benefit from premedication before coming to

the operating room. In these children, the inherent anxiety of transfer to unfamiliar surroundings, change in temperature, and parental separation may trigger infundibular spasm and reduce pulmonary blood flow, thereby leading to a "tet spell." This transient increase in pulmonary vascular resistance dramatically decreases pulmonary blood flow and increases the flow of desaturated blood to the body via VSD. Acute hypoxemia is not an optimal state in which to initiate an anesthetic induction. Therefore, sedation with oral midazolam or nasal dexmedetomidine is useful to allay preoperative anxiety and reduce the risk of provoking a hypoxemic spell. Premedication can make the perioperative experience for a child less frightening, produce variable degrees of amnesia, and decrease the risk of emergence delirium. Pharmacologic premedication is one of many tools a pediatric anesthesiologist has at his or her disposal to ensure a positive perioperative experience for the patients and their family. Studies have shown promising results with nonpharmacologic interventions including handheld video games or low sensory stimulation.

Bailliard F, Anderson RH. Tetralogy of Fallot. *Orphanet J Rare Dis*. 2009;4:2.

Manyande A, Cyna AM, Yip P, et al. Non-pharmacological interventions for assisting the induction of anaesthesia in children. *Cochrane Database Syst Rev*. 2015;(7):CD006447.

Jun JH, Kim KN, Kim JY, et al. The effects of intranasal dexmedetomidine premedication in children: a systematic review and meta-analysis. *Can J Anaesth*. 2017;64:947–961.

B.10. Before the planned surgery, the infant is scheduled for a magnetic resonance imaging (MRI) scan. You are asked to ensure that the baby remains immobile for 20 minutes to perform the scan adequately. How would you accomplish this?

Because this neonate has an already severely compromised

airway while awake, the safest anesthetic plan to assure immobility and adequate ventilation is to perform a general anesthetic via an endotracheal tube. Any form of sedation without an endotracheal tube already in place puts this patient at risk for complete airway obstruction and should not be used here. If the neonate has demonstrated a postprandial sleep cycle and can take oral fluids, it may be well worth an attempt to perform the MRI scan while the neonate is swaddled in a warm baby blanket sucking on a pacifier filled with dextrose solution ("Sweetie Soother pacifier"). In this manner, the patient remains "motionless" from the inherent feeling of comfort of being able to feed and bundled in a warm blanket.

Salerno S, Granata C, Trapenese M, et al. Is MRI imaging in pediatric age totally safe? A critical reprisal. *Radiol Med*. 2018;123:695–702.

C. Intraoperative Management

C.1. What anesthesia equipment, circuit, and monitors would you use?

This patient is especially susceptible to infection because of the baseline depressed cellular immunity. As with every patient, strict attention must be paid to maintaining a sterile technique during the central line placement and instrumentation of the patient. The anesthesiologist must wear a sterile gown and gloves to protect the neonate. Sterility of the disposable circle system, mask, endotracheal tube, fiberoptic bronchoscope, and laryngoscope should be ensured. Routine monitors for all surgery on infants include pulse oximetry, electrocardiogram, blood pressure, capnograph, spirometer, and temperature probe. Multiple pulse oximeters should be available to offer flexibility in the event of monitor dysfunction. In this neonate, the IAA prevents the ability to obtain saturation data from the lower body

and left arm. End-tidal expired gas concentrations should be recorded for anesthetic gases, nitrogen, and oxygen. Accurate capnography in small infants may be hampered by sidearm gas sampling resulting from the relatively high gas flows relative to the expired gas flow from the infant.

In this procedure, an arterial line should be inserted in the right upper extremity because the IAA will not allow for blood pressure determination on the left side. Because there is potential for significant blood loss, a central line should be placed under ultrasound guidance at the best available site (i.e., internal jugular, subclavian, or femoral). Obtaining central access in such a small patient with distorted anatomy may prove very difficult. If an internal jugular or subclavian central line is placed, a chest radiograph should be obtained after placement and reviewed for correct positioning and to rule out pneumothorax before proceeding with this complicated case. Catheter length must be taken into consideration during placement to avoid inadvertently inserting the central line inside the right atrium or across the tricuspid valve, leading to arrhythmias and misleading right ventricular pressures. The arterial line and central venous pressure (CVP) transducers should be placed at the approximate level of the right atrium and adjusted accordingly as the table height is changed. Cerebral and somatic oximetries are useful in providing early recognition of intraoperative hypoperfusion to the brain and body.

Burbano-Vera N, Zaleski KL, Latham GJ, et al. Perioperative and anesthetic considerations of interrupted aortic arch. *Semin Cardiothorac Vasc Anesth*. 2018;22(3):270–277.

Kussman BD, Wypij D, DiNardo JA, et al. Cerebral oximetry during infant cardiac surgery: evaluation and relationship to early postoperative outcome. *Anesth Analg*. 2009;108(4):1122–1131.

C.2. Describe techniques other than direct laryngoscopy that would be useful for securing the airway in this

baby.

It is highly unlikely that glottic visualization could be accomplished in this neonate with direct laryngoscopy alone. The following alternative forms of securing the airway can be used when direct laryngoscopy is not expected to provide easy visualization of the glottis.

Infant Video Laryngoscope

The various forms of this device on the market allow for excellent glottic visualization and facilitation of intubation if the patient's mouth opening is large enough to accommodate the blade and may provide a superior visualization compared to conventional direct laryngoscopy in some patients.

Intubation through a Laryngeal Mask Airway

First, securing the airway with an LMA and demonstrating that one can ventilate through it can add an extra margin of safety when performing an anticipated difficult pediatric intubation. The LMA is then used as a conduit for insertion of the fiberoptic-guided endotracheal tube into the glottis.

Retrograde Cricothyroid Wire

This technique is not ideal for this patient for many reasons. First, the size of the patient would make it technically difficult. Second, the large cystic hygroma is distorting the external anatomy landmarks that facilitate this type of intubation; nonetheless, for completeness, this method will be described. The retrograde cricothyroid wire technique is best for oral intubations. A guidewire is inserted through a large-gauge needle that is used to puncture the cricothyroid membrane. The guidewire is threaded cephalad until it visualized and retrieved through the mouth. Then, the guidewire is tied to "Murphy eye" of the endotracheal tube. Then, the other end of the guidewire (that is sticking out through the cricothyroid membrane) is

slowly pulled caudally to guide the endotracheal through the vocal cords. Even after the endotracheal tube is in correct position, the guidewire remains attached externally to the neck in case of unplanned extubation (to facilitate reintubation).

Blind Nasal Intubation

Although very successful in adult patients, the blind nasal intubation technique can be very challenging in infants or small children. Certainly, performing an awake, sedated intubation in this manner mandates giving adequate topical anesthesia to a less than cooperative infant. In addition, the smaller endotracheal tubes used in pediatrics are far more compliant than adult-sized tubes, especially when warmed with nasopharyngeal respiratory gases, which makes it difficult to maintain the anterior curve on the tube to enter the larynx.

Nasal Intubation with Laryngoscope and Magill Forceps

If the larynx cannot be visualized by direct laryngoscopy, an anesthetized, spontaneously breathing nasal intubation with laryngoscopic assistance can be carried out in some patients. In this case, great care is taken to ensure that the patient continues to maintain spontaneous and adequate ventilatory exchange during the inhalational induction. Sevoflurane is used for pediatric inhalational inductions because it is less pungent and more easily tolerated than other agents. The pediatric anesthesiologist should be mindful that total airway obstruction can happen at any point during the inhalation induction due to relaxation of pharyngeal tone and other airway abnormalities. If spontaneous breathing can be maintained, the intubation should be attempted after a surgical plane of anesthesia is achieved. The laryngoscope is then used to visualize the epiglottis. Using Magill forceps, the tip of the endotracheal tube is aligned with the subepiglottic region and slowly advanced. Capnographic

monitoring during this maneuver can help verify the direction of the endotracheal tube tip.

Fiberoptic Intubation

Fiberoptic intubation is most successful when it is carried out as the initial maneuver before the airway is traumatized from previous attempts at intubation. It may be nearly impossible to use after several unsuccessful attempts because the upper airway becomes hypersecretory and may ooze blood. The appropriate fiberoptic technology may not be widely available unless one is practicing at a tertiary pediatric hospital with a wide range of bronchoscopes on hand (including the smallest, "ultrathin" 2.2 mm in diameter scope necessary for this neonate). Due to their small size, pediatric bronchoscopes lack a suction port and need to be lubricated to facilitate the sliding of the endotracheal tube off the scope once it is through the glottis.

In older patients, three specialized fiberoptic methods can be useful in intubating pediatric patients with difficult airways. First, the clinician can pass a guidewire through the suction port of the larger instrument to serve as a stylet for the endotracheal tube. Second, the scope can be used to visualize and guide a nasal endotracheal tube inserted into the opposite nostril. Finally, a 4.5-mm tube can be placed at the laryngeal orifice to be used as a stent for inserting a small guidewire, which can in turn be used to place a smaller endotracheal tube.

Transtracheal jet ventilation can be used when applicable. In this technique, a 16-gauge intravenous catheter is placed through the cricothyroid membrane and jet ventilation with 100% oxygen is provided. A second intravenous catheter is placed through the cricothyroid membrane and a guidewire (0.021-in. diameter J-tip) is introduced with cephalad angulation. Jet ventilation continues as the guidewire is threaded through the nose and connected to the working part of a fiberoptic scope.

The scope is then advanced through the laryngeal inlet, and a tube is threaded over the scope and then the guidewire is removed. Sedation can be provided with a remifentanil drip (0.1 to 0.2 μg/kg/min). Because patient safety is the foremost consideration in any technique for inserting an artificial airway, the anesthesiologist and/or otolaryngologist should be immediately available to perform an emergent cricothyrotomy in case of a life-threatening loss of airway.

Of note, in the pediatric patient with a known difficult airway, a preemptive collaborative approach of securing the airway with a pediatric otolaryngologist can greatly increase the degree of safety and minimize harm done to the patient. When performing an emergency cricothyrotomy, a longitudinal incision is made in the skin and fascia above the cricothyroid membrane, after which the cricothyroid membrane is punctured and entered with a small endotracheal tube. Another technique utilizes an 18-gauge angiocatheter (or larger), which is inserted into the cricothyroid membrane. Intratracheal location is verified by the loss of resistance with an attached syringe and the aspiration of air. The catheter is attached to a 3-mL syringe (without plunger), which is then connected to the Y-piece of the anesthesia circuit by an adapter from a 3.0-mm internal diameter endotracheal tube.

Jagannathan, N. Difficult airway management in pediatrics: approaches for success. *ASA Annual Meeting Refresher Course Lectures*. Boston, MA: American Society of Anesthesiologists; 2017:323.

Tsao M, Vargas AA, Hajduk J, et al. Pediatric airway management devices: an update on recent advances and future directions. *Expert Rev Med Devices*. 2018;15(12):911–927.

C.3. How would you monitor blood loss in this patient?

In many of these procedures, the blood loss can be significant and easily exceed the patient's calculated blood volume. It is difficult to accurately measure blood loss when it is lost under

the drapes or irrigated away. Meticulous weighing of the sponges and observation of suction canisters are important, but blood loss can be continuous from the time of skin incision and may be seemingly relentless for an inexperienced clinician. Absolute changes in the CVP are a relative guide to the volume in the central compartment, but no one isolated value correlates with a known blood volume. A steady decrease in CVP in association with a downward trend in mean arterial pressures (MAPs) during periods of surgical intervention known to produce significant bleeding should be treated aggressively with crystalloid (20 mL per kg) or colloid (i.e., 5% albumin) replacement first, followed by a vasopressor supplementation as necessary. Ideally, with an arterial line in place and point of care testing, one can trend the hemoglobin and/or hematocrit prior to the initiation of a blood transfusion. Persistent hypotension with a normal hematocrit could be due to hypocalcemia either from parathyroid hormone insufficiency and/or from the citrate (used as an anticoagulant in the blood products), which binds ionized calcium if the patient was recently transfused.

C.4. What anesthetic technique should be used in a patient who may experience severe loss of blood intraoperatively?

Blood loss should be replaced milliliter for milliliter to prevent falling behind in volume. It is wise to choose an anesthetic technique that produces a relatively stable blood pressure throughout the surgery so that any new downward trend in blood pressure can be easily attributable to blood loss and not to pharmacologic action. For instance, if a steady level of desflurane or sevoflurane is given at 1.25 minimal alveolar concentration (MAC) with a resultant MAP 15% lower than awake, further dips in MAP during surgical intervention can be taken as intravascular volume depletion secondary to bleeding

and replaced accordingly. This interpretation would be obscured if there were frequent anesthetic interventions associated with MAP changes, such as intermittent narcotization, relaxant titration, or up and down titration of hypotension-inducing agents. An important clue to the blood volume loss of the patient is the blood pressure at an MAC of anesthesia. If a stable pressure is established at a given MAC of inhalational agent, a lower than expected blood pressure at this MAC is almost always indicative of hypovolemia and therefore calls for fluid or blood replacement. Another anesthetic technique for this procedure on a neonate is to use a high-dose narcotic technique with paralysis, which will lessen the impact of inhalational agents on the MAP. Serial hematocrit determinations drawn throughout the case should guide management. It is most unusual in an otherwise healthy infant to produce hypotension with intravascular overload unless there are other attendant problems.

C.5. How would you induce and maintain anesthesia in this neonate?

After securing the airway and verifying bilateral breath sounds, narcotic titration with fentanyl should be given in repeated doses. Remember, this neonate may be sensitive to any anesthetic agent because of his cardiovascular anomalies; therefore, titrating fentanyl to the patient's arterial blood pressure via the arterial line decreases the chance of inadvertent drops in perfusion. Because the neonate is not going to be extubated, fentanyl can be dosed safely at 50 μg per kg or higher to allow for dense analgesia. Neuromuscular blocking agents such as vecuronium and cisatracurium can be given and redosed at regular intervals to facilitate the surgical dissection. If tolerated, small concentrations of approximately 0.5% to 4% desflurane or sevoflurane 0.25% to 1.5% can be administered to

synergize with the narcotic. The prostaglandin infusion should be maintained throughout the entire surgery.

C.6. Intraoperatively, the surgeon must dissect the tumor in the anterior mediastinum and needs to have a quiet surgical field. How would you accomplish this in the infant?

Double-lumen tubes are not used in the neonatal age group because of the exceedingly small lumen and the technical difficulties of securing both lungs. Instead, a single-lumen endotracheal tube can be advanced into the right or left mainstem bronchus to allow for one-lung ventilation. This may be fraught with consequences in this infant with IAA, but it can still be attempted. Keep in mind that hypoxic pulmonary vasoconstriction may not occur readily in the neonate and excessive shunting may happen. In addition, having an infant on one-lung ventilation may lead to an elevated $PaCO_2$ from the pulmonary insufficiency. During thoracotomies in infants for pulmonary banding or Blalock-Taussig shunts, it is not uncommon to see extremely elevated $PaCO_2$ values from lung retraction, especially of the right side, which has almost 60% of the total lung surface area.

Cerchia E, Ferrero L, Molinaro F, et al. Pediatric thoracoscopy and bronchia blockers: the continued search for the ideal one-lung ventilation. *J Laparoendosc Adv Surg Tech A*. 2016;26(2):153–156.

Engum SA. Minimal access thoracic surgery in the pediatric population. *Semin Pediatr Surg*. 2007;16:14–26.

D. Postoperative Management

D.1. How would you manage this patient postoperatively?

Multiple factors about this case mandate that the neonate remain intubated or have a tracheostomy placed at the end of the case.

This surgery involves an extensive dissection of the patient's neck and upper thorax that will result in a tremendous amount of upper airway and neck edema. Consequently, this would make extubation life-threatening. High-dose narcotics and paralytics have been used, which also hamper safe extubation. The neonate should continue to remain well-narcotized and paralyzed to coordinate effective mechanical ventilation. Artificial ventilation and oxygen supplementation should be titrated to serial arterial blood gases. In addition, the prostaglandin drip must be continued to ensure ductal patency. Generous narcotic supplementation will ensure that the pulmonary vascular resistance stays in a state of relative quiescence. Approximately 24 hours postoperatively, a leak test can be performed to assess residual vocal cord edema. Fiberoptic visualization of the laryngeal inlet can provide useful information about the state of the laryngeal inlet for extubation.

Anatomic airway factors aside, the IAA and associated HF will make extubation of this baby more challenging. Assuming all other factors are under control, the following ventilatory parameters should be met before extubation: normal arterial blood gases with satisfactory oxygenation on 28% oxygen, spontaneous tidal volume greater than 5 mL per kg, and an inspiratory force greater than 12 cm H_2O. One needs to be vigilant for early signs of airway obstruction and be ready to reintubate or perform an emergent tracheostomy if prompt desaturation occurs.

44 Patent Ductus Arteriosus and Prematurity

Albert C. Yeung and Fun-Sun F. Yao

A 2-week-old male infant weighing 900 g is scheduled for ligation of patent ductus arteriosus (PDA). He was born at 27 weeks' gestation as part of a triplet pregnancy complicated by preterm labor. Immediately after delivery, he was intubated because of respiratory distress. He was given indomethacin prophylactically because of his prematurity and presumed PDA. A transthoracic echocardiogram (TTE) confirmed the patency of the ductus arteriosus and demonstrated its closure after one course of indomethacin. His respiratory function was gradually improving with ventilatory support until 2 weeks later when his oxygenation and ventilation suddenly worsened. A murmur was heard over his chest. A repeat TTE demonstrated left-to-right shunting through the ductus arteriosus. Another course of indomethacin was administered, but the ductus remained patent. His blood pressure was 50/20 mmHg and heart rate was 165 beats per minute. The laboratory data were as follows: white blood cell (WBC) count, 17,000 per μL; hemoglobin, 11 g per dL; hematocrit, 34%; urine specific gravity, 1.005; protein, 1+; sugar, 1+; serum calcium, 6.0 mg per dL; blood glucose, 60 mg per dL; arterial blood gases: pH, 7.30; $Paco_2$, 60 mmHg; Pao_2, 49 mmHg on fraction of inspired

oxygen (FIO_2) 50%; inspiratory pressure, 19/6 cm H_2O; and ventilation rate, 40 breaths per minute.

A. Medical Disease and Differential Diagnosis

1. How would you classify prematurity? What are the common problems associated with prematurity?
2. What are the survival rates of preterm infants?
3. What are the incidence and survival rates of respiratory distress syndrome (RDS)? Discuss its pathophysiology.
4. What is bronchopulmonary dysplasia (BPD)? How would you treat it?
5. What are apnea spells? What are the possible causes of apneic spells?
6. Discuss the incidence and pathophysiology of PDA in preterm infants.
7. How would you make a diagnosis of PDA? Describe its treatment.
8. Would you give digitalis to treat congestive heart failure in preterm infants? Why?
9. How does indomethacin close the ductus? What are the adverse effects of indomethacin?
10. When is surgical closure indicated? What are the complications associated with surgical ligation?
11. What is retinopathy of prematurity (ROP) (retrolental fibroplasia [RLF])? Discuss its etiology, pathophysiology, prognosis, prevention, and treatment.
12. Define neutral and critical temperatures. What are these values in the preterm neonate, in the term neonate, and in the adult? Discuss temperature regulation in the neonate.

B. Preoperative Evaluation and Preparation

1. How would you evaluate this patient preoperatively?

2. What are the normal values of arterial blood gases and pH in neonates and infants?
3. Interpret the arterial blood gases: pH, 7.30; $Paco_2$, 60 mmHg; Pao_2, 49 mmHg; HCO_3^-, 20 mEq per L on 50% oxygen; and 6 cm H_2O of positive end-expiratory pressure (PEEP). How would you improve them?
4. What are the normal values of arterial blood pressure, heart rate, and respiratory rate for preterm infants?
5. What are the normal values of WBC, red blood cells (RBCs), hemoglobin, glucose, electrolytes, calcium, blood urea nitrogen, and creatinine for preterm infants?
6. Would you transfuse blood to this patient preoperatively?
7. How would you interpret the urinalysis: specific gravity, 1.005; sugar, 1+; and protein, 1+?
8. Would you correct a serum calcium level of 6.0 mg per dL? What other information would you like to have? Which contains more calcium, 10 mL of 10% calcium chloride or 10 mL of 10% calcium gluconate? Could you hyperventilate this child safely?
9. How would you premedicate this patient?

C. Intraoperative Management

1. Where should the procedure take place? In the neonatal intensive care unit (NICU) or the operating room?
2. What monitors would you use for this child during surgery?
3. How does the oxygen analyzer work?
4. What is the Doppler effect? How does the Doppler transducer measure blood pressure?
5. What is the mechanism of pulse oximetry? Why is it important to monitor arterial oxygen saturation? What levels of arterial oxygen saturation would you like to keep during surgery?
6. How would you maintain the patient's body temperature?
7. How do the anesthetic requirements of the preterm infant differ

from those of the adult?

8. What size endotracheal tube would you have used if the patient had not been intubated?
9. How would you have induced anesthesia if the patient had not been intubated?
10. How would you maintain anesthesia?
11. How would you ventilate the patient? What tidal volume, respiratory rates, and FIO_2 would you set for the infant?
12. Discuss blood and fluid therapy in this preterm infant.
13. During dissection of the ductus arteriosus, the arterial oxygen saturation dropped from 92% to 80% and the heart rate decreased from 140 beats per minute to 80 beats per minute. What were the causes? How would you correct this situation?

D. Postoperative Management

1. Would you reverse the muscle relaxants and extubate the patient at the end of surgery?
2. How can one minimize the risk of transporting the patient to the NICU after surgery?
3. The patient's condition deteriorated postoperatively in the intensive care unit (ICU). Physical examination revealed persistent cardiac murmur. What was the possible diagnosis?

A. Medical Disease and Differential Diagnosis

A.1. How would you classify prematurity? What are the common problems associated with prematurity?

Live born infants delivered before 37 weeks from the first day of the last menstrual period are termed premature by the World Health Organization. Preterm infants can be classified into three groups, as shown in **Table 44.1**. Infants of borderline prematurity usually require no special care, but, because of their susceptibility to RDS, they should be observed closely for 24 to

48 hours in the newborn nursery. Furthermore, those with a poor suck reflex may require gavage feedings. Infants classified as moderately premature require intense neonatal care, and neonatal mortality correlates inversely with gestational age. Neonates of extreme prematurity constitute only 1% of all preterm infants; however, mortality in this group is extremely high, accounting for greater than 70% of all neonatal deaths. Furthermore, morbidity in surviving infants is substantial, often secondary to irreversible neurologic or respiratory insult.

TABLE 44.1 Classification of Prematurity

	Borderline Prematurity	Moderate Prematurity	Extreme Prematurity
Gestational age (weeks)	36–37	31–35	24–30
Percentage live births	16%	6%–7%	<1%
Weight (g)	2,500–3,200	1,500–2,500	500–1,500
Associated problems	Poor suck RDS Temperature regulation	Poor suck RDS Temperature regulation Sepsis Intracranial hemorrhage	Poor suck RDS Temperature regulation Sepsis Intracranial hemorrhage Necrotizing enterocolitis Congestive heart failure Birth asphyxia
Level of care	Careful observation in newborn nursery	Neonatal ICU	Neonatal ICU

ICU, intensive care unit; RDS, respiratory distress syndrome.

Coté C, Lerman J, Anderson B, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier; 2019:841.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:475–476.

Kliegman RM, St. Geme JW III, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:897–909.

A.2. What are the survival rates of preterm infants?

The survival rates of preterm infants depend mainly on their

maturity or birth weights. Because of the advancement in neonatal care, survival rates have continued to improve for extremely premature infants. Over the past 20 years, survival has increased for infants born at 23 and 24 weeks' gestation and survival without major comorbidities increased for infants born at 25 to 28 weeks. In a recent study looking at trends in the mortality of extremely premature infants, survival rates of infants born at 22, 23, 24, 25, and 26 weeks' gestation are 7%, 32%, 62%, 77%, and 85%, respectively.

Kliegman RM, St. Geme JW III, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:897–909.

Stoll BJ, Hansen NI, Bell EF, et al. Trends in care practices, morbidity, and mortality of extremely preterm neonates, 1993-2012. *JAMA*. 2015;314(10):1039–1051.

A.3. What are the incidence and survival rates of respiratory distress syndrome (RDS)? Discuss its pathophysiology.

RDS, formerly called hyaline membrane disease, is common in preterm infants. RDS is a life-threatening condition associated with 50% to 75% of all deaths of premature infants. The incidence of RDS is inversely related to gestational age and birth weight. RDS occurs in 60% to 80% of infants born at <28 weeks gestational age and 15% to 30% of infants between 32 and 36 weeks. The risk increases with maternal diabetes, multiple gestation, cesarean delivery, and precipitous delivery.

Survival depends on the infant's size and gestational age. Eighty percent of those weighing less than 750 g, 85% of those weighing less than 1,000 g, and >95% of those weighing 1,500 to 2,500 g survive. Maternal corticosteroid administration and administration of exogenous surfactant into the lungs of neonates of less than 28 weeks' gestation at birth has been associated with in an increase in survival and a decrease in

severity of RDS.

Deficiency of the alveolar phospholipid surfactant is thought to be the cause of RDS. The surfactant is produced by the type II alveolar cells and is necessary for the maintenance of alveolar stability. Surfactant production is usually inadequate before 35 weeks of gestational age. In its absence, alveolar collapse and a decrease in functional residual capacity (FRC) occur, with consequent right-to-left shunting, arterial hypoxemia, and metabolic acidosis. Administration of betamethasone to women 48 hours before the delivery of fetuses less than 34 weeks' gestation significantly reduces the incidence, mortality, and morbidity of RDS.

Physical examination of the infant with RDS will likely reveal cyanosis, tachypnea, intercostal retractions, and bilateral rales that fail to clear with suctioning. An arterial blood gas sample will demonstrate hypoxemia, metabolic acidosis, and respiratory alkalosis; a chest radiograph will show diffuse, hazy ("ground glass") infiltrates. RDS causes a decrease in lung volume and lung compliance, which may pose a problem for the anesthesiologist if these patients require surgery. Ventilation with high positive pressures and large volumes increases the likelihood of pneumothorax and lung injury.

Andropoulos DB, Stayer S, Mossad EB, et al, eds. *Anesthesia for Congenital Heart Disease*. 3rd ed. Hoboken, NJ: Wiley; 2015:345–347.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:477–478.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier Saunders; 2018:640.

Kliegman RM, St. Geme JW III, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:931–936.

A.4. What is bronchopulmonary dysplasia (BPD)? How would you treat it?

BPD is a chronic lung disease of prematurity. BPD is defined as

oxygen dependence at 36 weeks' postconceptual age with oxygen requirements to maintain Pa_{O_2} >50 mmHg beyond 28 days of life in infants with birth weight less than 1,500 g. BPD is thought to be a result of mechanical ventilation, oxygen toxicity, infection, or a combination of these factors that cause a lung injury–induced increase in cytokine production. Lung injury in the premature infant disrupts pulmonary maturation that normally occurs around 36 weeks' gestation, resulting in larger but fewer alveoli, decreased surface area for pulmonary gas exchange, and abnormal muscularization of peripheral pulmonary vessels. Infants with BPD may have interstitial fibrosis, lobar emphysema, and components of reactive airway disease. BPD results in mismatch of ventilation and perfusion, resulting in hypoxemia and hypercarbia. With progressive disease, it may lead to pulmonary hypertension and right heart failure.

The treatment for BPD is supportive ventilatory and medical therapies. Ventilatory goals include avoidance of intubation and hyperoxia if possible and use of smaller tidal volumes with permissive hypercapnia to avoid barotrauma. Medical therapies include diuretics (furosemide 5 to 10 mg per kg every 6 hours) to decrease pulmonary edema, bronchodilators to reduce airway resistance, corticosteroids, and inotropes as needed to support cardiac contractility.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:478.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier Saunders; 2018:640.

Kliegman RM, St. Geme JW III, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:936–940.

A.5. What are apnea spells? What are the possible causes of apneic spells?

Apnea spells are defined as cessation of breathing lasting more than 20 seconds or more than 10 seconds and produces oxygen desaturation and bradycardia. Apneic spells are common in preterm infants, especially after the first week of life and almost universal in infants who are less than 1,000 g at birth. Failure to breathe (central apnea) or failure to maintain a patent airway (obstructive apnea) may both be present. The causes are multiple and include the following:

- Hypothermia or hyperthermia
- Hypoglycemia or hyperglycemia
- Hypocalcemia or hypercalcemia
- Hypovolemia or hypervolemia
- Anemia
- Decreased FRC
- PDA
- Constipation
- Hypothyroidism
- Immature brainstem function
- Lack of type I muscle fibers in diaphragm
- Excessive handling
- Sepsis
- Gastroesophageal reflux disease

Repeated apnea increases the likelihood of central nervous system damage because of repeated episodes of hypoxemia. Infants who have apneic spells may not breathe during anesthesia; therefore, they should be ventilated throughout anesthesia, including the induction phase. Inhaled and intravenous anesthetics affect the control of breathing and contribute to upper airway obstruction, thereby increasing the likelihood of apnea during the postoperative period, especially in preterm infants less than 60 weeks postconception age.

Coté C, Lerman J, Anderson B, eds. *A Practice of Anesthesia for Infants and*

Children. 6th ed. Philadelphia, PA: Elsevier; 2019:844–845.

Finer NN, Higgins R, Kattwinkel J, et al. Summary proceedings from the Apnea-of-Prematurity Group. *Pediatrics*. 2006;117:S47–S51.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:478–479.

A.6. Discuss the incidence and pathophysiology of PDA in preterm infants.

In term infants, the ductus arteriosus closes soon after birth in response to the increased arterial oxygen tension. Closure is delayed in preterm infants, with the ductus remaining open on day 7 after birth in 2% of infants born at 30 through 37 weeks' gestation, 65% of those born at 25 through 29 weeks' gestation, and 87% of those born at 24 weeks' gestation. Compared to term infants, the ductus arteriosus in preterm infants has a thinner, more poorly contractile muscular layer with diminished responsiveness to the increasing oxygen levels after birth. In addition, preterm infants often suffer from hypoxemia because of RDS so that there are both a reduced stimulus to and a reduced response to physiologic closure. Shunting from the systemic to the pulmonary circulation results in pulmonary vascular overload and ultimately left heart failure. The pulmonary congestion worsens respiratory failure, resulting in further hypoxemia and carbon dioxide (CO_2) retention.

Prolonged patency is associated with increased mortality, BPD, pulmonary hemorrhage, necrotizing enterocolitis, and intraventricular hemorrhage.

Benitz WE. Patent ductus arteriosus in preterm infants. *Pediatrics*. 2016;137(1):E20153730.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:723–726.

A.7. How would you make a diagnosis of PDA? Describe its treatment.

The diagnosis of PDA in preterm infants may be suspected when there is sudden increase in respiratory failure, tachycardia, tachypnea, and a widened pulse pressure. The classic continuous or machinery murmur of PDA is usually not present in this population, but a systolic murmur, sometimes extending into diastole, and a hyperdynamic precordium are nearly always present. The diagnosis is confirmed by echocardiography to assess PDA diameter, shunt pattern, and shunt volume. Continuous-wave Doppler can detect abnormal flow in the pulmonary artery. Color Doppler can visualize the jet of abnormal flow.

The initial treatment of PDA is medical. It includes fluid restriction and administration of diuretics and indomethacin. Indomethacin, 0.1 to 0.2 mg per kg, three doses for every 12 hours, usually closes the ductus within 24 hours. If the ductus fails to close with medical treatment, surgical ligation may be indicated. Percutaneous closure with coils or occlusion devices in the catheterization laboratory may also be performed at some centers, but there are size limitations in small infants.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:723–726.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:479.

Jain A, Shah P. Diagnosis, evaluation, and management of patent ductus arteriosus in preterm neonates. *JAMA Pediatr*. 2015;169(9):863–872.

A.8. Would you give digitalis to treat congestive heart failure in preterm infants? Why?

Although digitalis was once a mainstay in treatment of congestive heart failure in both children and adults, there is controversy over digitalis use as newer therapies with fewer potential toxicities have been introduced. Digitalis should not be given to small preterm infants because it does not effectively

improve stroke volume or ventricular emptying. However, it does decrease the heart rate, resulting in detrimental decrease in cardiac output. Digitalis toxicity increases mortality in preterm infants.

Berman W Jr, Dubynsky O, Whitman V, et al. Digoxin therapy in low-birth-weight infants with patent ductus arteriosus. *J Pediatr*. 1978;93:652–655.

Kliegman RM, St. Geme JW III, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:2479–2481.

A.9. How does indomethacin close the ductus? What are the adverse effects of indomethacin?

The ductus arteriosus functionally closes shortly after birth in term infants when the vascular smooth muscle contracts. The muscular contraction of the ductus is initiated by the increased oxygen content and is influenced by other factors, such as release of vasoactive substances, the relative resistances in the aorta and pulmonary artery, and the differences in sensitivity of the vessel to oxygen. The ductus arteriosus produces several prostaglandins, including prostaglandin I_2 (PGI_2) and prostaglandin E_2 (PGE_2); both prostaglandins relax the smooth muscle of the ductus and keep the ductus patent. Meanwhile, the ductus of preterm infants is far more sensitive to the vasodilating effects of prostaglandins than is the ductus of term infants. Indomethacin is one of the most potent inhibitors of the prostaglandin-forming cyclooxygenase. Therefore, indomethacin decreases the synthesis of prostaglandins, resulting in closure of the ductus.

Adverse effects of indomethacin include decreased mesenteric, renal, and cerebral blood flow. Ibuprofen is another nonselective cyclooxygenase inhibitor that can be used effectively to treat PDA and has less side effects on organ blood circulation than indomethacin. When the agents are compared with each other, no differences were observed in the rate of PDA

closure, neonatal outcomes, or adverse effects.

Clyman RI. Ontogeny of the ductus arteriosus response to prostaglandins and inhibitors of their synthesis. *Semin Perinatol*. 1980;4:115–124.

Jain A, Shah P. Diagnosis, evaluation, and management of patent ductus arteriosus in preterm neonates. *JAMA Pediatr*. 2015;169(9):863–872.

Wyllie J. Treatment of patent ductus arteriosus. *Semin Neonatol*. 2003;8:425–432.

A.10. When is surgical closure indicated? What are the complications associated with surgical ligation?

Surgical ligation is indicated for infants with hemodynamically significant PDA where medical treatment has failed and the infant is unable to be weaned from respiratory support. Recently, the role of surgical ligation has come under scrutiny because of associations with adverse neonatal and neurodevelopmental outcomes. Systematic reviews have found that surgical ligation is associated with higher morbidity with lower mortality. Complications associated with surgical ligation include pneumothorax, chylothorax, vocal cord palsy, postligation cardiac syndrome, and abnormal neurodevelopmental outcome.

Benitz WE. Patent ductus arteriosus in preterm infants. *Pediatrics*. 2016;137(1):E20153730.

Jain A, Shah P. Diagnosis, evaluation, and management of patent ductus arteriosus in preterm neonates. *JAMA Pediatr*. 2015;169(9):863–872.

A.11. What is retinopathy of prematurity (ROP) (retrolental fibroplasia [RLF])? Discuss its etiology, pathophysiology, prognosis, prevention, and treatment.

ROP is a retinal disorder affecting preterm infants that can result in blindness if untreated. Some degree of ROP occurs in approximately 50% of infants weighing 1,000 to 1,500 g at

birth, 78% of those weighing 750 to 999 g, and more than 90% of those weighing less than 750 g. ROP is thought to be initiated by oxygen-induced retinal vasoconstriction with retinal vascular obliteration, which is followed by increased vascularity, hemorrhage, cicatrization, and finally retinal detachment. ROP refers to all stages of the disease and its sequelae. RLF, the term previously used for this disease, described only the cicatricial stages.

The factors that cause ROP and determine its outcome are not fully known, but prematurity, the degree of retinal immaturity at birth, and days on supplemental oxygen therapy are major factors. Other contributing factors include respiratory distress, apnea, bradycardia, heart disease, infection, hypoxia, hypercarbia, acidosis, anemia, and the need for transfusion. Generally, the lower the birth weight and the sicker the infant, the greater the risk for ROP.

The retinal vasculature in the developing fetus spreads outward from the optic disc, reaching the nasal side of the retinal periphery by 36 weeks' gestational age and the temporal side at 40 weeks. Classically, it was postulated that hyperoxia constricts the retinal arterioles, resulting in swelling and degeneration of the endothelium. This causes paradoxical retinal ischemia in spite of systemic hyperoxia. When normoxic conditions are restored, vascularization resumes in an aberrant manner, leading to retinal detachment and blindness.

ROP is divided into five stages:

Stage 1: A thin, white line separates the posterior vascularized portion of the retina from the anterior avascular retina.

Stage 2: The demarcation line increases in volume and elevates. At this point, it is known as the "ridge." The changes in stage 1 and 2 regress in 80% of patients. Between 5% and 10% of premature infants with stage 1 and 2 disease progress to stage 3.

Stage 3: Tissue proliferation develops from the ridge, usually posteriorly. Stage 3 can be mild, moderate, or severe, depending on the volume of the extraretinal tissue.

Stage 4: Partial retinal detachment occurs with the macula still attached (stage 4a). The macula is detached in stage 4b.

Stage 5: Total retinal detachment occurs.

Eighty-five percent of ROP cases undergo spontaneous recovery. Mild ROP regresses in 2 to 3 months, and moderate ROP in 6 months. The most severe ROP usually results in blindness or limited vision.

It is unclear what level of Pa_{O_2} causes ROP, but a Pa_{O_2} of 150 mmHg for as short a time as 1 to 2 hours can do so. Furthermore, the retinal vessels of these neonates certainly constrict maximally with a Pa_{O_2} of 100 mmHg. In addition, it is also possible that ROP will develop at lower Pa_{O_2} levels because infants of this age are normally exposed to a much lower Pa_{O_2} (30 to 40 mmHg) in utero than the levels found during the neonatal period. Therefore, in order to reduce the possibility of ROP, it is wise to maintain the Pa_{O_2} levels between 50 and 70 mmHg or the saturation of oxygen (Sa_{O_2}) between 87% and 92% for infants <44 to 50 weeks' gestation.

However, prevention of ROP ultimately depends on the prevention of premature birth and its attendant problems. Oxygen alone is neither sufficient nor necessary to produce ROP, and no safe level of oxygen has yet been determined. Therefore, each infant must be treated with whatsoever is necessary to sustain life and neurologic function. Treatment of ROP includes cryotherapy and laser photocoagulation for moderate disease and scleral buckling surgery and vitrectomy for severe disease.

Coté C, Lerman J, Anderson B, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier; 2019:866–867.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:482–483.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier Saunders; 2018:641.

Kliegman RM, St. Geme JW III, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia, PA: Elsevier; 2019:3377–3385.e1.

A.12. Define neutral and critical temperatures. What are these values in the preterm neonate, in the term neonate, and in the adult? Discuss temperature regulation in the neonate.

Neutral temperature is the ambient temperature that results in minimal oxygen consumption. Critical temperature is the ambient temperature below which an unclothed, unanesthetized individual cannot maintain a normal core temperature (**Table 44.2**).

TABLE 44.2 Neutral and Critical Temperature

	Neutral Temperature (°C)	Critical Temperature (°C)
Preterm neonate	34	28
Term neonate	32	23
Adults	28	1

Normally, body heat is lost by conduction, convection, radiation, and evaporation. The neonate is particularly susceptible to heat loss owing to a large surface: volume ratio, lack of insulating fat, and naturally flaccid and open posture. When stressed by a cold environment, vasoconstriction occurs, but the neonate is unable to shiver and relies on nonshivering thermogenesis. Cold stress stimulates norepinephrine release, promoting the exothermic metabolism of brown fat deposits in an attempt to maintain core temperature. However, under anesthesia nonshivering thermogenesis appears to be inhibited. Hypothermia can result in bradycardia, apnea, hypoglycemia, or metabolic acidosis and is a risk factor for infant mortality.

When the infant's rectal temperature reaches 36.6°C (97.88°F) to 37.3°C (99.14°F), dilation of peripheral vessels occurs. The term neonate will perspire at 37.2°C (98.96°F) in an attempt to maintain a normal core temperature, whereas those infants born before 37 weeks' gestation are unable to sweat.

Coté C, Lerman J, Anderson B, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier; 2019:848–849.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:477.

B. Preoperative Evaluation and Preparation

B.1. How would you evaluate this patient preoperatively?

The preoperative evaluation of preterm infants should be based on a clear understanding of the pathophysiology of prematurity. The preoperative evaluation of this patient should begin with a careful review of the medical record, followed by a systematic physical examination and laboratory evaluation, specifically:

- *History*—birth trauma, asphyxia, maternal drug history, respiratory, cardiovascular, and fluid status
- *Physical examination*—evaluation of the airway, cardiopulmonary system, fluid status (skin texture, turgor, mucous membranes, and fontanelles), and abdominal examination
- *Laboratory data*—WBC count; hemoglobin and hematocrit; serum electrolytes; serum coagulation profile, including prothrombin time, partial thromboplastin time, and platelet count; serum calcium and serum protein; arterial blood gases; urinalysis and urine specific gravity; and chest and abdominal radiographs

B.2. What are the normal values of arterial blood gases and pH in neonates and infants?

The normal blood gas and pH values for pediatric patients are shown in **Table 44.3**. The normal pH and $PaCO_2$ values for pediatric patients are similar to those for adults, whereas the normal PaO_2 values are lower in pediatric patients than in adult patients.

TABLE 44.3 Normal Values of Arterial Blood Gases and pH in Pediatric Patients

Age	Preterm	Term	1 Month	1 Year
pH	7.37 ± 0.03	7.40 ± 0.02	7.41 ± 0.04	7.39 ± 0.02
PaO_2 (mmHg)	60 ± 8	70 ± 11	95 ± 8	93 ± 10
$PaCO_2$ (mmHg)	37 ± 6	39 ± 7	40 ± 6	41 ± 7

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:1302–1303.

B.3. Interpret the arterial blood gases: pH, 7.30; $PaCO_2$, 60 mmHg; PaO_2, 49 mmHg; HCO_3^-, 20 mEq per L on 50% oxygen; and 6 cm H_2O of positive end-expiratory pressure (PEEP). How would you improve them?

The blood gases show respiratory and metabolic acidosis. The PaO_2 of 49 mmHg is low but acceptable for preterm infants with chronic lung disease. In order to prevent ROP, PaO_2 between 50 and 70 mmHg should be maintained. $PaCO_2$ of 60 mmHg indicates hypoventilation, which can be corrected by increasing respiratory rate or tidal volume. In order to avoid the pulmonary oxygen toxicity, FIO_2 should be lowered to less than 40% by increasing levels of PEEP. Mild metabolic acidosis may be corrected by improving fluid balance and circulation.

B.4. What are the normal values of arterial blood pressure, heart rate, and respiratory rate for preterm

infants?

The blood pressure is related to the size of infants, as shown in **Table 44.4**. The heavier the birth weight, the higher the blood pressure is. The normal heart rate is 120 to 160 beats per minute. The respiratory rate is normally between 30 and 60 breaths per minute. However, it can increase to 100 to 150 breaths per minute depending on how severely the lung compliance is decreased.

TABLE 44.4 Normal Blood Pressure of Infants Weighing between 1,000 and 4,000 g

	Birth Weight (g)			
	1,000	2,000	3,000	4,000
Systolic BP (mmHg)	50	55	60	70
Diastolic BP (mmHg)	25	30	35	40
Mean BP (mmHg)	35	40	45	50

BP, blood pressure.

Coté C, Lerman J, Anderson B, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier; 2019:18.

Versmold HT, Kitterman JA, Phibbs RH, et al. Aortic blood pressure during the first 12 hours of life in infants with birth weight 610 to 4,220 grams. *Pediatrics*. 1981;67(5):607–613.

B.5. What are the normal values of WBC, red blood cells (RBCs), hemoglobin, glucose, electrolytes, calcium, blood urea nitrogen, and creatinine for preterm infants?

The WBC count usually ranges from 9,000 to 30,000 per μL at birth and decreases to 5,000 to 20,000 per μL during the fifth week of life.

The normal RBC and hemoglobin are $5.1 \pm 1.0 \times 10^6$ per μL and 19.5 ± 5.0 g per dL, respectively, at birth and decrease to $4.5 \pm 0.7 \times 10^6$ per μL and 12.2 ± 2.3 g per dL, respectively, at 3

months of age. At birth, most of the hemoglobin is fetal hemoglobin, which has a greater affinity for oxygen. Therefore, the oxygen saturation (and content) of blood for a given Pa_{O_2} is higher. By 7 months of age, the circulating hemoglobin is of the adult type.

The normal blood glucose level is between 45 and 90 mg per dL. A glucose level below 40 mg per dL is common in preterm infants. It should be corrected with a bolus of 10% to 20% glucose (2 to 5 g per kg) given over 5 minutes, followed by a continuous infusion of glucose. Severe hypoglycemia (<10 mg per dL) may cause brain damage.

The serum calcium concentration of preterm infants is normally lower than that of term infants because preterm infants have decreased serum proteins. Normal calcium level is over 8.0 mg per dL.

The normal values of sodium, potassium, and chloride are 135 to 145, 3.0 to 5.0, and 105 to 115 mEq per L, respectively.

The creatinine levels of term infants at birth are 0.6 to 1.2 mg per dL but, within 1 month, fall to levels of 0.1 to 0.2 mg per dL. Preterm infants have relatively high serum creatinine levels compared with term infants. They are 0.8 to 1.8 mg per dL at birth and fall to 0.2 to 0.8 mg per dL in 1 month.

The normal blood urea nitrogen level is 10 to 20 mg per dL in term infants, whereas it is 16 to 28 mg per dL in preterm infants.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:1300–1314.

B.6. Would you transfuse blood to this patient preoperatively?

The patient has a hemoglobin of 11 g per dL; a transfusion is not indicated at this time. To ensure oxygen-carrying capacity, most clinicians agree that a hemoglobin of 10 g per dL is the lowest acceptable level if cardiorespiratory disease exists. If infants are

well, a hemoglobin level of above 7.0 g per dL is usually tolerable.

Coté C, Lerman J, Anderson B, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier; 2019:218–219.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:244.

B.7. How would you interpret the urinalysis: specific gravity, 1.005; sugar, 1+; and protein, 1+?

Normal urine specific gravity is 1.001 to 1.035. A higher specific gravity may be suggestive of dehydration. Mild glucosuria may be present in preterm infants, likely due to decreased renal tubular reabsorption of glucose. Albumin is normally filtered by the glomerulus and is completely reabsorbed. However, because of tubular immaturity, preterm infants have mild proteinuria.

Hughes H, Kahl I. *The Harriet Lane Handbook*. 21st ed. Philadelphia, PA: Elsevier; 2018:516–518.

B.8. Would you correct a serum calcium level of 6.0 mg per dL? What other information would you like to have? Which contains more calcium, 10 mL of 10% calcium chloride or 10 mL of 10% calcium gluconate? Could you hyperventilate this child safely?

Normally, the serum calcium is maintained at 8.0 mg per dL; however, in the preterm infant, a level of 7.0 mg per dL is acceptable. This child's serum calcium is 6.0 mg per dL. Therefore, supplementation with 30 to 100 mg per kg of calcium gluconate or 10 to 20 mg per kg of calcium chloride is appropriate.

Hypocalcemia in neonate is defined as serum calcium less than 3.5 mEq per L or serum ionized calcium less than 1.5 mEq

per L. When evaluating the serum calcium levels, it is important to know the serum protein concentration; neonatal hypocalcemia is usually due to hypoproteinemia. It is also important to determine the ionized calcium concentration (usually 45% of the total calcium concentration) because this is the calcium immediately available at the cellular level. The chloride molecule is approximately one-third the weight of the gluconate molecule. For this reason, approximately three times more calcium is given when an equivalent volume of calcium chloride is administered instead of 10% calcium gluconate. Respiratory alkalosis following hyperventilation will reduce serum ionized calcium levels and, for this reason, should be avoided in this infant.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:137–139.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:481.

B.9. How would you premedicate this patient?

Children under 1 year of age do not usually need sedation or anxiolysis. However, atropine, 0.01 to 0.02 mg per kg, may be given to attenuate the vagal response to a host of different stimuli.

Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:412–416.

C. Intraoperative Management

C.1. Where should the procedure take place? In the neonatal intensive care unit (NICU) or the operating room?

Surgical ligation of the PDA can occur either in the operating room or in the NICU. The decision is frequently institution

dependent. Studies have demonstrated the safety of PDA ligation in the NICU setting when performed by an experienced team. Advantages of performing ligation in the NICU include minimizing transport, continuity of care, and continuation of NICU interventions such as specialized ventilator settings or nitric oxide. Advantages of performing ligation in the operating room include familiarity of the environment for the surgical and anesthesia teams, availability of familiar equipment, potential for improved sterility, and proximity to other surgical and anesthesia personnel.

Gould DS, Montenegro LM, Gaynor JM, et al. A comparison of on-site and off-site patent ductus arteriosus ligation in premature infants. *Pediatrics*. 2003;112:1298–1301.

Jenkins IA, Kelly Ugarte LR, Mancuso TJ. Where should we operate on the preterm neonate? *Paediatr Anaesth*. 2014;24(1):127–136.

C.2. What monitors would you use for this child during surgery?

Proper monitoring of this child for safe administration of anesthesia includes the following:

- *Respiratory*—precordial or esophageal stethoscope, end-tidal CO_2, inspiratory oxygen monitor, pulse oximeter, arterial blood gases, inspiratory pressure gauge
- *Cardiovascular*—precordial or esophageal stethoscope, electrocardiogram, blood pressure cuff and Doppler transducer, and urinary bag
- *Thermoregulatory*—esophageal or axillary temperature probe with servo loop overhead heater and thermal blanket

If the patient has an umbilical artery catheter in place, it is useful for the measurement of blood pressure and arterial blood gases. However, it is probably unnecessary to establish an arterial line for the surgery alone because invasive monitoring in this age group is not without risk.

C.3. How does the oxygen analyzer work?

Oxygen analysis can be done by either parametric or amperometric analysis. Parametric analysis is based on the fact that oxygen is a dipole molecule. When a gas containing oxygen is passed through a magnetic field, the gas is deflected in proportion to the concentration of oxygen. Sensors can detect this deflection and give a readout of oxygen concentration. Amperometric analysis can be done with one of the two devices: the galvanic cell analyzer and the polarographic cell analyzer. In the galvanic or fuel cell analyzer, oxygen diffuses through a membrane of the sensor into an electrolyte solution from which the oxygen absorbs electrons and forms hydroxide ions. The hydroxide ions then diffuse to a lead anode where oxidation to lead oxide and water occurs with the resultant liberation of free electrons. An electron flow (current) is thereby generated between the anode and the cathode, which is proportional to the oxygen level at the sensor. This current is directly displayed by a meter that indicates oxygen percentage. These devices are relatively inexpensive to purchase but carry a high operating cost because the sensor is eventually exhausted and must be replaced.

The polarographic cell, or Clark electrode, uses a battery to induce a negative potential of 0.75 V between the anode and the cathode. As oxygen diffuses across a membrane and into the electrolyte solution separating the anode and cathode, the polarizing voltage at the cathode causes electrons to combine with oxygen molecules, reducing them to hydroxide ions. The hydroxide ions then move to the anode, causing electron flow (current) that is proportional to the initial oxygen concentration. This flow is read by a meter that translates to oxygen percentages. These monitors are initially more expensive than galvanic cell monitors, but they are less expensive to maintain, requiring only inexpensive electrolyte solution and battery

replacement.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1298–1339.

Saidman LJ, Smith NT, eds. *Monitoring in Anesthesia*. 3rd ed. Boston, MA: Butterworth-Heinemann; 1993:384.

C.4. What is the Doppler effect? How does the Doppler transducer measure blood pressure?

In 1841, Christian Doppler noted the change in observed frequency from a constant frequency sound generator when the source moved with respect to the observer. Ballot confirmed this "Doppler effect" in 1845 with the simple example of the frequency increase in a train's steam whistle as the train approached an observer. In the 1960s, a practical ultrasonic system for transducing arterial wall motion was described to obtain blood pressure. The ultrasonic system consists of an occlusive cuff and a dual crystal ultrasonic transducer placed over the artery distal to the occlusion. One crystal transmits the ultrasonic signal, whereas the other receives the signal reflected from the artery. Although the cuff occludes the artery, there is no arterial wall movement and the crystal receives a signal with an unchanged frequency. When the cuff pressure falls below systolic pressure, arterial wall motion occurs, causing a Doppler frequency shift, indicating systolic blood pressure. When the cuff pressure falls to diastolic pressure, the artery is open throughout the cycle: Rhythmic arterial opening and closing does not occur, and there is a loss of Doppler frequency shift. Therefore, one can easily and accurately obtain systolic and diastolic blood pressure.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1145–1193.

Saidman LJ, Smith NT, eds. *Monitoring in Anesthesia*. 3rd ed. Boston, MA: Butterworth-Heinemann; 1993:121.

C.5. What is the mechanism of pulse oximetry? Why is it important to monitor arterial oxygen saturation? What levels of arterial oxygen saturation would you like to keep during surgery?

The mechanism of pulse oximetry is described in Chapter 2, section C.10, and Chapter 59, section A.5.

Safe anesthesia practice requires the monitoring of arterial oxygen saturation in all patients to prevent hypoxia. However, in ex-premature infants less than 44 weeks' postconceptional age, it is also vital to guard against hyperoxia, which may cause ROP.

The arterial oxygen saturation should be kept between 85% and 95% during the neonatal period.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:558–559.

Purohit DM, Ellison RC, Zierler S, et al. Risk factors for retrolental fibroplasia: experience with 3,025 premature infants. National Collaborative Study on Patent Ductus Arteriosus in Premature Infants. *Pediatrics*. 1985;76:339–344.

C.6. How would you maintain the patient's body temperature?

Hypothermia greatly increases the metabolic rate and oxygen consumption of preterm infants. The preterm infant is particularly susceptible to heat loss because of a large surface-to-volume ratio, lack of insulating fat, and a naturally flaccid and open posture. In addition, the preterm infant often has impaired thermal regulatory ability; therefore, all precautions must be taken to ensure normothermia. The patient should be transported to the operating room in a heated isolette. If unavailable, the infant should be covered with a plastic sheet or warm blanket, and a cap should be put on the head to prevent heat loss. The operating room should be warmed to >27°C

(80°F) and a servo-controlled infrared heater placed over the operating table. A water-circulating heating blanket or forced air warmer should be used. All extremities should be covered if possible. All intravenous fluids and inspired gases should be warmed and humidified to help maintain the patient's body temperature. If the appropriate setup and equipment are available, then in very low birth weight infants, the procedure can be done at the bedside using the ICU ventilator for airway management. This helps minimize the risks associated with transportation and also minimize the incidence of hypothermia.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:577.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:341–342.

C.7. How do the anesthetic requirements of the preterm infant differ from those of the adult?

Achieving proper anesthetic depth in the preterm infant presents a unique challenge to the anesthesiologist. Anesthetic requirements (as determined by minimal alveolar concentration) are decreased in the preterm infant as compared with the adult, possibly due to immaturity of the central nervous system and to increase circulating concentrations of progesterone and β-endorphins. Cardiovascular sensitivity is greatly pronounced because of greater myocardial depression and a reduced peripheral response to catecholamines. Furthermore, the baroreceptor reflex that maintains blood pressure is often poorly developed in the preterm infant and can be abolished by even light levels of inhalation anesthesia. Therefore, the preterm infant is extremely susceptible to anesthetic overdose, which produces cardiovascular depression leading to hypotension or cardiovascular collapse.

Unfortunately, an inadequate depth of anesthesia is also

uniquely hazardous in the neonate. Because there is a lack of cerebral autoregulation, systemic hypertension from inadequate depth of anesthesia may be transmitted directly to the cerebral circulation, resulting in intraventricular hemorrhage.

For these reasons, it is essential to carefully tailor anesthetic depth to surgical conditions because the therapeutic margin between underdose and overdose is extremely narrow.

Coté C, Lerman J, Anderson B, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier; 2019:852–853.

Gregory GA. The baroresponses of preterm infants during halothane anaesthesia. *Can Anaesth Soc J*. 1982;29:105–107.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:352.

Lou HC, Lassen PH, Friis-Hansen B. Impaired autoregulation of cerebral blood flow in the distressed newborn infant. *J Pediatr*. 1979;94:118–121.

C.8. What size endotracheal tube would you have used if the patient had not been intubated?

The larynx of a full-term neonate usually accommodates a 3.0- or 3.5-mm endotracheal tube, whereas infants weighing less than 3,500 g tolerate a 3.0-mm tube. In infants weighing less than 1,500 g, a 2.5-mm (internal diameter) tube is usually recommended. The endotracheal tube should be large enough to allow easy ventilation but small enough to permit leaking of gas between the tube and trachea when the lung is ventilated with 15 to 20 cm H_2O pressure. However, a higher leak pressure of 25 to 35 cm H_2O may be necessary if high peak inspiratory pressures are required during anesthesia such as during a thoracotomy or an upper laparotomy or if the patient has decreased pulmonary compliance.

Coté C, Lerman J, Anderson B, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier; 2019:841–842.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed.

West Sussex, United Kingdom: Wiley-Blackwell; 2012:314–315.

C.9. How would you have induced anesthesia if the patient had not been intubated?

Preterm infants require adequate anesthesia and analgesia for painful procedures. Although use of premedication for intubation in the NICU may be institution dependent, studies have demonstrated that premedication in the newborn improves intubating conditions, decreases the time and number of attempts to secure airway, decreases potential intubation-related airway injury, and attenuates the physiologic responses to laryngoscopy and intubation. After preoxygenation with 100%, premedication with fentanyl 1 to 4 μg per kg and 0.05 to 0.1 mg per kg of pancuronium or 0.6 to 1.2 mg per kg of rocuronium can be used to facilitate intubation. After intubation, breath sounds should be checked bilaterally to ensure that the tube is properly positioned.

Alternatively, anesthesia may be induced in the operating room with an inhalation anesthetic such as sevoflurane followed by muscle relaxation with pancuronium or rocuronium before intubation.

Kumar P, Denson SE, Mancuso TJ. Clinical report—premedication for nonemergency endotracheal intubation in the neonate. *Pediatrics*. 2010;125:608–615.

C.10. How would you maintain anesthesia?

Because preterm infants are extremely sensitive to cardiovascular depression from volatile anesthetics, an intravenous anesthetic technique using opioids such as fentanyl and a neuromuscular blocker can be used for maintenance of anesthesia. Increments of fentanyl, 3 to 5 μg per kg, are titrated to maintain hemodynamic stability. A bolus injection of high-dose fentanyl, 30 to 50 μg per kg, often causes hypotension because the infant is usually dehydrated as a result of fluid

restriction and diuretic therapy for congestive heart failure from PDA.

Pancuronium, 0.1 mg per kg, is an attractive choice for muscle relaxation because it causes mild tachycardia and the infant's blood pressure is dependent on heart rate.

Andropoulos DB, Stayer S, Mossad EB, et al, eds. *Anesthesia for Congenital Heart Disease*. 3rd ed. Hoboken, NJ: Wiley; 2015:471–472.

Coté C, Lerman J, Anderson B, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier; 2019:410–411.

Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:412–416.

Robinson S, Gregory GA. Fentanyl-air-oxygen anesthesia for ligation of patent ductus arteriosus in preterm infants. *Anesth Analg*. 1981;60:331–334.

C.11. How would you ventilate the patient? What tidal volume, respiratory rates, and FIO_2 would you set for the infant?

Controlled ventilation should be employed because preterm infants do not breathe well under anesthesia. The patient may be ventilated by hand with a Jackson-Rees device. This technique potentially allows for instantaneous compensation for changes in pulmonary compliance and resistance, especially during thoracotomy. It also permits the use of PEEP. However, manual ventilation may be unreliable for sensing changes in compliance. Mechanical ventilation, preferably with a pediatric bellows or NICU ventilator, may be used to ventilate the infant.

During spontaneous respiration, normal tidal volume is 7 mL per kg for all ages. However, the ventilator tidal volumes calculated on the basis of body weight for adult patients, such as 10 mL per kg, may not be applicable for pediatric patients, especially small infants. A ventilator-delivered tidal volume may be lost from the leak around the uncuffed endotracheal tube. Traditional anesthesia ventilators were not designed to deliver

small tidal volumes accurately, but modern ventilators can compensate for the compliance of the breathing system. However, most modern anesthesia ventilators have a minimal tidal volume of 20 mL, which might not be appropriate for the smallest patients. In cases where a leak cannot be eliminated such as with an uncuffed tube, or the desired tidal volumes are below the limitations of the ventilator, pressure control ventilation is appropriate. Usually, the peak inspiratory pressures are set between 15 and 25 cm H_2O, depending on the patient's respiratory condition, to ensure adequate chest expansion.

The respiratory rates and inspiratory pressures are adjusted as needed to maintain the $PaCO_2$ between 35 and 40 mmHg or the end-tidal CO_2 between 30 and 35 mmHg. The FIO_2 is adjusted to keep the PaO_2 between 50 and 70 mmHg or the arterial oxygen saturation between 87% and 95%.

Feldman JM. Optimal ventilation of the anesthetized pediatric patient. *Anesth Analg*. 2015;120:165–175.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:340.

C.12. Discuss blood and fluid therapy in this preterm infant.

Fluid therapy should be aimed at correcting the preoperative deficit; providing maintenance fluid; and replacing intraoperative evaporative, third space, and blood loss.

Intraoperative blood loss must be carefully estimated by weighing the sponges and using small-calibrated suction bottles in plain view of the anesthesiologist. The preterm infant's blood volume is only 80 to 95 mL (85 to 100 mL per kg); therefore, even a 10-mL blood loss can be critical. Despite these precautions, estimation of blood loss is inevitably inaccurate because of the unmeasured loss in the drapes and tissues. For

this reason, it is recommended that 125% to 150% of measured blood loss be replaced. Each milliliter of estimated blood loss is replaced with 3 mL of Ringer's lactate or 1 mL of 5% albumin in saline. If the hematocrit is low (<30%) to begin with, blood losses are replaced with packed RBC.

Maintenance fluids consisting of 5% dextrose in one-fourth strength normal saline are given at 4 mL/kg/hr, whereas evaporative and third-space losses are replaced with Ringer's lactate at 8 to 12 mL/kg/hr for abdominal or thoracic procedures. The adequacy of blood and fluid therapy may be ensured by stable blood pressure, normal central venous pressure (over 3 cm H_2O), and adequate urine output of >0.75 mL/kg/hr and specific gravity of less than 1.010. In addition, the infant's fontanel should be above the inner table of the skull if there is no volume depletion.

Coté C, Lerman J, Anderson B, eds. *A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier; 2019:205–209.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:352–354.

C.13. During dissection of the ductus arteriosus, the arterial oxygen saturation dropped from 92% to 80% and the heart rate decreased from 140 beats per minute to 80 beats per minute. What were the causes? How would you correct this situation?

Pediatric patients, especially preterm infants, develop hypoxemia quickly after hypoventilation because they have high metabolism (increased oxygen demand) and low FRC (decreased oxygen reserve). During dissection of the ductus arteriosus, the ipsilateral lung is retracted and compressed by the surgeon. Therefore, the pulmonary resistance increases and pulmonary compliance decreases. Consequently, the delivered tidal volume to the patient decreases, and the gas leak around the

endotracheal tube increases if the inspiratory pressures remain unchanged. Decreasing tidal volume causes hypoventilation, resulting in hypoxemia and CO_2 retention. In addition, compressing the lung tissue increases intrapulmonary shunt, which causes further hypoxemia. In pediatric patients, bradycardia is most commonly caused by hypoxemia. During dissection of the ductus arteriosus, surgical manipulation of the vagus nerve and lung tissue may initiate vagal reflex, with resultant bradycardia.

The infant should be manually ventilated with 100% oxygen to correct hypoxemia and bradycardia. If bradycardia persists, atropine, 0.01 to 0.02 mg per kg, should be given. The surgical manipulation should be stopped and the collapsed lung reexpanded. Blood loss or hypovolemia should also be corrected.

When the hemodynamic status and oxygenation are stabilized, the F_{IO_2} and respiratory pressures should be adjusted to ensure adequate ventilation and oxygenation.

D. Postoperative Management

D.1. Would you reverse the muscle relaxants and extubate the patient at the end of surgery?

No. Postoperative ventilatory support would be necessary for this preterm infant with RDS; therefore, reversal of muscle relaxation and extubation are not indicated.

D.2. How can one minimize the risk of transporting the patient to the NICU after surgery?

The anesthesiologist's responsibilities do not end with the successful completion of the operative procedure. Removal of the surgical drapes must be done with caution to prevent inadvertent extubation or removal of the arterial or venous

cannula. Transportation of the infant to the NICU is an extremely hazardous transition and requires watchful vigilance.

Arrangements must be made in advance so that elevators are waiting and the nursery is ready to accept the patient. The anesthesiologist must accompany the child until satisfied that care has been appropriately transferred to the neonatal nursery staff.

The same monitors that were employed for surgery must be used in transport, including electrocardiogram and monitors for arterial blood pressure and oxygen saturation. Ventilation should be maintained by hand with a Jackson-Rees device or by a battery-operated transport ventilator, and the child should not be transported with 100% oxygen unless it was used for the operative procedure. A precordial stethoscope is especially helpful to monitor the adequacy of respiration and heart sounds. Finally, every effort to ensure thermal stability must be made, including the use of a heated Isolette (if possible), plastic sheet, warm blankets, and a cap on the infant's head.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. West Sussex, United Kingdom: Wiley-Blackwell; 2012:488–489.

D.3. The patient's condition deteriorated postoperatively in the intensive care unit (ICU). Physical examination revealed persistent cardiac murmur. What was the possible diagnosis?

It has been reported that a large ductus arteriosus arising from the aortic arch proximal to the subclavian artery creates the illusion of the arch, leading to surgical closure of the distal left pulmonary artery instead of ductus arteriosus (**Fig. 44.1**). A sign of successful PDA ligation is an increase in diastolic blood pressure from the elimination of pulmonary runoff during diastole. To help identify the ductus, some surgeons place a temporary clip on what they believe is the ductus and observe

whether the diastolic pressure increases correspondingly.

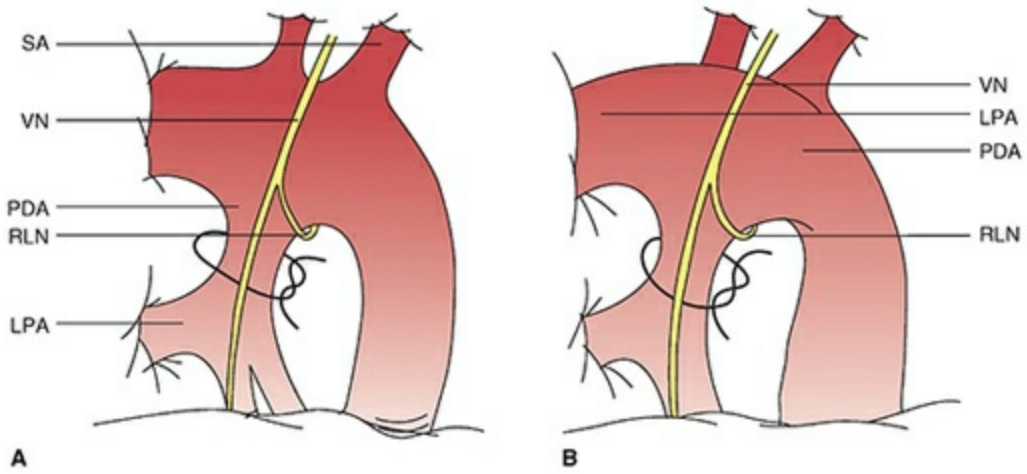

FIGURE 44.1. A. Anatomically, atypical patent ductus arteriosus (PDA) arising proximal to the left subclavian artery (SA). **B.** Large patent ductus arteriosus sweeping into the descending aorta and appearing to be the arch. The ductus overlies the arch and hides it from view. A large distal left pulmonary artery is misinterpreted as the patent ductus (encircled by ligature). LPA, left pulmonary artery; RLN, recurrent laryngeal nerve; VN, vagus nerve. (*Adapted from Pontius RG, Danielson GK, Noonan JA, et al. Illusions leading to surgical closure of the distal left pulmonary artery instead of the ductus arteriosus.* J Thorac Cardiovasc Surg*. 1981;82[1]:107–113. Copyright © 1981 Elsevier. With permission.*)

In this case, the ductus arteriosus was not ligated; therefore, the ductus murmur persisted. Inadvertent ligation of the distal left pulmonary artery resulted in pulmonary ischemia distal to the ligation. Meanwhile, the right lung was further flooded with the shunted blood through the unligated PDA. The resultant ventilation/perfusion mismatch caused further hypoxemia and CO_2 retention in this infant. The patient should be brought to the operating room for repair of the left pulmonary artery and ligation of the ductus arteriosus.

Lake CL, Booker PD, eds. *Pediatric Cardiac Anesthesia*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:414.

Pontius RG, Danielson GK, Noonan JA, et al. Illusions leading to surgical closure of the distal left pulmonary artery instead of the ductus arteriosus. *J Thorac Cardiovasc Surg*. 1981;82:107–113.

45 Post-tonsillectomy Hemorrhage

Dana L. Gurvitch, Jessica A. Latzman, and Hugh C. Hemmings Jr.

The patient is a 10-year-old male with a history of diagnosed obstructive sleep apnea (apnea–hypopnea index [AHI] of 27) who presents to the emergency department with bleeding in the posterior oropharynx 7 days post-tonsillectomy. On physical exam, the patient is lethargic with pallor and decreased capillary refill. His vital signs are significant for tachycardia to 140 beats per minute, hypotension with blood pressure of 70/40 mmHg, and tachypnea with a respiratory rate of 25 breaths per minute. His oxygen saturation is 97%. The patient is accompanied by his mother, who states that the bleeding started 2 hours ago after the child ate a sandwich.

A. Medical Disease and Differential Diagnosis

1. Approximately how many pediatric tonsillectomies are performed in the United States each year? What are the indications for tonsillectomy?
2. What is the differential diagnosis for this patient?
3. What is the treatment for a patient with von Willebrand disease?

4. Describe the vascular anatomy of the tonsils. What is the incidence of post-tonsillectomy hemorrhage?
5. What are the risk factors for post-tonsillectomy hemorrhage? Does age matter?
6. Describe the morbidity and mortality of post-tonsillectomy hemorrhage.

B. Preoperative Evaluation and Preparation

1. What is your approach to assessing this patient?
2. What will you set up in the operating room for this patient? How will your preparation be different from a routine general anesthetic set up?
3. Should you plan to use vasopressors?
4. The patient seems anxious. Will you administer a sedative to calm the patient down?
5. How do you plan on interpreting this patient's laboratory results?
6. What are your expectations of the surgeon, specifically as it relates to induction of anesthesia?

C. Intraoperative Management

1. What is your plan for induction of anesthesia? During the initial procedure, this patient underwent an uneventful inhalational induction, with postinduction intravenous (IV) placement. Would you perform an inhalational induction again? Why or why not?
2. What is your plan for management of blood in the oropharynx?
3. What is your plan for airway management?
4. Laryngoscopy and intubation prove challenging due to blood in the airway. What options do you have now?
5. What is your plan for maintenance of the anesthetic? What other medications might you want to give?
6. Assuming the surgical intervention is successful, what is your plan for emergence and extubation?

D. Postoperative Management

1. Is postoperative management in the pediatric intensive care unit (PICU) indicated?
2. What would you require for safe transport from the operating room to the PICU?
3. Discuss potential postoperative complications for this patient.
4. What discharge instructions should be given post-tonsillectomy?

A. Medical Disease and Differential Diagnosis

A.1. Approximately how many pediatric tonsillectomies are performed in the United States each year? What are the indications for tonsillectomy?

Approximately 500,000 pediatric tonsillectomies are performed in the United States each year, making it the second most common pediatric ambulatory procedure (behind myringotomy tube insertion).

There are two indications for tonsillectomy in children: sleep-disordered breathing (SDB) and infection. SDB exists on a continuum, with the mildest end being snoring. Obstructive sleep apnea syndrome (OSAS) exists on the severe end of the spectrum and is now the most common indication for tonsillectomy in the pediatric population. The severity of OSAS can be evaluated via polysomnography. Results of polysomnography are graded by the AHI (i.e., the average number of apneic and hypopneic episodes per hour). The AHI allows OSAS to be classified as mild ($1 < \text{AHI} \leq 5$), moderate ($5 < \text{AHI} \leq 10$), or severe ($\text{AHI} > 10$). Patients with SDB and OSAS can exhibit problems such as enuresis, daytime sleepiness or hyperactivity, poor concentration, aggression, anxiety, depression, and other behavioral disorders. In addition, patients

with SDB may have a lower intelligence quotient (IQ) and quality of life.

A second indication for tonsillectomy in children is infection. This can include recurrent tonsillitis, chronic tonsillitis, or peritonsillar abscess. The American Academy of Otolaryngology-Head and Neck Surgery recommends tonsillectomy for recurrent throat infections (7 infections in the past year, 5 infections per year for the last 2 years, or 3 infections per year for at least 3 years, also known as the Paradise Criteria) with documentation of either temperature greater than 38.3°C, cervical adenopathy, tonsillar exudates/erythema, or a positive test for Group A β-hemolytic streptococcus.

Baugh RF, Archer SM, Mitchell RB, et al. Clinical practice guideline: tonsillectomy in children. *Otolaryngol Head Neck Surg*. 2011;144(suppl 1):S1–S30.

Cullen KA, Hall MJ, Golosinskiy A. *Ambulatory Surgery in the United States, 2006*. Hyattsville, MD: National Center for Health Statistics; 2009. National Health Statistic reports no. 11, revised.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:820–842.

Dehlink E, Tan HL. Update on paediatric obstructive sleep apnoea. *J Thorac Dis*. 2016;8(2):224–235.

Paradise JL, Bluestone CD, Bachman RZ, et al. Efficacy of tonsillectomy for recurrent throat infection in severely affected children. Results of parallel randomized and nonrandomized clinical trials. *N Engl J Med*. 1984;310(11):674–683.

A.2. What is the differential diagnosis for this patient?

Blood in the posterior oropharynx could have several etiologies, and it is important to start with a broad differential. Given this patient's recent tonsillectomy, postoperative bleeding from the surgical site is the most likely diagnosis. However, other possible causes of bleeding may be due to trauma, underlying coagulopathy or vascular malformations, or it may be

spontaneous. Bleeding from the tonsillar bed is the most likely cause of this patient's surgical bleeding. However, damage to nearby structures, including the uvula, should not be overlooked. Epistaxis secondary to trauma, and possibly unrelated to the prior surgery, may also be a cause of bleeding into the posterior pharynx. Additionally, underlying coagulopathies, such as von Willebrand disease (incidence of 1% in the general population), may be a cause for continued bleeding postsurgery. And finally, spontaneous hemorrhage has also been reported.

Centers for Disease Control and Prevention. Data & Statistics on von Willebrand Disease. Centers for Disease Control and Prevention Web site. https://www.cdc.gov/ncbddd/vwd/data.html. Accessed December 18, 2018.

Salem A, Healy S, Pau H. Management of spontaneous tonsillar bleeding: review. *J Laryngol Otol*. 2010;124:470–473.

A.3. What is the treatment for a patient with von Willebrand disease?

To combat the dual defects of hemostasis (abnormal coagulation due to low levels of expressed factor VIII and abnormal platelet adhesion), there are three main treatment options:

- Desmopressin (raises endogenous factor VIII and von Willebrand factor levels)
- von Willebrand factor concentrate
- Transfusion therapy with blood products

Eighty percent of patients with von Willebrand disease have type 1 von Willebrand disease, which is responsive to desmopressin. In patients with type 2 or type 3 von Willebrand disease, desmopressin is not effective, and plasma concentrates containing factor VIII and von Willebrand factor concentrate must be used.

Mannucci PM. Treatment of von Willebrand's disease. *J Intern Med Suppl*. 1997;740:129–132.

Rick M. Treatment of von Willebrand disease. UpToDate Web site.

https://www.uptodate.com/contents/treatment-of-von-willebrand-disease. Accessed December 19, 2018.

A.4. Describe the vascular anatomy of the tonsils. What is the incidence of post-tonsillectomy hemorrhage?

The arterial blood supply of the tonsils comes from several branches of the external carotid artery, including the ascending pharyngeal artery, descending palatine artery, ascending palatine artery, facial artery branches, and dorsal lingual artery (**Fig. 45.1**). The internal carotid artery may have an aberrant course, allowing it to run close to the tonsillar bed. Venous return is to the peritonsillar plexus, the lingual vein, and the pharyngeal plexus. Sources of tonsillar bleeding can be arterial, venous, or involve vascular anomalies.

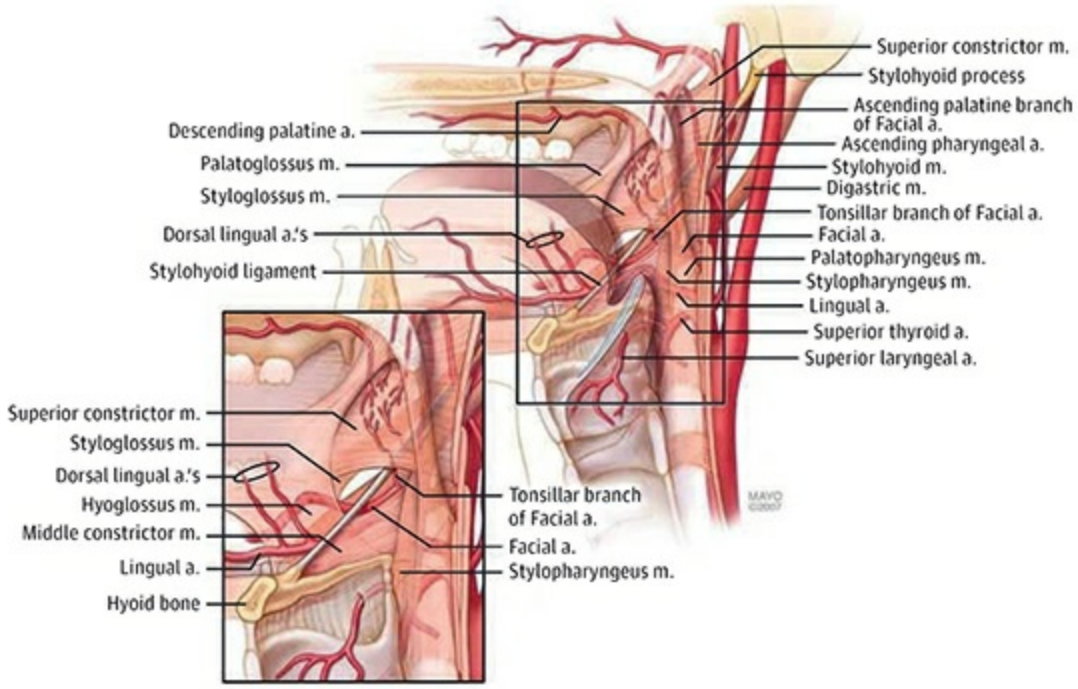

FIGURE 45.1. Blood supply to the lateral oropharynx. a, artery; m, muscle. (*From Pollei TR, Hinni ML, Moore EJ, et al. Analysis of postoperative bleeding and risk factors in transoral surgery of the oropharynx*. JAMA Otolaryngol Head Neck Surg. *2013;139[11]:1212–1218; used with permission of Mayo Foundation for Medical Education and Research, all rights reserved.*)

Stages of tonsillectomy healing are shown in **Figure 45.2**.

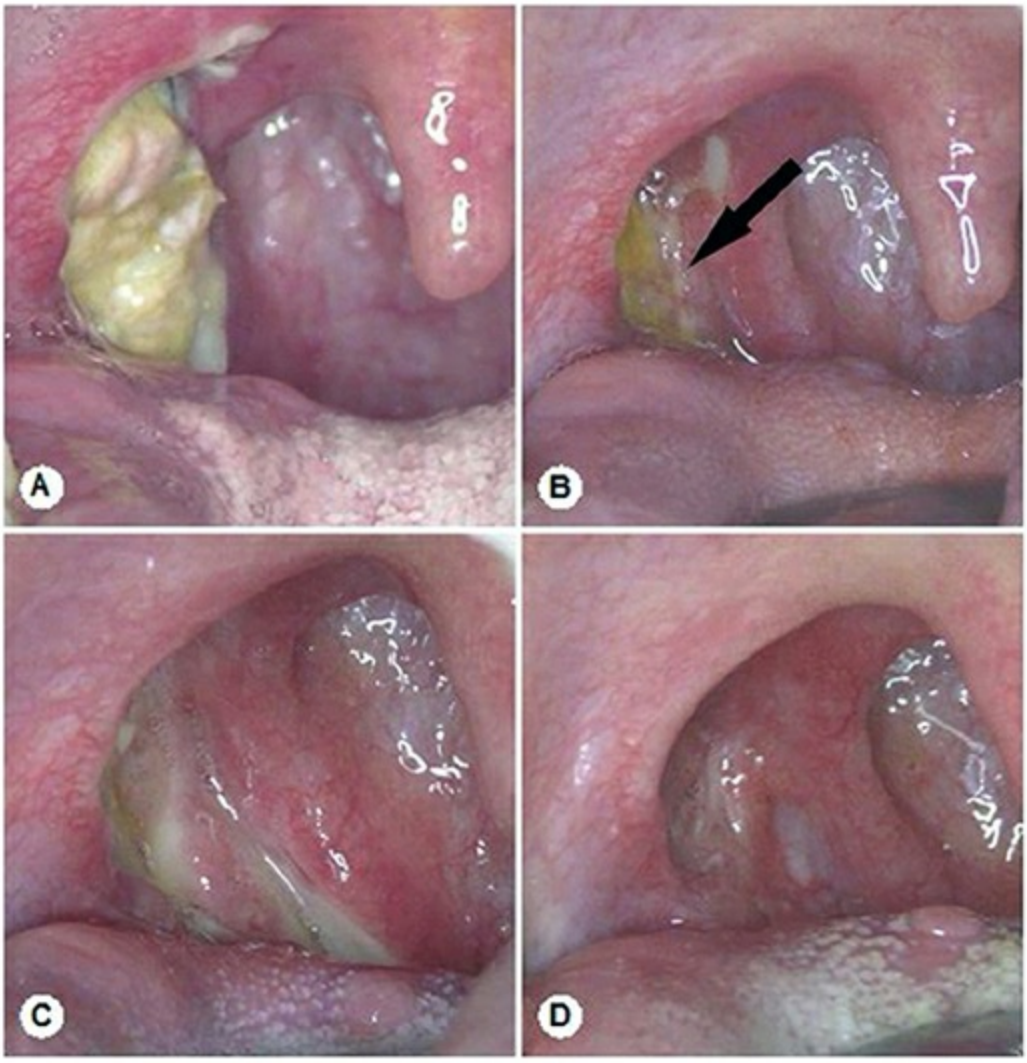

FIGURE 45.2. Stages of tonsillectomy healing. A. Postoperative day (POD) 5: Exudative fibrin clot fills tonsillar fossa, protruding beyond tonsillar pillars. **B.** POD 7: Fibrin clot has separated from tonsillar fossa. New stroma lines the tonsillar fossa. Initial ingrowth of posterior pillar epithelium is discernible (*arrow*). **C.** POD 9: Bridge of epithelium has widened, advancing laterally across tromal bed. **D.** POD 17: Tonsillar fossa is covered by layer of epithelium. Initial epithelium bridge has thickened and resembles normal mucosa. (*Reprinted with permission from Isaacson G. Tonsillectomy healing*. Ann Otol Rhinol Laryngol. *2012;121[10]:645–649. Copyright © 2012 SAGE Publications*.)

Post-tonsillectomy hemorrhage occurs at an overall rate of 3.5% and can be a surgical emergency. Primary bleeding occurs within 24 hours of surgery in approximately 0.55% of cases, with ranges reported in the literature of 0.2% to 2.2% of tonsillectomy patients. Secondary bleeding occurs in approximately 3% of patients (ranges have been reported from

0.1% to 4.8%) and occurs more than 24 hours after surgery, usually between postoperative days 5 through 7. Primary hemorrhage is usually a result of inadequate surgical hemostasis, whereas secondary hemorrhage occurs when the fibrin clot, or eschar, sloughs off of the tonsillar bed.

Isaacson G. Tonsillectomy healing. *Ann Otol Rhinol Laryngol*. 2012;121(10):645–649.

Lowe D, van der Meulen J, Cromwell D, et al. Key messages from the National Prospective Tonsillectomy Audit. *Laryngoscope*. 2007;117:717–724.

Paulsen F, Tillman B, Christofides C, et al. Curving and looping of the internal carotid artery in relation to the pharynx: frequency, embryology and clinical implications. *J Anat*. 2000;197:373–381.

Standring S, Borley NR, Collins P, et al, ed. *Gray's Anatomy: The Anatomical Basis of Clinical Practice*. 40th ed. Edinburgh, Scotland: Churchill Livingstone Elsevier; 2008:566–567.

Windfuhr JP, Chen YS, Remmert S. Hemorrhage following tonsillectomy and adenoidectomy in 15,218 patients. *Otolaryngol Head Neck Surg*. 2005;132(2):281–286.

A.5. What are the risk factors for post-tonsillectomy hemorrhage? Does age matter?

Risk factors for post-tonsillectomy hemorrhage include age, male sex, history of recurrent tonsillitis/peritonsillar abscess, and, in rare cases, underlying coagulopathies (such as von Willebrand disease). There are also rare cases of unsuspected vascular anomalies. The incidence of post-tonsillectomy bleeding increases with age, particularly after age 12 years. Patients age 12 years and older are 1.5 times more likely to experience primary hemorrhage and 3.3 times more likely to experience secondary hemorrhage following tonsillectomy.

Tomkinson A, Harrison W, Owens D, et al. Postoperative hemorrhage following adenoidectomy. *Laryngoscope*. 2012;122:1246–1253.

Tomkinson A, Harrison W, Owens D, et al. Risk factors for postoperative hemorrhage following tonsillectomy. *Laryngoscope*. 2011;121:279–288.

A.6. Describe the morbidity and mortality of post-tonsillectomy hemorrhage.

Efficient and early intervention and resuscitation should be implemented in the face of active bleeding post-tonsillectomy to prevent hypovolemia, decreased cardiac output, and airway obstruction. Morbidity and mortality occur secondary to aspiration, laryngospasm, and hemorrhagic shock. Mortality rates range from 1 in 10,000 to 1 in 35,000.

Windfuhr JP, Schloendorff G, Baburi D, et al. Lethal outcome of post-tonsillectomy hemorrhage. *Eur Arch Otorhinolaryngol*. 2008;265:1527–1534.

B. Preoperative Evaluation and Preparation

B.1. What is your approach to assessing this patient?

The preoperative assessment must be focused and efficient, with emphasis on the airway, vital signs, and cardiovascular status. Important questions to ask yourself during preoperative assessment include the following:

- Is the patient alert and maintaining his or her airway?
- Is the bleeding active?
- Has the patient been adequately resuscitated?

Inadequate volume resuscitation, anemia, swallowing of blood (increasing the risk of aspiration), and compromised airway visualization are all critical issues. As the patient continues to manifest hypotension and tachycardia, more aggressive volume resuscitation should be employed. Laboratory values will help identify the severity of anemia (and thus the need for preoperative transfusion), coagulation issues (platelet count, prothrombin time, partial thromboplastin time, and international normalized ratio values), and the need to order clotting factors or platelets. Additionally, laboratory values can help determine acidosis and volume contraction necessitating

additional crystalloid administration.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:828–829.

Fields R, Gencorelli F, Litman R. Anesthetic management of the pediatric bleeding tonsil. *Paediatr Anaesth*. 2010;20(11):982–986.

Randall DA, Hoffer ME. Complications of tonsillectomy and adenoidectomy. *Otolaryngol Head Neck Surg*. 1998;118(1):61–68.

Windfuhr JP, Schloendorff G, Sesterhenn AM, et al. A devastating outcome after adenoidectomy and tonsillectomy: ideas for improved prevention and management. *Otolaryngol Head Neck Surg*. 2009;140:191–196.

B.2. What will you set up in the operating room for this patient? How will your preparation be different from a routine general anesthetic set up?

Along with standard operating room equipment, additional items to have prepared in the procedure room include the following:

- Blood transfusion tubing along with a fluid warmer
- Double suction set up with Yankauer suction tips, as one may become occluded with blood clots)
- Multiple sizes of stylet cuffed endotracheal tubes
- Backup laryngoscope blades/handles
- Emergency airway equipment (McGrath videolaryngoscope, GlideScope, fiberoptic intubation equipment)
- Resuscitation medications
- A tracheostomy set in the unlikely need of an emergency surgical airway

The temperature in the operating room should also be increased to minimize heat loss in the patient.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:828–829.

Fields R, Gencorelli F, Litman R. Anesthetic management of the pediatric bleeding tonsil. *Paediatr Anaesth*. 2010;20(11):982–986.

B.3. Should you plan to use vasopressors?

If the patient is hemodynamically unstable, vasopressors can be titrated until the patient is able to be adequately volume resuscitated. A blood type and crossmatch should be done, laboratory tests should be sent, and the patient should be given fluids and/or blood products in the operating room. Vasopressors should also be considered if the patient has a cardiac history, pulmonary hypertension, or if there is a need to manage the blood pressure tightly.

B.4. The patient seems anxious. Will you administer a sedative to calm the patient down?

The decision to administer preoperative sedation should be weighed against the patient's increased risk for regurgitation and aspiration as well as the potential for respiratory depression. Thus, preoperative sedation in this patient is likely not a wise decision.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 7th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:1359.

B.5. How do you plan on interpreting this patient's laboratory results?

The need for blood transfusion should be based on hemoglobin/hematocrit assessment and ongoing blood loss. Although recognizing optimal oxygen-carrying capacity is imperative, the threshold for transfusion should be addressed and discussed with the parents and surgical team preoperatively.

B.6. What are your expectations of the surgeon, specifically as it relates to induction of anesthesia?

The surgeon should be gowned and gloved with a headlight on when the patient enters the operating room. The surgeon should have a rigid bronchoscope and a tracheotomy set ready in addition to standard surgical equipment.

Windfuhr JP, Schloendorff G, Sesterhenn AM, et al. A devastating outcome after adenoidectomy and tonsillectomy: ideas for improved prevention and management. *Otolaryngol Head Neck Surg*. 2009;140:191–196.

C. Intraoperative Management

C.1. What is your plan for induction of anesthesia? During the initial procedure, this patient underwent an uneventful inhalational induction, with postinduction intravenous (IV) placement. Would you perform an inhalational induction again? Why or why not?

Adequate preoxygenation is essential to ensuring maximal oxygen reserves in the functional residual volume in the unlikely event of an airway issue. A preinduction nasogastric tube should also be placed to evacuate any gastric contents and/or blood. Rapid sequence induction should be performed with cricoid pressure (Sellick maneuver) using IV propofol if the patient is hemodynamically stable, or etomidate or ketamine if the patient is unstable. High-dose rocuronium or succinylcholine can be administered for rapid paralysis. If succinylcholine is deemed appropriate and safe, an anticholinergic, such as glycopyrrolate, should be administered prior to succinylcholine to minimize vagal response.

Curley GF. Rapid sequence induction with rocuronium—a challenge to the gold standard. *Crit Care*. 2011;15(5):190.

Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*. 9th ed. Philadelphia, PA: Elsevier; 2017:828–829.

C.2. What is your plan for management of blood in the oropharynx?

There should be two large-bore suction catheters ready prior to anesthesia induction and intubation. Suctioning should be done

carefully, as disruption of formed clots may cause an exacerbation of the bleeding. If suctioning is needed, the suction catheter should be directed into the midline of the oropharynx, avoiding the tonsillar fossae. Once the bleeding is surgically controlled, suctioning of the stomach can be done carefully and with direct visualization of the oropharynx.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. Chichester, United Kingdom: Wiley-Blackwell; 2012:786.

C.3. What is your plan for airway management?

Airway management must proceed with a plan. Airway adjuvants, including a fiberoptic bronchoscope and a videolaryngoscope (if the patient's size warrants) should be in the operating room and ready for use. Multiple styleted, cuffed endotracheal tubes should also be in the operating room. Additionally, a double suction set up, a backup anesthesiologist, and an ear, nose and throat (ENT) surgeon should be present.

Fields R, Gencorelli F, Litman R. Anesthetic management of the pediatric bleeding tonsil. *Paediatr Anaesth*. 2010;20(11):982–986.

Weiss M, Dullenkopf A. Cuffed tracheal tubes in children: past, present and future. *Expert Rev Med Devices*. 2007;4:73–82.

C.4. Laryngoscopy and intubation prove challenging due to blood in the airway. What options do you have now?

Gently pressing on the chest to simulate respiration can create air bubbles at the glottic opening to guide placement of the endotracheal tube. Simultaneous suctioning of blood in the oropharynx by a second anesthesia provider may also be warranted to help the laryngoscopist focus on intubation.

Gregory GA, Andropoulos DB, eds. *Gregory's Pediatric Anesthesia*. 5th ed. Chichester, United Kingdom: Wiley-Blackwell; 2012:786.

C.5. What is your plan for maintenance of the anesthetic? What other medications might you want to give?

Maintenance of the anesthetic will depend both on the patient's hemodynamic stability and surgical cessation of bleeding. Given the usual brevity of these procedures, it is important to exercise caution when choosing to administer IV narcotics as this can prolong respiratory depression. As such, IV acetaminophen (12.5 mg/kg) might be considered a better alternative for analgesia. Inhalational anesthetics are appropriate for maintenance. Antiemetics, such as ondansetron (0.15 mg/kg) and dexamethasone (0.15 mg/kg) should also be administered.

Baugh RF, Archer SM, Mitchell RB, et al. Clinical practice guideline: tonsillectomy in children. *Otolaryngol Head Neck Surg*. 2011;144(suppl 1):S1–S30.

C.6. Assuming the surgical intervention is successful, what is your plan for emergence and extubation?

Once hemostasis and hemodynamic stability are achieved, and the decision is made to extubate, gastric contents should be suctioned, paralysis reversal should be confirmed by a twitch monitor, and the patient should be awake and responsive with laryngeal reflexes.

Fields R, Gencorelli F, Litman R. Anesthetic management of the pediatric bleeding tonsil. *Paediatr Anaesth*. 2010;20(11):982–986.

Tomkinson A, Harrison W, Owens D, et al. Postoperative hemorrhage following adenoidectomy. *Laryngoscope*. 2012;122:1246–1253.

D. Postoperative Management

D.1. Is postoperative management in the pediatric intensive care unit (PICU) indicated?

Deciding whether to admit patients to the PICU status post-tonsillectomy hemorrhage should be jointly determined by the

anesthesiologist and surgeon. Assuming the patient does not have significant comorbidities and had an uneventful intraoperative course, admission to the postanesthesia care unit (PACU) is appropriate and safe for management until discharge criteria are met and the patient is able to go home (**Table 45.1**).

TABLE 45.1 PACU Discharge Criteria for the Pediatric (Under 13 Years of Age) Patient

Infant <1 Year			
Optimal Pain Relief Achieved	□ YES	□ NO	
1. BP within Pre-op Value/Age-specific range	□ YES	□ NO	
2. HR 120-160	□ YES	□ NO	
A. Unchanged from Pre-op Rhythm?	□ YES	□ NO	□ N/A
3. LOC: Awake or at Pre-op Baseline	□ YES	□ NO	
4. Temp 36-38 Centigrade	□ YES	□ NO	
5. Respiratory Rate 30-60	□ YES	□ NO	
A. O2 Sat ≥ 94% or at Pre-op Baseline (if < 94%)	□ YES	□ NO	
6. Dressing Dry	□ YES	□ NO	□ N/A
7. Urinary Output Adequate for Size	□ YES	□ NO	□ N/A
Age 1 to 5 Year			
Optimal Pain Relief Achieved	□ YES	□ NO	
1. BP within Pre-op Value/Age-specific range	□ YES	□ NO	
2. HR 80-150	□ YES	□ NO	
A. Unchanged from Pre-op Rhythm?	□ YES	□ NO	□ N/A
3. LOC: Awake or at Pre-op Baseline	□ YES	□ NO	
4. Temp 36-38 Centigrade	□ YES	□ NO	
5. Respiratory Rate 20-30	□ YES	□ NO	
A. O2 Sat ≥ 94% or at Pre-op Baseline (if < 94%)	□ YES	□ NO	
6. Dressing Dry	□ YES	□ NO	□ N/A
7. Urinary Output Adequate for Size	□ YES	□ NO	□ N/A
Age 6 to 12 Year			
Optimal Pain Relief Achieved	□ YES	□ NO	
1. BP within Pre-op Value/Age-specific range	□ YES	□ NO	
2. HR 60-130	□ YES	□ NO	
A. Unchanged from Pre-op Rhythm?	□ YES	□ NO	□ N/A
3. LOC: Awake or at Pre-op Baseline	□ YES	□ NO	
4. Temp 36-38 Centigrade	□ YES	□ NO	
5. Respiratory Rate 12-20	□ YES	□ NO	

A. O2 Sat ≥ 94% or at Pre-op Baseline (if ≤ 94%)	□ YES	□ NO	
6. Dressing Dry	□ YES	□ NO	□ N/A
7. Urinary Output Adequate for Size	□ YES	□ NO	□ N/A

Reprinted with permission from the New York-Presbyterian Perioperative Nursing Post Anesthesia Record.

Lescanne E, Chiron B, Constant I, et al. Pediatric tonsillectomy: clinical practice guidelines. *Eur Ann Otorhinolaryngol Head Neck Dis*. 2012;129:264–271.

Windfuhr JP. Lethal post-tonsillectomy hemorrhage. *Auris Nasus Larynx*. 2003;30:391–396.

D.2. What would you require for safe transport from the operating room to the PICU?

Positioning the patient in the left or right lateral position can reduce the risk of airway obstruction. Supplemental oxygen, emergency airway equipment, and emergency medications are essential for safe transport. If transport over a long distance is required, monitoring equipment should also be employed.

Randall DA, Hoffer ME. Complications of tonsillectomy and adenoidectomy. *Otolaryngol Head Neck Surg*. 1998;118(1):61–68.

D.3. Discuss potential postoperative complications for this patient.

Potential postoperative complications include fever, intravascular volume depletion, airway edema, coagulopathy, anemia, and electrolyte disturbances. Although rare, a rebleed may also occur. If stridor is present postextubation, humidified oxygen and nebulized racemic epinephrine (0.25 mL of 2.25% solution diluted to 3 mL with normal saline) should be promptly administered.

Guida RA, Mattucci KF. Tonsillectomy and adenoidectomy: an inpatient or outpatient procedure? *Laryngoscope*. 1990;100(5):491–493.

Leach J, Manning S, Schaefer S. Comparison of two methods of tonsillectomy. *Laryngoscope*. 1993;103:619–622.

D.4. What discharge instructions should be given post-tonsillectomy?

After discharge criteria are met, patients (and their parents) should be instructed to visit the nearest emergency room in the event of ongoing bleeding. In addition, patients should be encouraged to hydrate and add soft solids to their diet as tolerated. Pharmacologic interventions for pain management should be determined on an individual basis but should aim to minimize the use of narcotics and maximize the use of acetaminophen.

Baugh RF, Archer SM, Mitchell RB, et al. Clinical practice guideline: tonsillectomy in children. *Otolaryngol Head Neck Surg*. 2011;144(suppl 1):S1–S30.

SECTION 11 Pain Management and Neuraxial Blocks

46 Brachial Plexus Block

Tiffany Tedore and William Urmey

A 72-year-old man presents after sustaining a fall and right proximal humeral fracture. The patient's history is remarkable for hypertension and significant chronic obstructive pulmonary disease (COPD). He has a 30 pack-year cigarette smoking history. His only other remarkable history is that he claims to have fainted several times in his life. Recent pulmonary function tests 6 months before admission include a forced vital capacity (FVC) of 1.4 L (33% predicted). The patient's routine medications include atenolol and chlorthalidone. Hydromorphone 1 mg was administered intravenously in the emergency room.

A. Medical Disease and Differential Diagnosis

1. What are the presenting problems in this patient?
2. What additional medical history would you want to obtain?
3. What implications does the use of atenolol have on the

patient's coexisting medical condition?

4. Why is immobilization of the arm important following humeral fracture?
5. What nerve is at particular risk for injury from humeral fracture?

B. Preoperative Evaluation and Preparation

1. What testing would be helpful to elucidate the cause of this patient's fainting spells?
2. What premedication would you order?
3. What are the respiratory effects of benzodiazepines?

C. Intraoperative Management

1. What anesthetic technique would you use?
2. Describe the relevant anatomy of the brachial plexus.
3. What relevant anatomic structures in the neck and below the neck can be injured or injected accidentally during brachial plexus block?
4. What regional technique would you choose to block the brachial plexus in this patient?
5. What are the advantages and disadvantages of the following blocks?
   a. Interscalene block
   b. Supraclavicular block
   c. Infraclavicular block
   d. Axillary block
6. Describe the landmarks and procedures for nerve stimulator and ultrasound-guided interscalene block.
7. Describe the landmarks and procedures for supraclavicular block.
8. Describe the landmarks and procedures for infraclavicular block.
9. Describe the landmarks and procedures for axillary block.
10. The patient requests to have the brachial plexus block

performed after you administer general anesthesia. Would you agree to this request?

11. What relevant respiratory complications or side effects are you concerned about in this patient?
12. What is the incidence of hemidiaphragmatic paresis following interscalene brachial plexus block? Can this complication be avoided by decreasing the volume or concentration of local anesthetic injected or by using ultrasound-guided supraclavicular block?
13. Describe the pulmonary function changes that occur after interscalene brachial plexus block.
14. What would you do if the patient complained of dyspnea after you performed an interscalene or supraclavicular block?
15. The surgeon prefers to perform the surgical procedure in the sitting position. What are the advantages and disadvantages of this position compared to the lateral position in this patient?
16. Which nerves are most commonly missed with axillary brachial plexus block? With interscalene block? With all brachial plexus blocks?
17. What is the expected duration of brachial plexus block with 30 mL of 1.5% mepivacaine with 5 μg per mL epinephrine?
18. What is the maximum safe dose of local anesthetic for brachial plexus block?

D. Postoperative Management

1. What regimen would you suggest for postoperative pain management?
2. In the postanesthesia care unit, the patient complains of dyspnea. How would you evaluate and manage this?
3. On the third postoperative day after removal of the brachial plexus catheter, the patient complains of persistent numbness and paresthesia in the ulnar nerve distribution. What would you tell the patient? How would you manage neurologic

dysfunction after brachial plexus block that persists for 1 week?

A. Medical Disease and Differential Diagnosis

A.1. What are the presenting problems in this patient?

The patient presented for urgent surgery for a proximal humeral fracture and may have some internal bleeding. The patient has significant COPD, most likely secondary to his long cigarette smoking history, and has a history of multiple fainting episodes in the past. He also has chronic hypertension.

A.2. What additional medical history would you want to obtain?

It is important to know if the patient's fall was precipitated by a fainting episode or if the patient simply tripped or lost footing. The patient should be questioned whether any additional trauma occurred at the time of the fall. Has the patient's history of fainting been evaluated in the past? Does the patient have any known cardiac problems? Does he have any history of stroke or carotid disease?

A.3. What implications does the use of atenolol have on the patient's coexisting medical condition?

The patient's use of atenolol may exacerbate COPD, especially if there is a reversible component of airway disease. It would be useful to determine whether the atenolol is being taken for the treatment of hypertension or syncope. Although β-blockers have been commonly used for vasovagal reflex syncope, large long-term controlled trials do not support their efficacy. The American College of Cardiology/American Heart Association/Heart Rhythm Society (ACC/AHA/HRS) and the European Society of Cardiology (ESC) guidelines do not

recommend their use. There is some evidence that in adults older than 42 years of age, β-blockers may be protective with regard to development of severe bradycardia or sudden asystole during surgical procedures performed in the "beach chair" or head-up position.

Brignole M, Moya A, deLange FJ, et al. 2018 ESC guidelines for the diagnosis and management of syncope. *Eur Heart J*. 2018;39:1883.

Shen WK, Sheldon RS, Benditt DG, et al. 2017 ACC/AHA/HRS guideline for the evaluation and management of patients with syncope: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *Circulation*. 2017;136(5):e60–e122.

A.4. Why is immobilization of the arm important following humeral fracture?

Immobilization of the arm following humeral fracture is important to avoid injury to the brachial plexus or its terminal branches.

A.5. What nerve is at particular risk for injury from humeral fracture?

The axillary nerve is at greatest risk from a proximal humerus fracture, and the radial nerve is at risk with midshaft humeral fracture. Following proximal humeral fracture, the shoulder can be dislocated and malpositioning can cause stretching or pressure on components of the brachial plexus, especially the axillary nerve. To this extent, it is important to verify and document any preexisting neurologic findings on examination, especially if brachial plexus block is being considered.

B. Preoperative Evaluation and Preparation

B.1. What testing would be helpful to elucidate the cause of this patient's fainting spells?

Syncope is defined by a complete loss of consciousness that is of rapid onset and short duration, accompanied by loss of postural tone and a complete and spontaneous recovery. The major categories of syncope include reflex or neurally mediated syncope (vasovagal, situational, carotid sinus), orthostatic syncope (autonomic failure, drug-induced, hypovolemia), and cardiac syncope (arrhythmia, drug-induced, structural disease). Syncope is fairly common, affecting approximately 11% of the population. Vasovagal syncope is the most common cause, accounting for 21% of cases. Most affected patients experience a first episode between the ages of 10 and 30 years; only 5% of patients experience their first episode after age 40 years. The incidence of syncope increases with age, peaking after the age of 65 years.

The workup of syncope should include a detailed history and physical examination, including a measurement of orthostatic blood pressure and an electrocardiogram. An echocardiogram is indicated if the history or physical exam is suggestive of cardiac disease. Tilt-table testing or a neurologic workup may also be appropriate depending on the history and physical exam.

This patient had a prior evaluation that documented an abnormal response to head-up tilt-table testing during isoproterenol infusion and received a diagnosis of reflex (vasovagal) syncope. He has managed this conservatively with physical maneuvers (sitting, leg crossing) upon feeling faint and has not experienced a complete loss of consciousness for over 20 years.

Brignole M, Moya A, deLange FJ, et al. 2018 ESC guidelines for the diagnosis and management of syncope. *Eur Heart J*. 2018;39:1883.

Shen WK, Sheldon RS, Benditt DG, et al. 2017 ACC/AHA/HRS guideline for the evaluation and management of patients with syncope: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *Circulation*. 2017;136(5):e60–e122.

Soteriaces E, Evans J, Larson M, et al. Incidence and prognosis of syncope. *N Engl J Med*. 2002;347:878–885.

B.2. What premedication would you order?

This patient has already received a recent significant intravenous dose of hydromorphone in the emergency room. The patient may not require any additional medication. If the patient is anxious, and assuming that a careful history rules out any significant problems or other drug intake, intravenous midazolam can be carefully administered in the operating room while the patient is monitored with pulse oximetry in the presence of the anesthesia practitioner. Additional opioids may be avoided if he is not in pain.

B.3. What are the respiratory effects of benzodiazepines?

Although benzodiazepines cause a dose-related, centrally mediated respiratory depression, overall respiratory depression is not nearly as profound as with the administration of intravenous opioids. Use of carefully administered smaller therapeutic doses of midazolam is usually well tolerated, without significant respiratory depression. Use of benzodiazepines has been shown to elevate the seizure threshold during local anesthetic administration.

Arcangeli A, Antonelli M, Mignani V, et al. Sedation in PACU: the role of benzodiazepines. *Curr Drug Targets*. 2005;6:745–748.

C. Intraoperative Management

C.1. What anesthetic technique would you use?

Both interscalene and supraclavicular brachial plexus blocks provide excellent operating conditions and allow for postoperative analgesia. Interscalene block may provide better coverage if arthrotomy is required. Concomitant intravenous sedation and oxygen via nasal cannula may be appropriate, or

laryngeal mask airway or endotracheal intubation may be preferred depending on the surgical positioning and access to the airway.

C.2. Describe the relevant anatomy of the brachial plexus.

The brachial plexus supplies the nerves to the upper limb. It is formed by the ventral primary divisions of the fifth to the eighth cervical and the first thoracic nerves, with possible contributions from the fourth cervical and second nerve thoracic roots. The roots join to form the superior, middle, and inferior trunks, which divide into anterior and posterior divisions (**Fig. 46.1**). The three posterior divisions form the posterior cord, whose major branches are the radial and the axillary nerves. The upper two anterior divisions form the lateral cord, whose major branches are the musculocutaneous nerve and the lateral root of the median nerve. The lowest anterior division forms the medial cord, which gives the medial root to the median nerve and terminates as the ulnar nerve. The sympathetic contributions to the brachial plexus are derived from the middle cervical ganglion and the stellate ganglion.

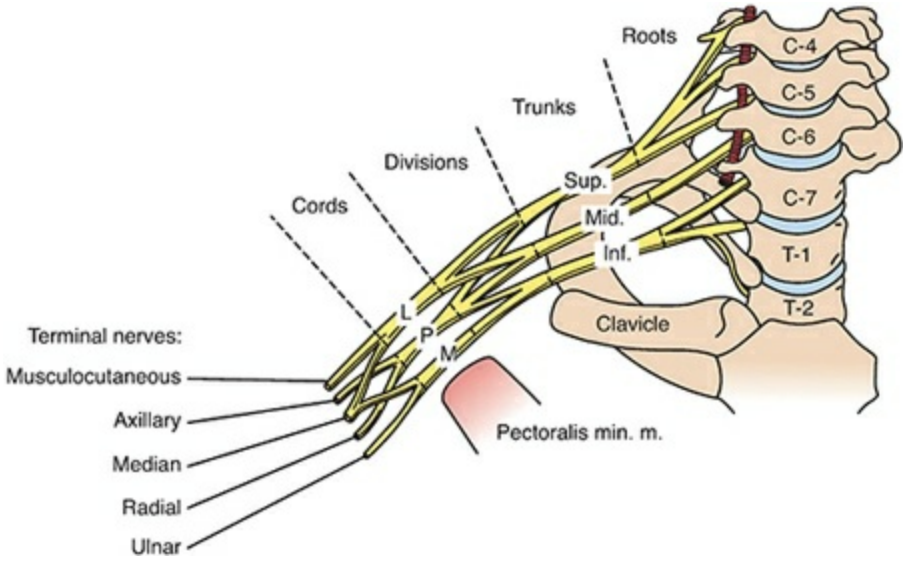

FIGURE 46.1. The brachial plexus. The roots join to form the superior (Sup.), middle (Mid.), and inferior (Inf.) trunks, which divide into anterior and posterior divisions. L, lateral; M, medial; P, posterior.

The brachial plexus begins at the level of the nerve roots, usually at C5–T1. It is at this level that the interscalene brachial plexus block, first described by Winnie, is performed. Injections at this level result in a block with central characteristics, much like a one-sided neuraxial block. Resulting sensory block at this level is characterized by a dermatomal pattern. If the block is incomplete, the typical cause is inadequate spread of local anesthetic to certain nerve roots. For example, the C8–T1 nerve roots are often spared during interscalene block anesthesia because local anesthetic distribution fails to include the lower, most caudal, nerve roots of the brachial plexus. As the brachial plexus courses more peripherally from the neck to the axilla, the nerve roots transform to trunks, divisions, and cords and finally form fully differentiated peripheral nerves. At the level of the axilla, where axillary block is performed, the plexus is composed of terminal nerves that include the median, radial, ulnar, and musculocutaneous nerves. At this level, an incomplete block typically spares sensory or motor blockade in the distribution of a given peripheral nerve, for example, the lateral antebrachial cutaneous nerve (the terminal sensory branch of the musculocutaneous nerve), which exits the surrounding fascia high in the brachial plexus. At this level, the nerves are spread out anatomically around the axillary artery and, depending upon the location of the needle tip during injection and the volume of local anesthetic, any of the four nerves could be spared. This has resulted in the description of multiple injection techniques for axillary block to ensure complete brachial plexus anesthesia.

At the level of the nerve roots or trunks, the brachial plexus is simply a neural plexus, being devoid of major consistently identifiable blood vessels. At this level, brachial plexus identification (i.e., needle tip location) relies on a neural response (paresthesia or motor response to electrical nerve

stimulation) or direct imaging (e.g., using ultrasonographic guidance) of the neural tissue itself. At the level of the clavicle and first rib, the plexus is adjacent to the subclavian artery, which continues as the axillary artery. At this level or below, one can use the blood vessels as landmarks by palpation, Doppler flow guidance, or ultrasonographic guidance to assist in the performance of brachial plexus block.

Mian A, Chaudhry I, Huang R, et al. Brachial plexus anesthesia: a review of the relevant anatomy, complications, and anatomical variations. *Clin Anat*. 2014;27(2):210–221.

Neal JM, Gerancher JC, Hebl JR, et al. Upper extremity regional anesthesia: essentials of our current understanding, 2008. *Reg Anesth Pain Med*. 2009;34:134–170.

Urmey WF. Pulmonary complications. In: Neal JM, Rathmell J, eds. *Complications in Regional Anesthesia and Pain Medicine*. Philadelphia, PA: Saunders; 2007:147–156.

Winnie AP. Interscalene Brachial Plexus Block. *Anesth Analg*. 1970;49:455–466.

C.3. What relevant anatomic structures in the neck and below the neck can be injured or injected accidentally during brachial plexus block?

The brachial plexus in the neck has multiple significant anatomic relationships that include the phrenic nerve, subarachnoid space, epidural space, spinal cord, proximal nerve roots, vertebral artery, jugular veins, and the apex of the lung. Errant needle passes can hit any one of these, and in fact, there are published case reports of complications from needle injury or local anesthetic injection for each of these anatomic structures.

Below the neck, the major relevant structures are the blood vessels in the neurovascular plexus, which include the subclavian artery and vein, which more distally become the axillary artery and vein, as well as the parietal pleural, visceral

pleural, and lung.

Mian A, Chaudhry I, Huang R, et al. Brachial plexus anesthesia: a review of the relevant anatomy, complications, and anatomical variations. *Clin Anat*. 2014;27(2):210–221.

C.4. What regional technique would you choose to block the brachial plexus in this patient?

Interscalene block provides the most complete anesthetic block for shoulder surgery. The supraclavicular block has not historically been used for shoulder surgery due to the concern that it may spare the supraclavicular (C3–C4) and suprascapular (C5–C6) nerves and thus not provide anesthesia for the entire shoulder joint and skin over the cape of the shoulder. Recent experience suggests that at higher volumes of local anesthetic (50 mL), supraclavicular block provides equivalent anesthetic conditions to interscalene block. The supraclavicular block may also have a decreased incidence of phrenic nerve blockade when compared to the interscalene block when lower volumes of local anesthetic (20 mL) are used, although this is not guaranteed. If coverage of the shoulder cape is a concern with the use of lower volumes of local anesthetic, the supraclavicular nerve can be anesthetized separately with a superficial cervical plexus block. If the avoidance of phrenic nerve block is to be assured, a combination of more distal blocks, such as the suprascapular and axillary nerve blocks, can be used for shoulder analgesia but will not provide full anesthetic coverage.

Eckmann MS, Bickelhaupt B, Fehl J, et al. Cadaveric study of the articular branches of the shoulder joint. *Reg Anesth Pain Med*. 2017;42:564–570.

Liu S, Gordon M, Shaw P, et al. A prospective clinical registry of ultrasound-guided regional anesthesia for ambulatory shoulder surgery. *Anesth Analg*. 2010;111:617–623.

Neal JM, Gerancher JC, Hebl JR, et al. Upper extremity regional anesthesia: essentials of our current understanding, 2008. *Reg Anesth Pain Med*. 2009;34:134–170.

Renes SH, Spoormans HH, Gielen MJ, et al. Hemidiaphragmatic paresis can be avoided in ultrasound-guided supraclavicular brachial plexus block. *Reg Anesth Pain Med*. 2009;34:595–599.

Tran DQ, Elgueta MF, Aliste J, et al. Diaphragm-sparing nerve blocks for shoulder surgery. *Reg Anesth Pain Med*. 2017;42:32–38.

C.5. What are the advantages and disadvantages of the following blocks?

a. Interscalene block
b. Supraclavicular block
c. Infraclavicular block
d. Axillary block

Interscalene Block

One advantage of the interscalene block is a superficial location that makes it easily accessible by paresthesia, nerve stimulation, or ultrasonographic guidance techniques. Injection of an adequate volume of local anesthetic at the interscalene level results in reliably complete anesthesia or analgesia for surgery on or about the shoulder, including proximal humeral surgery. A single injection results in success rates approaching 100%. A catheter can be easily placed at this site. This technique blocks the axillary nerve to the deltoid and the musculocutaneous nerve to the biceps brachialis derived from the C5–C6 nerve roots and therefore guarantees reliable relaxation of the deltoid and biceps muscles. This block also reliably anesthetizes the distribution of the supraclavicular nerve (C3–C4), which supplies sensory innervation to the cape of the shoulder, as well as the suprascapular (C5–C6) and lateral pectoral nerves (C5–C7), which innervate the shoulder joint, adjacent ligaments, and soft tissues. This allows optimal surgical exposure and facilitates dislocation of the humeral head from the glenoid socket. If performed properly, it is unlikely to cause a pneumothorax with an appropriate-sized needle using this approach.

Disadvantages include the close proximity of the phrenic

nerve, or perhaps nerve root marginalization of those fibers contributing to phrenic nerve formation, which has rarely resulted in injury to these structures and reported cases of permanent phrenic nerve palsy. Interscalene block with a volume of local anesthetic adequate for surgery results in 100% incidence of ipsilateral hemidiaphragmatic paresis.

Supraclavicular Block

The supraclavicular block is used for surgeries distal to and including the shoulder, although this block may spare the supraclavicular nerve (C3–C4) supplying sensation to the skin over the top of the shoulder, as well as the suprascapular nerve (C5–C6), which innervates the shoulder joint and adjacent ligaments and soft tissues. If being performed for shoulder surgery, the supraclavicular block may be supplemented with a superficial cervical plexus block and/or a suprascapular block. The supraclavicular block is most commonly performed using ultrasound guidance. It can also be performed with the subclavian perivascular or "plumb-bob" approaches. Advantages of ultrasound-guided supraclavicular block include superficial location of the artery and plexus that allow for easy imaging and perivascular block. Also, one is able to visualize two-dimensional local anesthetic distribution and can avoid inadvertent puncture or injection into the vessels. Disadvantages include the intimate proximity to the apex of the lung with a risk of pneumothorax following this block. Supraclavicular block is associated with a variable incidence of diaphragmatic paresis.

Infraclavicular Block

The infraclavicular block is used for procedures distal to the shoulder. It can be performed with nerve stimulation or ultrasound guidance. One advantage of the ultrasound-guided infraclavicular block is the visualization of the artery, which facilitates imaging for perivascular brachial plexus block. The

block does not require positioning of the upper extremity. It is easy to place a catheter at a central location of the plexus via this approach. Disadvantages are related to the depth of the plexus at this level. This may cause more discomfort during placement as the needle must pass through both the pectoralis major and minor muscles.

Axillary Block

The axillary block is utilized for anesthesia distal to the elbow. This block is characterized by the major advantage of the superficial location of the individual terminal branches of the brachial plexus. Thus, one can target the fully differentiated terminal nerves by using either nerve stimulation, paresthesia, or ultrasound-guided techniques. Disadvantages include the need to locate more than one nerve to guarantee successful brachial plexus block at this level. The musculocutaneous nerve is often located relatively distant to the other terminal nerves, lying within the body of the coracobrachialis muscle or between the coracobrachialis and biceps muscles and usually requires a separate injection.

Chan V. *A Practical Guide to Ultrasound Imaging for Regional Anesthesia: Part 2—Upper Limb Blocks. Version 1.1*. Toronto, Canada: Toronto Centre for Ultrasound Education; 2013:72–73.

Macfarlane AJ, Perlas A, Chan V, et al. Eight ball, corner pocket ultrasound-guided supraclavicular block: avoiding a scratch. *Reg Anesth Pain Med*. 2008;33:502–504.

Neal JM, Gerancher JC, Hebl JR, et al. Upper extremity regional anesthesia: essentials of our current understanding, 2008. *Reg Anesth Pain Med*. 2009;34:134–170.

Neal JM, Moore JM, Kopacz DJ, et al. Quantitative analysis of respiratory, motor, and sensory function after supraclavicular block. *Anesth Analg*. 1998;86:1239–1244.

Petrar SD, Seltenrich ME, Head SJ, et al. Hemidiaphragmatic paralysis following ultrasound-guided supraclavicular versus infraclavicular brachial plexus blockade: a randomized clinical trial. *Reg Anesth Pain Med*. 2015;40:133–138.

Renes SH, Spoormans HH, Gielen MJ, et al. Hemidiaphragmatic paresis can be avoided in ultrasound-guided supraclavicular brachial plexus block. *Reg Anesth Pain Med*. 2009;34:595–599.

Soares LG, Brull R, Lai J, et al. Eight ball, corner pocket: the optimal needle position for ultrasound-guided supraclavicular block. *Reg Anesth Pain Med*. 2007;32:94–95.

Urmey WF. Pulmonary complications. In: Neal JM, Rathmell J, eds. *Complications in Regional Anesthesia and Pain Medicine*. Philadelphia, PA: Saunders; 2007:147–156.

C.6. Describe the landmarks and procedures for nerve stimulator and ultrasound-guided interscalene block.

For interscalene block by electrical nerve stimulation, the patient's head is turned away from the side of the block at an approximately 45-degree angle with the surface of the bed or table. The interscalene groove (between the anterior and middle scalene muscles) is located by palpation just posterior to the lateral border of the sternocleidomastoid muscle. The electrically shielded stimulating needle is introduced in a dorsal, medial, and caudal direction until an appropriate motor response is elicited. Because of the orientation of the nerve roots in a cephalocaudad plane, a response from C5–C6 nerve roots is most frequently obtained first. C5–C6 motor response is characterized by deltoid, biceps, or brachioradialis muscle contractions. Reduction of electrical current amplitude below 0.5 mAmp at a pulse duration of 0.1 millisecond results in a success rate with single injection close to 100%.

For interscalene block by ultrasonographic guidance (**Figs. 46.2** to **46.4**, **Video 46.1**), either an in-plane or out-of-plane approach can be used, depending on the experience and preference of the operator. For an in-plane approach, the needle is inserted in a posterolateral to anteromedial direction along the long axis of a high-frequency linear array transducer with the needle shaft and tip visualized. The middle and anterior scalene muscles should be visualized, and the hypoechoic nerve roots

are usually stacked in a somewhat cephalocaudad arrangement. Injection should be made so that real-time spread of anesthetic can be visualized within the brachial plexus sheath spreading the cross-sectional nerve roots apart.

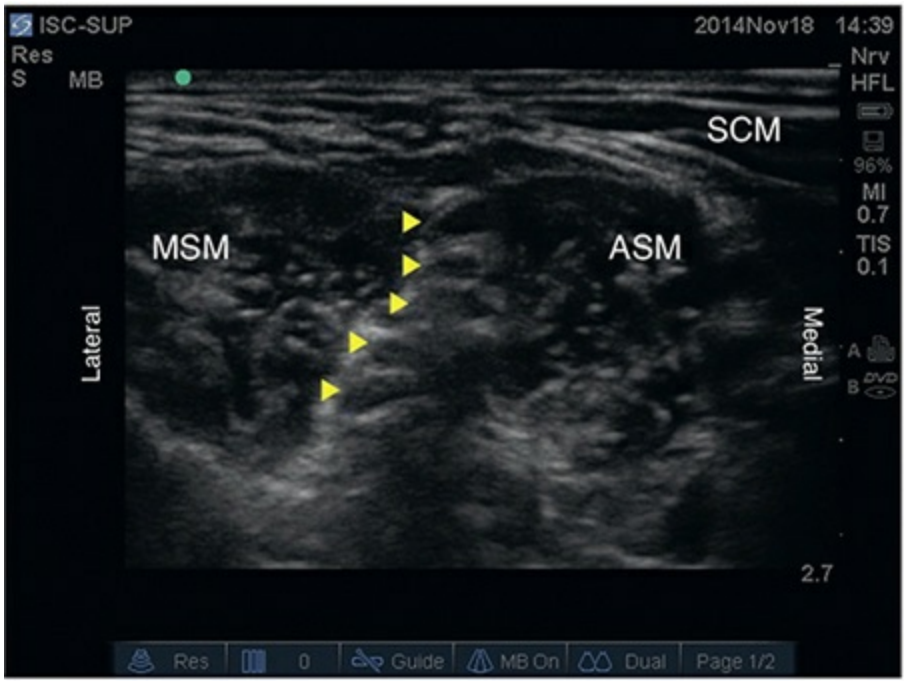

FIGURE 46.2. Ultrasound image of interscalene groove. The hypoechoic nerve roots of the brachial plexus *(yellow arrowheads)* can be seen between the anterior scalene muscle (ASM) and middle scalene muscle (MSM). SCM, sternocleidomastoid muscle.

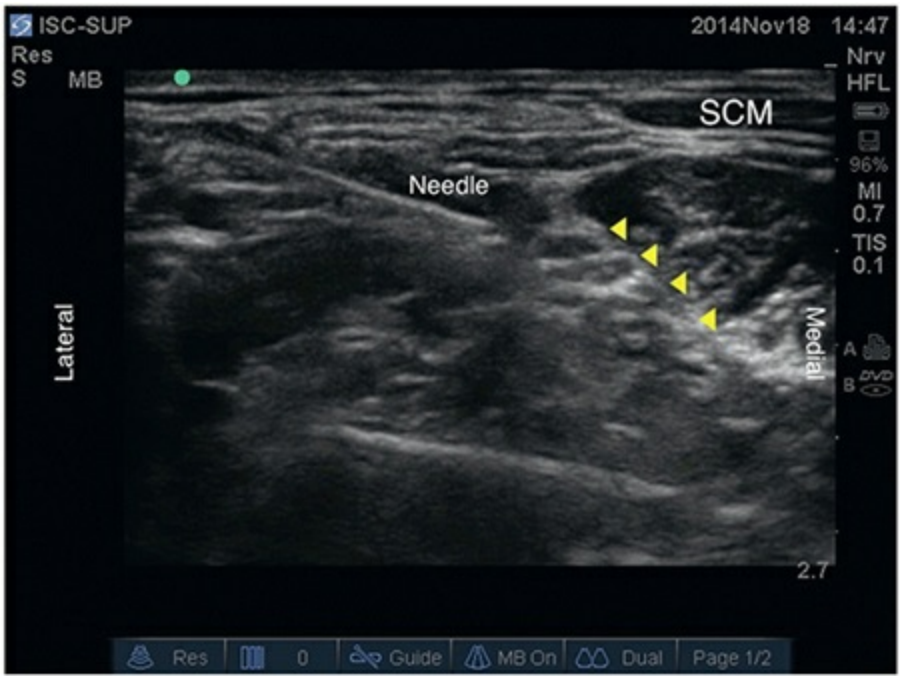

FIGURE 46.3. Ultrasound-guided interscalene block. The needle can be seen approaching the nerve roots *(yellow arrowheads)* in the interscalene groove from the lateral to medial direction. SCM, sternocleidomastoid muscle.

FIGURE 46.4. Ultrasound-guided interscalene block. Hypoechoic local anesthetic *(white arrowheads)* can be seen surrounding the brachial plexus in the interscalene groove. SCM, sternocleidomastoid muscle.

For an out-of-plane approach, the high-frequency linear array

transducer may be placed just caudal to the conventional interscalene block injection point and just above the clavicle. The longitudinal axis of the transducer is oriented in a posterolateral to anteromedial direction, with the center of the probe overlying the interscalene space and the image of the nerve roots, which again will be hypoechoic in cross-section. The needle is introduced in a slightly dorsal, medial, and caudal direction, as originally described in the conventional technique by Winnie. It is technically challenging to observe the needle tip when using the out-of-plane approach. Tissue movement as seen on the ultrasound image can be used to guide needle placement, as can intermittent injection of small volumes of local anesthetic. Nerve stimulation can also be used to confirm position of the needle tip within the brachial plexus.

Chan V. *A Practical Guide to Ultrasound Imaging for Regional Anesthesia: Part 2—Upper Limb Blocks. Version 1.1*. Toronto, Canada: Toronto Centre for Ultrasound Education; 2013:17–32.

Goutier PE, Vandepitte C, Lopez AM. Ultrasound-guided interscalene block. In: Hadzic A, ed. *Hadzic's Textbook of Regional Anesthesia and Acute Pain Management*. 2nd ed. New York: McGraw-Hill; 2017:558–567.

Kapral S, Greher M, Huber G, et al. Ultrasonographic guidance improves the success rate of interscalene brachial plexus blockade. *Reg Anesth Pain Med*. 2008;33:253–258.

Winnie AP. Interscalene Brachial Plexus Block. *Anesth Analg*. 1970;49:455–466.

C.7. Describe the landmarks and procedures for supraclavicular block.

The divisions of the brachial plexus in the supraclavicular area are located cephaloposterior to the subclavian artery and superior to the first rib. Due to the high risk of subclavian artery puncture and pneumothorax with the perivascular and "plumb-bob" techniques, this block is predominately performed using ultrasound guidance. A high-frequency linear array transducer is

placed just above and parallel to the clavicle in the supraclavicular fossa (**Figs. 46.5** and **46.6**). In the resulting ultrasound image, the plexus can be visualized superior and lateral to the subclavian artery and directly above the first rib. The dome of the lung can be seen medial to the first rib. An in-plane posterolateral to anteromedial technique is generally used, making sure that the needle tip and shaft are visualized throughout manipulation of the needle and that the pleura is clearly seen. Local anesthetic is deposited at the superior aspect of the plexus for proximal procedures (shoulder, humerus) and in the "eight ball, corner pocket" between the subclavian artery, first rib, and brachial plexus for distal procedures (forearm, hand).

FIGURE 46.5. Ultrasound image of the supraclavicular fossa. The hypoechoic divisions of the brachial plexus *(yellow arrowheads)* can be seen superior and lateral to the subclavian artery (SA).

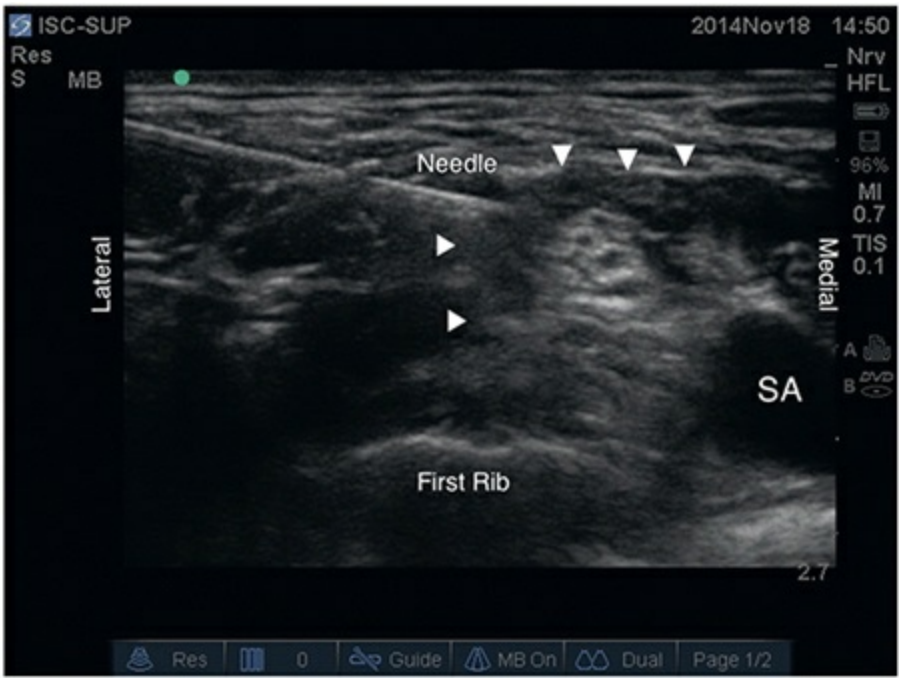

FIGURE 46.6. Ultrasound-guided supraclavicular block. The needle is positioned just superior and lateral to the brachial plexus. Hypoechoic local anesthetic *(white arrowheads)* can be seen surrounding the plexus. SA, subclavian artery.

Farag E, Mounir-Soliman L, eds. *Brown's Atlas of Regional Anesthesia*. 5th ed. Philadelphia, PA: Elsevier; 2017:45–54.

Hadzic A, ed. *Hadzic's Textbook of Regional Anesthesia and Acute Pain Management*. 2nd ed. New York: McGraw-Hill; 2017:568–573.

Soares LG, Brull R, Lai J, et al. Eight ball, corner pocket: the optimal needle position for ultrasound-guided supraclavicular block. *Reg Anesth Pain Med*. 2007;32:94–95.

C.8. Describe the landmarks and procedures for infraclavicular block.

The infraclavicular block is performed at the cord level of the brachial plexus near the second portion of the axillary artery. For the nerve stimulator approach, the patient is placed supine with the arm to be blocked abducted 90 degrees at the elbow. The coracoid process is palpated, and the needle insertion site is located 2 cm medial and 2 cm caudad to the process. The needle is inserted in a vertical parasagittal plane until a distal upper extremity motor response is elicited. The needle may be

redirected in a cephalocaudad arc if a response is not elicited on the initial attempt. The depth of the brachial plexus can vary from 3 to 10 cm depending on patient size.

The ultrasound-guided infraclavicular block (**Fig. 46.7**) is usually performed with the patient supine and with the arm either adducted at the side or abducted 90 degrees at the elbow. The ultrasound probe is placed in the deltopectoral groove just medial to the coracoid process. There is a large amount of variation in the precise location of the cords, but in this position, the lateral cord is most often located cephalad, the posterior cord posterior, and the medial cord caudad to the axillary artery. The medial cord may lie between the axillary artery and vein. Abduction of the arm to 90 degrees may improve visualization of the cords and will pull the clavicle down and away from the needle insertion site. A 10-cm needle is inserted in-plane and cephalad to the long axis of the probe, and the tip is positioned posterior to the axillary artery near the posterior cord. The steep insertion angle required and the depth of the brachial plexus at this level often results in poor visualization of the needle. The use of a small curvilinear probe and an echogenic needle may enhance needle visualization. The curvilinear probe allows greater room for needle entry and a wide sector view of the involved structures at the expense of reduced resolution when compared to a high-frequency linear probe. If all three cords are not easily identifiable, deposition of a ring of local anesthetic surrounding the axillary artery is associated with an effective block in 95% of cases. It may be necessary to reposition the needle and give multiple injections in order to surround all three cords.

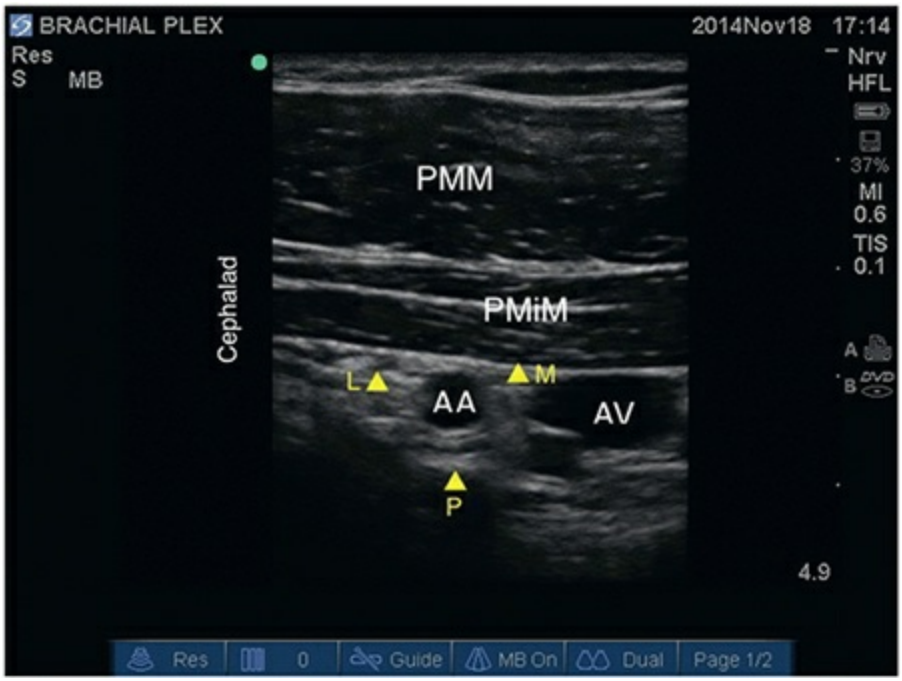

FIGURE 46.7. Ultrasound image of the infraclavicular region using a high-frequency linear probe. The lateral (L), posterior (P), and medial (M) cords can be seen surrounding the axillary artery (AA). AV, axillary vein; PMiM, pectoralis minor muscle; PMM, pectoralis major muscle.

Atchabatian A, Vandepitte C, Lopez AM. Ultrasound-guided infraclavicular block. In: Hadzic A, ed. *Hadzic's Textbook of Regional Anesthesia and Acute Pain Management*. 2nd ed. New York: McGraw-Hill; 2017:574–579.

Chan V. *A Practical Guide to Ultrasound Imaging for Regional Anesthesia: Part 2—Upper Limb Blocks. Version 1.1*. Toronto, Canada: Toronto Centre for Ultrasound Education; 2013:64–73.

Farag E, Mounir-Soliman L, eds. *Brown's Atlas of Regional Anesthesia*. 5th ed. Philadelphia, PA: Elsevier; 2017:59–68.

Ootaki C, Hayashi H, Amano M. Ultrasound-guided infraclavicular brachial plexus block: an alternative technique to anatomical landmark-guided approaches. *Reg Anes Pain Med*. 2000;25:600–604.

C.9. Describe the landmarks and procedures for axillary block.

In the axilla, the median, ulnar, and radial nerves lie close to the axillary artery and are surrounded by the biceps, triceps, and coracobrachialis muscles. The radial nerve generally lies between the axillary artery and the humerus. The musculocutaneous nerve separates from the lateral cord

proximal to the axilla and is often found between the biceps and coracobrachialis muscles.

For the nerve stimulator technique, the patient is positioned supine and the arm is abducted to 90 degrees and bent at the elbow. The patient's axillary artery is palpated, and a small-gauge electrically shielded stimulating needle is introduced just below the artery to elicit motor response from the radial nerve (deep to the artery) or ulnar nerve (medial to the artery; i.e., immediately below with the arm in this position). The needle is repositioned and advanced superficial to the artery for a median nerve motor response. Highest success rate correlates with at least two motor responses in which one response is from radial nerve stimulation. By insisting on current amplitude levels of 0.5 mAmp or below, at short pulse duration (0.1 millisecond), success rates in the 95% to 100% range can be expected.

The ultrasound-guided axillary block (**Fig. 46.8**) utilizes the same patient position as the nerve stimulator technique. The ultrasound probe is placed along the axillary crease in order to obtain a transverse view of the vessels and nerves. Care should be taken to identify the location of axillary veins because even slight pressure from the ultrasound transducer can collapse these vessels and obscure their identification. The nerves will appear hyperechoic with a honeycomb-like texture and can be traced distally in the arm to confirm their identification. The block is usually performed in-plane with a 5-cm needle oriented from lateral to medial, or out-of-plane with the needle oriented perpendicular to the long axis of the transducer. A shallow needle angle is utilized due to the superficial location of the nerves in the axilla and generally results in a clear image of the needle. If an out-of-plane technique is used, injections of small amounts of local anesthetic during needle advancement can assist in identifying the location of the needle tip. If the individual radial, median, and ulnar nerves are difficult to

identify, a perivascular ring of local anesthetic surrounding the axillary artery usually ensures a successful block of these nerves.

FIGURE 46.8. Ultrasound image of the axilla. The median (M), radial (R), and ulnar (U) nerves can be seen surrounding the axillary artery (AA). The musculocutaneous nerve (MC) lies between the body of the biceps and the coracobrachialis muscles.

Chan V. *A Practical Guide to Ultrasound Imaging for Regional Anesthesia: Part 2—Upper Limb Blocks. Version 1.1*. Toronto, Canada: Toronto Centre for Ultrasound Education; 2013:64–73.

Hadzic A, ed. *Hadzic's Textbook of Regional Anesthesia and Acute Pain Management*. 2nd ed. New York: McGraw-Hill; 2017:580–585.

Neal JM, Gerancher JC, Hebl JR, et al. Upper extremity regional anesthesia: essentials of our current understanding, 2008. *Reg Anesth Pain Med*. 2009;34:134–170.

C.10. The patient requests to have the brachial plexus block performed after you administer general anesthesia. Would you agree to this request?

In a landmark publication, Benumof reported four cases of permanent injury to the cervical spinal cord resulting from interscalene block performed during general anesthesia. Imaging

of the cervical spinal cord showed vacuolization of the cord or the presence of a syrinx. Intraneural injection of local anesthetic under pressure has been found to spread along the longitudinal axis along the nerve during experimental studies. Thus, theoretically, injection into a proximal nerve root can spread and disrupt the cervical spinal cord.

Performance of regional anesthesia in the anesthetized patient does not allow the patient to report painful paresthesia or other sensations. Sudden severe pain on injection during peripheral nerve block is a time-honored signal that neural tissue is endangered and that the needle should be promptly withdrawn and repositioned. It has been shown that needle contact with the nerve is often not associated with the ability to elicit a motor response during electrical stimulation. Reports of accidental intraneural injection during ultrasonographic needle guidance have been published. Therefore, no available modality can ensure against this complication and hence the caution that regional blocks not be performed in patients who are heavily sedated or following induction of general anesthesia. There are certain important exceptions to this rule, including children and adults who may suffer from dementia, developmental delay, or for other reasons are unable to tolerate regional block under only minimal sedation.

Auroy Y, Benhamou D, Bargues L, et al. Major complications of regional anesthesia in France: the SOS Regional Anesthesia Hotline Service. *Anesthesiology*. 2002;97:1274–1280.

Benumof JL. Permanent loss of cervical spinal cord function associated with interscalene block performed under general anesthesia. *Anesthesiology*. 2000;93:1541–1544.

Hadzic A, Dilberovic F, Shah S, et al. Combination of intraneural injection and high injection pressure leads to fascicular injury and neurologic deficits in dogs. *Reg Anesth Pain Med*. 2004;29:417–423.

Neal J, Barrington MJ, Brull R, et al. The second ASRA practice advisory on neurologic complications associated with regional anesthesia and pain

medicine. *Reg Anesth Pain Med*. 2015;40:401–430.

Urmey W, Stanton J. Inability to consistently elicit a motor response following sensory paresthesia during interscalene block administration. *Anesthesiology*. 2002;96:552–554.

C.11. What relevant respiratory complications or side effects are you concerned about in this patient?

Ipsilateral hemidiaphragmatic paresis is a consistent side effect associated with interscalene block. It occurs with an incidence of 100% when utilizing local anesthetic volumes of 20 mL or greater. It is also a variable side effect of supraclavicular block. This expected side effect takes on added importance if the patient has respiratory comorbidities, including contralateral phrenic or diaphragmatic pathology, severe chronic obstructive cardiopulmonary disease, neuromuscular disorders in which a 25% reduction in FVC would not be tolerated, or conditions that restrict rib cage motion such as ankylosing spondylitis. If these conditions are present, significant atelectasis or respiratory failure can occur. With proper technique and needle size, the risk of pneumothorax is minimal. Introduction of a catheter, nevertheless, could theoretically reach the apex of the lung.

El-Boghdadly K, Chin KJ, Chan VWS. Phrenic nerve palsy and regional anesthesia for shoulder surgery. *Anesthesiology*. 2017;127:173–191.

Urmey W, Talts K, Sharrock N. One hundred percent incidence of hemidiaphragmatic paresis associated with interscalene brachial plexus anesthesia as diagnosed by ultrasonography. *Anesth Analg*. 1991;72:498–503.

C.12. What is the incidence of hemidiaphragmatic paresis following interscalene brachial plexus block? Can this complication be avoided by decreasing the volume or concentration of local anesthetic injected or by using ultrasound-guided supraclavicular block?

Hemidiaphragmatic paresis cannot be reliably avoided by reducing the volume of local anesthetic injected. Volumes as

low as 5 mL (which is inadequate for surgical anesthesia) have been associated with a 45% incidence of hemidiaphragmatic paresis. Similarly, reductions in local anesthetic concentration do not avoid this side effect, with concentrations of bupivacaine as low as 0.125% being associated with 100% incidence of hemidiaphragmatic paresis. The use of ultrasound-guided supraclavicular blocks can reduce the incidence of hemidiaphragmatic paresis from 100% but will still be expected to be associated with a variable incidence. Blocks above the clavicle are associated with spread of local anesthetic into the cervical plexus. The mechanism for phrenic nerve paresis is motor blockade of the C3–C5 nerve roots before forming the phrenic nerve. The main nerve root contributing to formation to the phrenic nerve is the C4 nerve root. Any block causing sensory blockade of C5, C4, or C3 would be expected to have associated phrenic paresis. A recent publication suggests that with careful deposition of lower volumes of local anesthetic by ultrasonographic guidance at the intersection of the first rib and subclavian artery, the incidence of hemidiaphragmatic paresis may indeed be avoided during supraclavicular block.

Kang RA, Chung YH, Ko JS, et al. Reduced hemidiaphragmatic paresis with a "corner pocket" technique for supraclavicular brachial plexus block: single center; observer-blinded, randomized controlled trial. *Reg Anesth Pain Med*. 2018;443:720–724.

Renes SH, Spoormans HH, Gielen MJ, et al. Hemidiaphragmatic paresis can be avoided in ultrasound-guided supraclavicular brachial plexus block. *Reg Anesth Pain Med*. 2009;34:595–599.

Riazi S, Carmichael N, Awad I, et al. Effect of local anaesthetic volume (20 vs 5 mL) on the efficacy and respiratory consequences of ultrasound-guided interscalene brachial plexus block. *Br J Anaesth*. 2008;101:549–556.

Sinha SK, Abrams JH, Barnett JT, et al. Decreasing the local anesthetic volume from 20 to 10 mL for ultrasound-guided interscalene block at the cricoid level does not reduce the incidence of hemidiaphragmatic paresis. *Reg Anesth Pain Med*. 2011;36:17–20.

Urmey W, Gloeggler P. Pulmonary function changes during interscalene

block: effects of decreasing local anesthetic injection volume. *Reg Anesth*. 1993;18:244–249.

Urmey W, Talts K, Sharrock N. One hundred percent incidence of hemidiaphragmatic paresis associated with interscalene brachial plexus anesthesia as diagnosed by ultrasonography. *Anesth Analg*. 1991;72:498–503.

C.13. Describe the pulmonary function changes that occur after interscalene brachial plexus block.

Pulmonary function (such as FVC and forced expiratory volume in 1 second) reductions of 25% to 30% occur routinely. These changes are usually complete within 15 minutes of completion of the injection. Increased upper rib cage expansion and ipsilateral paradoxical inward motion of the hemiabdomen have been reported. The combined effect of these changes is a reduced ability to cough and clear secretions, which may be poorly tolerated by a patient with severe COPD.

Hortense A, Perez MV, Amaral JL, et al. Interscalene brachial plexus block. Effects on pulmonary function. *Rev Bras Anestesiol*. 2010;60(2):130–137, 174–178.

Melton MS, Monroe HE, Qi W, et al. Effect of interscalene brachial plexus block on the pulmonary function of obese patients: a prospective, observational cohort study. *Anesth Analg*. 2017;125(1):313–319.

Urmey W, McDonald M. Hemidiaphragmatic paresis during interscalene brachial plexus block: effects on pulmonary function and chest wall mechanics. *Anesth Analg*. 1992;74:352–357.

C.14. What would you do if the patient complained of dyspnea after you performed an interscalene or supraclavicular block?

The patient should be reassured and observed. Most patients complaining of dyspnea will have more than adequate pulmonary function for normal respiration. Symptoms of dyspnea may be relieved by placing the patient in the upright or sitting position as tolerated. This position optimizes diaphragmatic geometry and function and increases functional

residual capacity. Auscultation often reveals diminished or silent breath sounds on the side of the block. Chest radiography may be obtained if pneumothorax is suspected. Application of a face mask to assess ventilation or end-tidal carbon dioxide may be done, and assisted or controlled ventilation can be used if necessary. Endotracheal intubation should be performed if clinically indicated.

C.15. The surgeon prefers to perform the surgical procedure in the sitting position. What are the advantages and disadvantages of this position compared to the lateral position in this patient?

As discussed earlier, the seated position optimizes chest wall mechanics. The sitting position also allows easier access to the airway and is more comfortable for the patient if sedation is preferred over general anesthesia. However, placing the patient in the seated position may be associated with hypotensive bradycardiac episodes (HBE). Severe bradycardia or asystole may occur. It is suggested that these events occur as a result of the Bezold-Jarisch reflex (paradoxical cardiac inhibition and bradycardia in response to decreased ventricular volume resulting from venous pooling in sitting position). The sitting position may be thought of as a variation of the tilt-table test. This patient would be at particular risk for developing intraoperative bradycardia in the sitting position because of the history of syncopal episodes and positive findings on the tilt test. The use of β-blockers to decrease the likelihood of HBEs advocated on basis of observational studies has not been corroborated by large randomized studies in the literature. Ephedrine appears to be the drug of choice for HBEs. Epinephrine, atropine, α-agonists, and intravenous fluids are effective treatments for hypotension and bradycardia. Vigilance and rapid response are of critical importance.

The seated position has also been associated with case reports of stroke and neurologic deficit following shoulder surgery. There is some evidence to suggest improved cerebral perfusion when spontaneous, rather than positive pressure, ventilation is used for shoulder procedures in the upright position.

Gold BS, Weitz SR, Lurie KG. Intraoperative "syncope": evaluation with tilt-table testing. *Anesthesiology*. 1992;76:635–637.

Kinsella SM, Tuckey JP. Perioperative bradycardia and asystole: relationship to vasovagal syncope and the Bezold-Jarisch reflex. *Br J Anaesth*. 2001;86:859–868.

Pohl A, Cullen DJ. Cerebral ischemia during shoulder surgery in the upright position: a case series. *J Clin Anesth*. 2005;17:463–469.

Sheldon R, Connolly S, Rose S, et al. Prevention of syncope trial (POST): a randomized, placebo-controlled study of metoprolol in the prevention of vasovagal syncope. *Circulation*. 2006;113:1164–1170.

Weiner MM, Fischer GW, Rosenblatt MA. The beach-chair position and general anesthesia. *Reg Anesth Pain Med*. 2012;37:120.

Yadeau JT, Casciano M, Liu SS et al. Stroke, regional anesthesia in the sitting position, and hypotension: a review of 4169 ambulatory surgery patients. *Reg Anesth Pain Med*. 2011;36:430–435.

C.16. Which nerves are most commonly missed with axillary brachial plexus block? With interscalene block? With all brachial plexus blocks?

Axillary brachial plexus block commonly misses the musculocutaneous nerve, which arises from C5–C6 nerve roots and exits the plexus above the axilla. The interscalene block commonly spares the ulnar nerve, which is formed by the C8–T1 nerve roots at the lower extent of the brachial plexus. The intercostobrachial nerve is a branch of the second thoracic nerve and is not anesthetized by brachial plexus blocks. A separate injection is required for procedures involving the medial upper arm or axilla, or if a tourniquet will be inflated for extended periods on the upper arm.

Mian A, Chaudhry I, Huang R, et al. Brachial plexus anesthesia: a review of the relevant anatomy, complications, and anatomical variations. *Clin Anat*. 2014;27(2):210–221.

Neal JM, Gerancher JC, Hebl JR, et al. Upper extremity regional anesthesia: essentials of our current understanding, 2008. *Reg Anesth Pain Med*. 2009;34:134–170.

C.17. What is the expected duration of brachial plexus block with 30 mL of 1.5% mepivacaine with 5 μg per mL epinephrine?

Such an injection typically lasts 4 to 5 hours for surgical anesthesia.

C.18. What is the maximum safe dose of local anesthetic for brachial plexus block?

There is no absolute maximum safe dose of local anesthetic. The brachial plexus is characterized by relatively low systemic absorption compared to that of other blocks, such as epidural or intercostal. Absorption of local anesthetic following regional anesthetic injection is site specific. The American Society of Regional Anesthesia and Pain Medicine has published guidelines for local anesthetic toxicity. One should be cognizant of the recent publications demonstrating the efficacy of intravenous infusion of lipid emulsion in reversing local anesthetic–induced cardiac toxicity in animals and in multiple case reports involving human patients. Background information as well as advice concerning resuscitation equipment and procedure, including recommended dosing of lipid emulsion, can be obtained by accessing lipidrescue.org.

Neal JM, Barrington MJ, Fettiplace MR, et al. The Third American Society of Regional Anesthesia and Pain Medicine Practice Advisory on Local Anesthetic Systemic Toxicity. *Reg Anesth Pain Med*. 2018;43:113–123.

Rosenberg PH, Veering BT, Urmey WF. Maximum recommended doses of local anesthetics: a multifactorial concept. *Reg Anesth Pain Med*. 2004;29:564–575.

D. Postoperative Management

D.1. What regimen would you suggest for postoperative pain management?

Patient-controlled regional analgesia with a continuous infusion of local anesthetic is superior to intravenous patient-controlled analgesia for the treatment of pain after major shoulder surgery and also results in a faster time to discharge and increased patient satisfaction when used as part of a multimodal pain regimen. A supraclavicular or interscalene infusion of 0.2% ropivacaine at 4 to 8 mL per hour with patient administered boluses of 2 to 4 mL every 20 to 30 minutes is a good starting point. This can be combined with standing acetaminophen, COX-2 selective nonsteroidal anti-inflammatory drugs, gabapentinoids, and oral or intravenous opioids as needed.

Borgeat A, Tewes E, Biasca N, et al. Patient-controlled interscalene analgesia with ropivacaine after major shoulder surgery: PCIA vs PCA. *Br J Anaesth*. 1998;81:603–605.

Grosh T, Elkassabany NM. Enhanced recovery after shoulder arthroplasty. *Anesthesiol Clin*. 2018;36:417–430.

Herrick MD, Liu H, Davis M, et al. Regional anesthesia decreases complications and resource utilization in shoulder arthroplasty patients. *Acta Anaesthesiol Scand*. 2018;62(4):540–547.

Ilfeld BM, Vandenborne K, Duncan PW, et al. Ambulatory continuous interscalene nerve blocks decrease the time to discharge readiness after total shoulder arthroplasty. *Anesthesiology*. 2006;105:999–1007.

D.2. In the postanesthesia care unit, the patient complains of dyspnea. How would you evaluate and manage this?

The patient's vital signs should be monitored, including the oxygen saturation. Duration of hemidiaphragmatic paresis following brachial plexus block with mepivacaine or bupivacaine with added epinephrine lasts 3 to 4 hours or 9 to 18

hours, respectively. If a catheter has been placed, it should be checked via imaging to ascertain that it is not in the cervical plexus. Chest radiography should be performed to rule out pneumothorax or significant atelectasis. The patient should be supported by placement into the sitting position and ventilation assisted or controlled if necessary.

Urmey W, Gloeggler P. Effects of bupivacaine 0.5% compared with mepivacaine 1.5% used for interscalene brachial plexus block (abstract). *Reg Anesth*. 1992;17:13.

D.3. On the third postoperative day after removal of the brachial plexus catheter, the patient complains of persistent numbness and paresthesia in the ulnar nerve distribution. What would you tell the patient? How would you manage neurologic dysfunction after brachial plexus block that persists for 1 week?

Postoperative neurologic symptoms may be due to block-, surgical-, or patient-related factors. Causes unrelated to the brachial plexus block can include restrictive casts, compartment syndrome, or surgical causes such as tourniquet or traction injuries. The incidence of peripheral nerve injury after general anesthesia is approximately 0.04%. The incidence of block-related neurologic symptoms in the first several postoperative days ranges from 0.9/1,000 to 3/100 (0.18% to 3%). The incidence of symptoms lasting longer than 6 months ranges from 0.14 to 0.9/1,000 (0.014% to 0.09%).

It is appropriate to reassure the patient and tell him that these symptoms will likely resolve over time. If the symptoms persist for more than 1 week, a neurologist should be consulted to evaluate for neuropathy or brachial plexopathy. Electromyography (EMG) studies provide information on the location and degree of injury. It can take up to 4 weeks for an injury to cause sufficient wallerian degeneration of axons to

result in muscle denervation. EMG testing immediately after the injury can help to define any preexisting neurologic injury but should be repeated after 3 to 4 weeks. Serial testing can help to assess the evolution or recovery of the initial injury. Magnetic resonance imaging (MRI) is also considered a standard tool for the workup of neurologic injuries. It is especially suited to image the brachial plexus, where injuries often present with enhancement. The diagnostic ability of MRI is limited due to the fact that abnormalities seen on MRI can be nonspecific.

Aminoff MJ. Electrophysiologic testing for the diagnosis of peripheral nerve injuries. *Anesthesiology*. 2004;100:1298–1303.

Auroy Y, Benhamou D, Bargues L, et al. Major complications of regional anesthesia in France: the SOS Regional Anesthesia Hotline Service. *Anesthesiology*. 2002;97:1274–1280.

Barrington MJ, Morrison W, Sutherland T, et al. Case scenario: postoperative brachial plexopathy associated with infraclavicular brachial plexus blockade: localizing postoperative nerve injury. *Anesthesiology*. 2014;121:383–387.

Barrington MJ, Watts SA, Gledhill SR, et al. Preliminary results of the Australasian Regional Anaesthesia Collaboration: a prospective audit of more than 7000 peripheral nerve and plexus blocks for neurologic and other complications. *Reg Anesth Pain Med*. 2009;34:534–541.

Brull R, McCartney CJ, Chan VW, et al. Neurological complications after regional anesthesia: contemporary estimates of risk. *Anesth Analg*. 2007;104:965–974.

Sites BD, Taenzer AH, Herrick MD, et al. Incidence of local anesthetic systemic toxicity and postoperative neurologic symptoms associated with 12,668 ultrasound-guided nerve blocks: an analysis from a prospective clinical registry. *Reg Anesth Pain Med*. 2012;37:478–482.

Welch MG, Brummett CM, Welch TD, et al. Perioperative peripheral nerve injuries: a retrospective study of 380,680 cases during a 10-year period at a single institution. *Anesthesiology*. 2009;111:490–497.

47 Nerve Blocks of the Lower Extremity

Roniel Weinberg, Melvin La, and Danielle M. Gluck

A 60-year-old male was struck by a car while walking across a street. Upon arrival to the emergency room (ER), he complained of severe right lower extremity pain. His Glasgow Coma Score was 13 because he was slightly confused and only opened his eyes to speech. His past medical history was significant for paroxysmal atrial fibrillation and chronic low back pain. Prior surgeries include a right anterior cruciate ligament (ACL) repair 4 years ago and an L4–S1 fusion. His medications include dabigatran (Pradaxa), methadone 15 mg every 6 hours, and oxycodone 15 to 30 mg every 6 hours as needed for breakthrough pain. The patient's heart rate is irregular at a rate of 85 beats per minute, and his blood pressure is 130/70 mmHg. An electrocardiogram shows atrial fibrillation. Head computed tomography (CT) scan in the ER reveals a small subdural hematoma. He has lacerations of the skin on both the medial and lateral aspects of his right ankle, and plain film x-rays show a high right ankle fracture of the tibia and fibula. The consulting neurosurgical service has determined that the patient does not require immediate interventions and will be followed with close observation. The orthopedic surgery team wants to take the patient for an open reduction and internal fixation (ORIF) of his ankle as soon as medical conditions allow.

A. Preoperative Evaluation

1. What is the Glasgow Coma Scale and its significance in this patient?
2. Should surgery be allowed to proceed in this patient who has a subdural bleed?
3. Does the patient's atrial fibrillation need to be addressed prior to surgery, and if so, how?

B. Preoperative Preparation

1. What is dabigatran (Pradaxa)? How is its effect measured? How far in advance of elective surgery should it be stopped? Can its effect be reversed?
2. What concerns do you have regarding neuraxial anesthesia in this patient who has a subdural hematoma?
3. What concerns do you have regarding neuraxial anesthesia in this patient who has prior back surgery?
4. The surgeon is willing to wait a few days prior to surgery while the swelling around the injury decreases. When would you feel comfortable proceeding with surgery in this patient?

C. Intraoperative Management

The patient presents to the operating room (OR) 72 hours after his injury. He was medically cleared for the ORIF of his right ankle. You have decided to proceed with a regional nerve block anesthetic technique.

1. What two nerve plexuses need to be blocked in this case? What nerve roots contribute to each plexus? Name the major nerves that come from each plexus.
2. What is the innervation to the medial and lateral aspects of the ankle? What nerves need to be blocked for his surgery?
3. What nerves are blocked with an ankle block? Would you do an ankle block in this case?
4. Explain the posterior landmark technique to blocking the lumbar plexus. What motor response would be elicited with a

nerve stimulator? At what stimulation level would you feel safe injecting the patient? Why not at a lower level of stimulation? Can ultrasound guidance be utilized for this injection?

5. What is a fascia iliaca block (three-in-one block)?
6. Describe the different ultrasound approaches to blocking the saphenous nerve above the knee.
7. What benefits might a saphenous nerve block above the knee provide compared to a femoral nerve block?
8. How would pain from a midthigh tourniquet dictate which peripheral nerve blocks to use in this patient? Describe the landmark technique of sciatic nerve block in the gluteal region. What is seen while performing an ultrasound technique to block the sciatic nerve?
9. Why does a popliteal nerve block have a high failure rate if performed too proximate to the popliteal fossa when using a landmark/nerve stimulator technique? Describe how this can be avoided when using ultrasound-based popliteal block.
10. What is the IPACK block? In what situations would this block be useful?

D. Postoperative Pain Management

1. Describe compartment syndrome and how that risk would influence your postoperative plan for peripheral regional analgesia.
2. How would the addition of dexamethasone to your local anesthetic influence the duration of the blocks placed in the OR?
3. What is liposomal bupivacaine?
4. What benefit would a peripheral nerve catheter provide over a long-acting local anesthetic? Are there any downsides?
5. You were able to perform a continuous spinal epidural (CSE) at L3–L4 and used 0.125% bupivacaine via epidural route for

postoperative pain control. The patient reports that he is comfortable regarding both his back pain and his ankle pain. What benefit would continuing the patient's methadone confer in this case?

6. How can regional analgesia aid in fast-track postoperative care?

A. Preoperative Evaluation

A.1. What is the Glasgow Coma Scale and its significance in this patient?

The Glasgow Coma Scale (Score) was developed as a practical structured assessment of consciousness in patients following acute brain trauma. The scale, first described in 1974 and later revised in 1979, scores three different components of responsiveness for a score range of 3 to 15. The levels of response include eye opening (none, to pressure, to speech, spontaneous), verbal response (none, sounds, words, confused, oriented), and best motor response (none, extension, abnormal flexion, normal flexion or withdrawal, localizing, obeying commands), with the worse response receiving a lower number. Generally, scores of 13 to 15 signify mild head injury, 9 to 12 as moderate, and 8 and below as severe. Components of the scale and the overall score seem to strongly correlate to outcome after acute brain injury. A baseline score should be established upon patient presentation, with a revised and more predictive score upon stabilization of respiratory, circulatory, and metabolic abnormalities.

Teasdale G, Maas A, Lecky F, et al. The Glasgow Coma Scale at 40 years: standing the test of time. *Lancet Neurol*. 2014;13:844–854.

A.2. Should surgery be allowed to proceed in this patient who has a subdural bleed?

Although the patient suffered acute brain trauma and appears stable, he remains at risk for sudden deterioration secondary to increased hematoma formation or cerebral edema. Following acute brain trauma, preservation of normal intracranial pressures and avoiding hypotension while maintaining cerebral perfusion pressure between 60 and 70 mmHg are essential to decrease poor outcomes. Subdural hematomas are the result of bleeding from bridging veins into the space between the dura and arachnoid. These can develop over the course of a few days and may often result from a seemingly benign injury or spontaneously. Patients will complain of a headache and often appear drowsy or obtunded. The diagnosis is via CT scan, and the patient can be managed conservatively or with surgical evacuation. Assuming the patient's medical condition does not change over the course of 24 to 48 hours, it would then be safe to proceed with repair of the ankle fracture.

Carney N, Totten AM, O'Reilly C, et al. Guidelines for the management of severe traumatic brain injury, fourth edition. *Neurosurgery*. 2017;80:6–15.

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:290–291.

A.3. Does the patient's atrial fibrillation need to be addressed prior to surgery, and if so, how?

This patient has preexisting paroxysmal atrial fibrillation. Prior to surgery, he should be asked if he knows when his last episode of atrial fibrillation was, if he has symptoms when it occurs, if he is typically rate controlled, if he has ever taken medications for rate control, and if he ever required a cardioversion or an ablation. Because these patients are more likely to have cardiac disease, a preoperative transthoracic echocardiogram in non-emergent cases is often helpful in evaluating cardiac and valvular functions. Although our patient's heart rate is controlled, consider the addition of a β-blocker or calcium

channel blocker in non–rate-controlled patients, as tolerated by their blood pressure. In addition to inquiring about our patient's last dabigatran (Pradaxa) use, discuss with the surgical team the plan for possible perioperative anticoagulation.

January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *Circulation*. 2014;130:e199–e267.

Schleifer JW, Ramakrishna H. Perioperative atrial fibrillation: a systematic review of evolving therapeutic options in pharmacologic and procedural management. *Ann Card Anaesth*. 2015;18(4):565–570.

B. Preoperative Preparation

B.1. What is dabigatran (Pradaxa)? How is its effect measured? How far in advance of elective surgery should it be stopped? Can its effect be reversed?

Patients with atrial fibrillation will often take an oral anticoagulant to reduce their risk of stroke. Dabigatran etexilate (Pradaxa) is a direct thrombin (factor IIa) inhibitor that is among a group of drugs known as direct oral anticoagulants (DOACs). Unlike warfarin, DOACs are generally easier to manage and do not require laboratory monitoring, but until recently, specific reversal agents for these drugs did not exist. Thrombin activates factors V, VIII, and IX; helps convert fibrinogen to fibrin; and stimulates platelet aggregation. Dabigatran inhibits both free and clot-bound thrombin. It is a prodrug that is hydrolyzed by serum esterases into its active form. Peak plasma level occurs within 0.5 to 2 hours of administration, and its half-life is 12 to 17 hours in healthy patients and up to 28 hours in patients with end-stage renal disease. Eighty percent of the medication is excreted unchanged via the kidneys. In patients with normal renal function, the medication should be stopped 24 hours prior to

low-risk surgery and 48 hours prior to high-risk surgery. These time intervals are extended up to 4 times depending on the patient's renal impairment. In terms of anesthetic management, it is recommended that dabigatran be discontinued 120 hours (5 days) prior to neuraxial block. However, in patients with a normal creatinine clearance and no additional risk factors for bleeding (e.g., elderly patients, concomitant antiplatelet medications, hypertension), it may be appropriate to wait 72 hours (i.e., 4 to 6 half-lives) from cessation of dabigatran prior to neuraxial injection.

Prothrombin time (PT) and international normalized ratio (INR) cannot be used reliably to determine anticoagulation status in a patient receiving dabigatran. Although activated partial thromboplastin time (aPTT) has a nonlinear correlation to dabigatran plasma levels and can be used to provide some qualitative measure of anticoagulation status in emergency situations, there remains considerable variability between patients. The most sensitive assays to monitor quantitative dabigatran activity are thrombin time (TT) and dilute thrombin time (dTT), but the availability of these specialized tests may be limited. Idarucizumab (Praxbind) is a monoclonal antibody fragment that binds to dabigatran and can be used for the emergency reversal of life-threatening bleeding in patients on dabigatran. The recommended dose is 5 g via intravenous infusion. If idarucizumab is not available, activated prothrombin complex concentrate (PCC) or unactivated three-factor or four-factor PCC has been suggested for reversal of dabigatran associated bleeding. In addition, gastric lavage with activated charcoal within 2 hours of administration can be attempted. Ultimately, dialysis will remove the anticoagulant effects of dabigatran.

Doherty JU, Gluckman TJ, Hucker WJ, et al. 2017 ACC Expert Consensus

decision pathway for periprocedural management of anticoagulation in patients with nonvalvular atrial fibrillation: a report of the American College of Cardiology Clinical Expert Consensus Document Task Force. *J Am Coll Cardiol*. 2017;69(7):871–898.

Horlocker TT, Vandermeuelen E, Kopp SL, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine evidence-based guidelines (fourth edition). *Reg Anesth Pain Med*. 2018;43(3):263–309.

Pollack CV Jr, Reilly PA, van Ryn J, et al. Idarucizumab for dabigatran reversal—full cohort analysis. *N Engl J Med*. 2017;377(5):431–441.

Schulman S, Carrier M, Lee AY, et al. Perioperative management of dabigatran: a prospective cohort study. *Circulation*. 2015;132(3):167–173.

B.2. What concerns do you have regarding neuraxial anesthesia in this patient who has a subdural hematoma?

The sheering of bridging veins, generally at their thinnest point in the subdural space, is the likely etiology in the development of subdural hematomas associated with trauma and those associated with postdural puncture headaches and low cerebrospinal fluid (CSF) pressure. A review documented 46 cases of subdural hematoma, which developed following intentional dural puncture during spinal procedures or unintentional violation of the dura mater during epidural catheter placement. Given that this patient has already developed a subdural hematoma, neuraxial anesthesia would need to be undertaken with great care, and if done, a spinal should be avoided in favor of an epidural technique.

Edlow JA, Caplan LR, O'Brien K, et al. Diagnosis of acute neurological emergencies in pregnant and post-partum women. *Lancet Neurol*. 2013;12(2):175–185.

Zeidan A, Farhat O, Maaliki H, et al. Does postdural puncture headache left untreated lead to subdural hematoma? Case report and review of the literature. *Int J Obstet Anesth*. 2006;15:50–58.

B.3. What concerns do you have regarding neuraxial

anesthesia in this patient who has prior back surgery?

Neuraxial anesthesia should be considered with caution in this patient with a history of a lumbar fusion at L4–S1. Neuraxial anesthesia can be challenging in this patient population due to abnormalities of the usual landmarks, scar formation, presence of hardware, and bone grafts. These patients are at higher risk for false loss of resistance, inability to access the epidural or subarachnoid space, patchy and failed blocks, unintentional dural puncture, and traumatic needle placement. In a retrospective review of 937 patients with a history of spinal stenosis and/or lumbar disc disease, Hebl et al. showed that prior spinal surgery in 207 of the patients did not affect the block success rate or the frequency of complications. However, of the 207 patients, only 5 had prior spinal fusion. Care should be taken to confirm that the fusion is at the level that the patient reports. If available, imaging of the patient's spine should be reviewed to identify relevant anatomy, deformity, or surgical implants. In addition, ultrasound can be helpful in determining the best interspace, correct level, midline, and epidural space depth.

Hebl JR, Horlocker TT, Kopp SL, et al. Neuraxial blockade in patients with preexisting spinal stenosis, lumbar disk disease, or prior spine surgery: efficacy and neurologic complications. *Anesth Analg*. 2010;111(6):1511–1519.

Neal JM, Barrington MJ, Brull R, et al. The Second ASRA Practice Advisory on neurologic complications associated with regional anesthesia and pain medicine: executive summary 2015. *Reg Anesth Pain Med*. 2015;40(5):401–430.

B.4. The surgeon is willing to wait a few days prior to surgery while the swelling around the injury decreases. When would you feel comfortable proceeding with surgery in this patient?

After assessing the patient's current medical status and prior medical history, an anesthetic plan of general, regional, or neuraxial should be considered. If choosing an anesthetic plan of neuraxial anesthesia or one involving deep regional blocks, the anticoagulation status of the patient must be taken into account. The most recent guidelines from the American Society of Regional Anesthesia and Pain Medicine (ASRA) recommend waiting 120 hours from the last dose of dabigatran prior to neuraxial block. However, these same guidelines also suggest that patients with stable renal function, creatinine clearance of 80 mL per minute or greater, and no other risk factors for bleeding need only wait 72 hours prior to neuraxial block. Otherwise, for a general anesthetic or superficial peripheral nerve block, surgery can proceed within 24 to 48 hours, assuming that his atrial fibrillation is stable with preserved cardiac function and that his mental status does not deteriorate secondary to his subdural hematoma.

Doherty JU, Gluckman TJ, Hucker WJ, et al. 2017 ACC Expert Consensus decision pathway for periprocedural management of anticoagulation in patients with nonvalvular atrial fibrillation: a report of the American College of Cardiology Clinical Expert Consensus Document Task Force. *J Am Coll Cardiol*. 2017;69(7):871–898.

Horlocker TT, Vandermeuelen E, Kopp SL, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine evidence-based guidelines (fourth edition). *Reg Anesth Pain Med*. 2018;43(3):263–309.

Schulman S, Carrier M, Lee AY, et al. Perioperative management of dabigatran: a prospective cohort study. *Circulation*. 2015;132(3):167–173.

C. Intraoperative Management

The patient presents to the operating room (OR) 72 hours after his injury. He was medically cleared for the ORIF of his right ankle. You have decided to proceed with a regional nerve block anesthetic technique.

C.1. What two nerve plexuses need to be blocked in this case? What nerve roots contribute to each plexus? Name the major nerves that come from each plexus.

Peripheral regional anesthesia for almost all major orthopedic surgery of the lower extremity involves blocking the whole or branches of both the lumbar and the lumbosacral plexuses. In broad terms, the lumbar plexus innervates the ventral aspect of the lower extremity, whereas the sacral plexus innervates the dorsal aspect. The lumbar plexus is made up of the ventral rami of L1–L3, part of L4, and, in 50% of patients, a branch from T12. The plexus is located within the psoas muscle, anterior to the transverse processes of the lumbar vertebra. The plexus gives off the iliohypogastric (T12–L1), ilioinguinal (L1), genitofemoral (L1–L2), lateral femoral cutaneous (L2–L3), femoral (L2–L4), and obturator nerves (L2–L4) (**Fig. 47.1**).

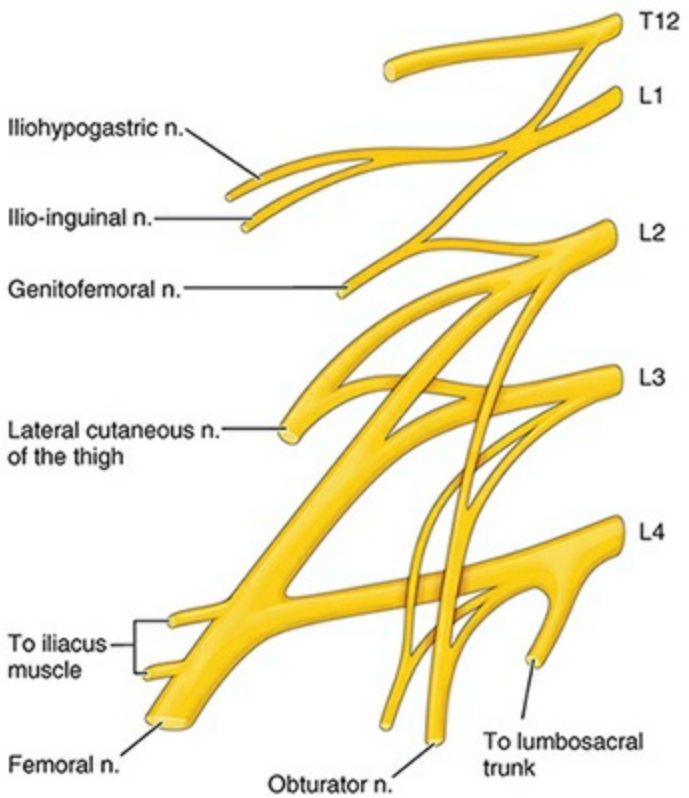

FIGURE 47.1. Lumbar plexus. (*From Drake RL, Vogl AW, Mitchell AWM*. Gray's Anatomy for

Students. *3rd ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2014: Fig. 4.160, 253–420, with permission*.)

The lumbosacral trunk is formed from ventral rami of L4 and L5 and the anterior branch of S1. The sacral plexus is composed of the union of the lumbosacral trunk with S1–S3 and occasionally S4. The sciatic nerve contains the tibial nerve, which is made up of the anterior divisions of the ventral rami of L4, L5, and S1–S3, and the common peroneal nerve, which is made of the dorsal branches of the same nerve roots. The sciatic nerve splits into the tibial and common peroneal nerves in the popliteal fossa. The common peroneal nerve branches into the superficial and deep tibial nerves. The tibial nerve branches into the medial plantar, calcaneal, and sural (with contribution from communicating superficial peroneal branches) nerves. Other nerves from the lumbosacral plexus include the superior gluteal (L4–S1), inferior gluteal (L5–S2), posterior femoral cutaneous (S1–S3), piriformis (S1–S2), obturator internus (L5, S1–S2), and quadratus femoris (L4–L5, S1) (**Fig. 47.2**).

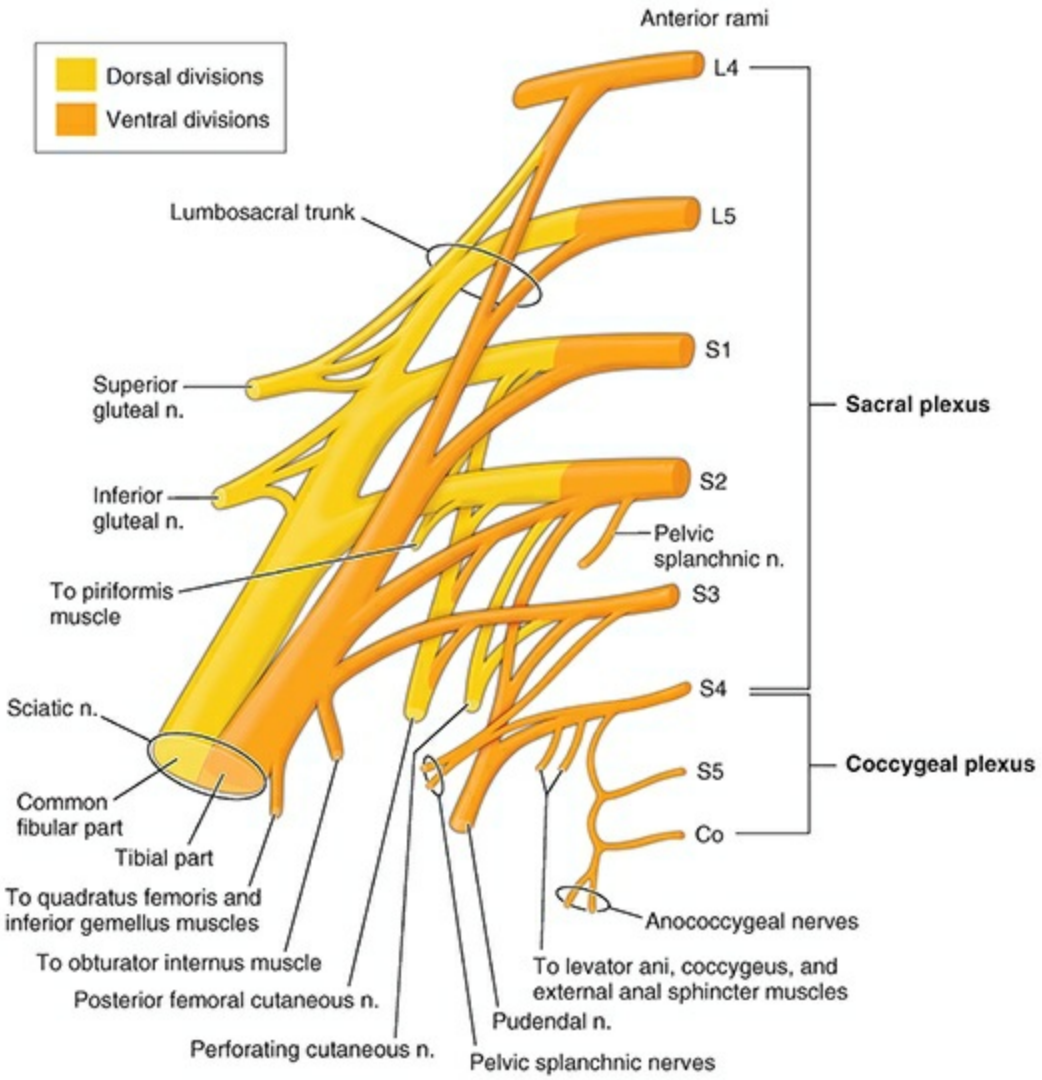

FIGURE 47.2. Sacral plexus.

Farag E, Mounir-Soliman L, eds. *Brown's Atlas of Regional Anesthesia*. 5th ed. Philadelphia, PA: Elsevier; 2017:89–96.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1450–2155.

Hadzic A, ed. *Hadzic's Textbook of Regional Anesthesia and Acute Pain Management*. 2nd ed. New York: McGraw-Hill; 2017:39–70.

Narouze SN, ed. *Atlas of Ultrasound-Guided Procedures in Interventional Pain Management*. New York: Springer; 2011:240–258.

C.2. What is the innervation to the medial and lateral aspects of the ankle? What nerves need to be blocked for his surgery?

Below the knee, the saphenous nerve provides innervation to the medial aspect of the lower extremity. The lateral aspect is innervated by the common peroneal nerve, with the tibial nerve providing innervation in the posterior aspect. The superficial peroneal nerve innervates the dorsal aspect of the foot, whereas the deep peroneal nerve provides innervation to the deep dorsal structures and the web space between the first and second digits. The sural nerve innervates the lateral aspect of the foot, whereas the calcaneal and medial plantar nerves innervate the plantar aspect of the foot.

In our case, to provide effective surgical anesthetic peripheral nerve blockade, both the medial and lateral aspects of the ankle would need to be anesthetized. Thus, the tibial, common peroneal, and the saphenous branch of the femoral nerve would require surgical blockade.

Farag E, Mounir-Soliman L, eds. *Brown's Atlas of Regional Anesthesia*. 5th ed. Philadelphia, PA: Elsevier; 2017:153–155.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1450–1479.

Narouze SN, ed. *Atlas of Ultrasound-Guided Procedures in Interventional Pain Management*. New York: Springer; 2011:240–258.

C.3. What nerves are blocked with an ankle block? Would you do an ankle block in this case?

The posterior tibial, deep and superficial peroneal, sural, and saphenous nerves require blockade for anesthesia of the foot. Typically, an ankle block is performed at the level of the medial and lateral malleoli. The posterior tibial nerve is blocked by inserting a fine needle along the medial aspect of the Achilles tendon at the level of the medial malleolus and advanced until the posterior tibia/medial malleolus is contacted (**Fig. 47.3**). Three to 5 mL of local anesthetic is deposited superficial to the periosteum. The deep peroneal nerve at the level of the malleoli

lies deep between the tendons of the tibialis anterior and the extensor hallucis longus (EHL). These tendons are identified by asking the patient to dorsiflex the big toe (EHL) and the foot (tibialis anterior). Another 2 to 3 mL of local anesthetic can be deposited here just superficial to the periosteum. The deep peroneal nerve can also be blocked distal to the level of the malleoli on the dorsum of the foot by injecting local anesthetic deep to the fascia lateral to the EHL and medial to the dorsalis pedis artery (**Fig. 47.4**). At the level of the malleoli, the needle can be redirected to block the branches of the superficial peroneal and saphenous nerves by making a subcutaneous ring across the dorsum of the foot using 5 to 10 mL of the anesthetic solution. The sural nerve can be blocked by inserting a needle lateral to the Achilles tendon at the level of the lateral malleolus. The needle is advanced until the periosteum is contacted and another 3 to 5 mL of local anesthetic is deposited superficial to the periosteum.

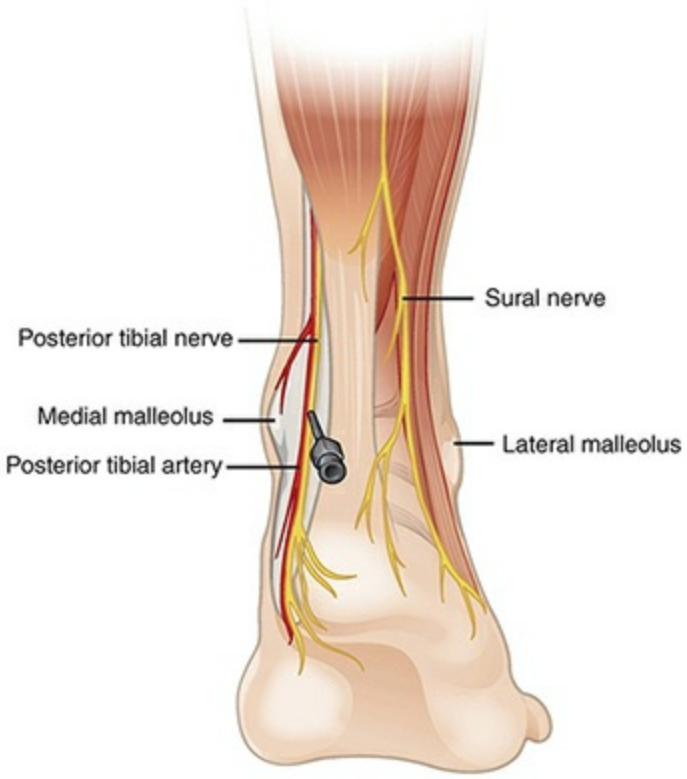

FIGURE 47.3. The posterior tibial nerve block.

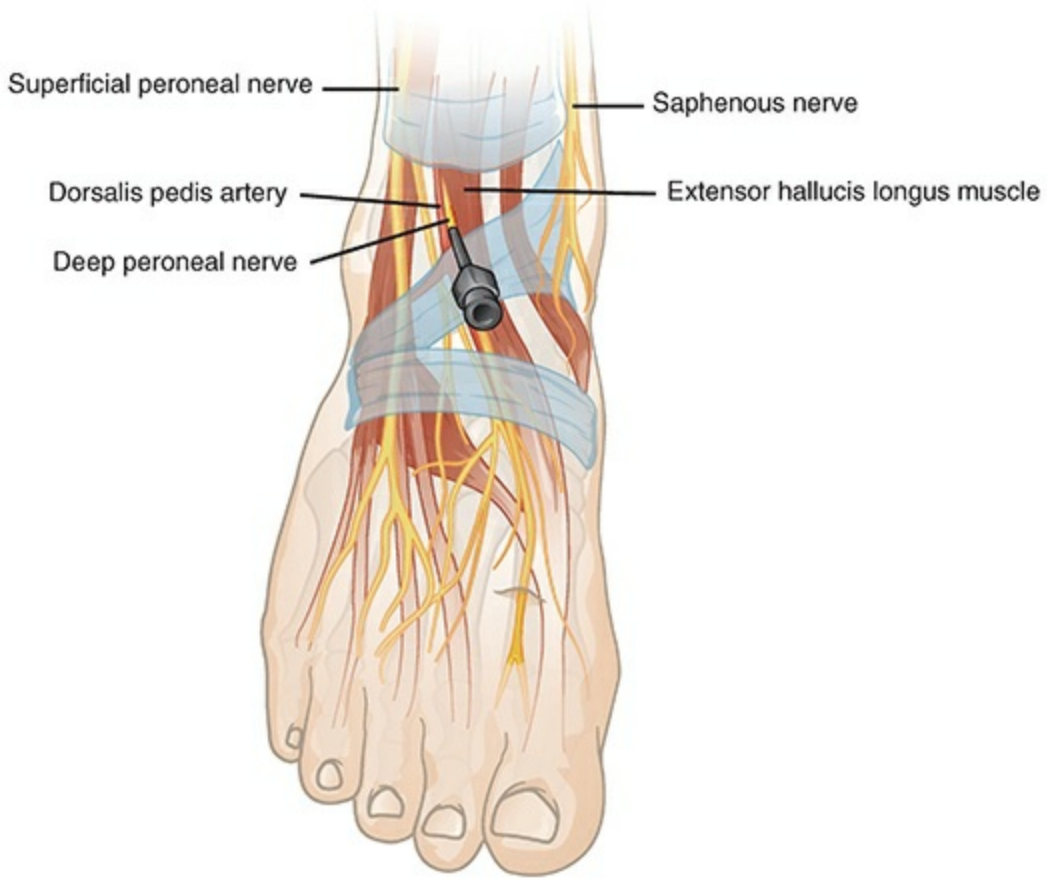

FIGURE 47.4. The deep peroneal nerve block.

Our patient would require anesthesia cephalad to the level of the malleoli, given that he has sustained a high ankle fracture. Thus, an ankle block would likely not provide adequate surgical anesthesia and should not be employed as the primary anesthetic in this case.

Farag E, Mounir-Soliman L, eds. *Brown's Atlas of Regional Anesthesia*. 5th ed. Philadelphia, PA: Elsevier; 2017:153–155.

Sharrock NE, Waller JF, Fierro LE. Midtarsal block for surgery of the forefoot. *Br J Anaesth*. 1986;58:37–40.

C.4. Explain the posterior landmark technique to blocking the lumbar plexus. What motor response

would be elicited with a nerve stimulator? At what stimulation level would you feel safe injecting the patient? Why not at a lower level of stimulation? Can ultrasound guidance be utilized for this injection?

The posterior approach to the lumbar plexus block, also known as a psoas compartment block, is performed by injecting 20 to 40 mL of local anesthetic into a lumbar paravertebral location. For this injection, the patient should be in the lateral decubitus position. The classic approach was described by Winnie et al. at the L4 level using a paresthesia technique that can be modified with the use of a nerve stimulator. The point of puncture is at the intersection of the intercristal line (line joining the iliac crests) and a caudad-cephalad line that passes through the posterior superior iliac spine (PSIS) and is parallel to the spinal column. If the lumbar plexus is not located, the needle should be directed more medially. Mannion et al. recommended a medial needle redirection of no more than 15 degrees to reduce the risk of bilateral spread. Capdevila et al. described a modification of this approach by using a point of puncture at the lateral two-thirds of the distance between the spinous process and the PSIS and 1 cm above the intercristal line. The needle should be advanced in a perpendicular plane and contact made with the L4 transverse process. The needle should then be redirected caudally, until a quadriceps femoris twitch is obtained, usually at the depth of another 18 mm.

With the near ubiquitous use of ultrasound for peripheral nerve blocks, ultrasound can similarly be utilized to image the relevant anatomy and to guide needle placement in the lumbar plexus block. First described by Kirchmair et al., ultrasound technique allows for the visualization of the lumbar paravertebral region, which includes the psoas major muscle, erector spinae muscle, and quadratus lumborum muscle. For

most techniques, the block needle is advanced under ultrasound guidance to the posterior aspect of the psoas muscle. Because the lumbar plexus nerves cannot always be delineated within the psoas muscle, ultrasound-guided approaches are often combined with nerve stimulation.

Although inadvertent spinal anesthesia, intravascular injections, incorrect catheter placement, and renal and psoas hematoma have all been reported, the most common complication of a lumbar plexus block is inadvertent epidural anesthesia and bilateral spread. Motor stimulation should be elicited between 0.5 and 1.0 mA, as twitches evoked at lower currents may indicate needle placement in a dural sleeve, which might increase the risk of epidural or spinal spread.

Capdevila X, Coimbra C, Choquet O. Approaches to the lumbar plexus: success, risks, and outcome. *Reg Anesth Pain Med*. 2005;30(2):150–162.

Capdevila X, Macaire P, Dadure C, et al. Continuous psoas compartment block for postoperative analgesia after total hip arthroplasty: new landmarks, technical guidelines, and clinical evaluation. *Anesth Analg*. 2002;94:1606–1613.

Hadzic A, ed. *Hadzic's Textbook of Regional Anesthesia and Acute Pain Management*. 2nd ed. New York: McGraw-Hill; 2017:711–739.

Karmakar MK, Li JW, Kwok WH, et al. Ultrasound-guided lumbar plexus block using a transverse scan through the lumbar intertransverse space: a prospective case series. *Reg Anesth Pain Med*. 2015;40(1):75–81.

Kirchmair L, Entner T, Kapral S, et al. Ultrasound guidance for the psoas compartment block: an imaging study. *Anesth Analg*. 2002;94(3):706–710.

Mannion S, O'Callaghan S, Walsh M, et al. In with the new, out with the old? Comparison of two approaches for psoas compartment block. *Anesth Analg*. 2005;101:259–264.

Winnie AP, Ramamurthy S, Durrani Z, et al. Plexus blocks for lower extremity surgery: new answers to old problems. *Anesthesiol Rev*. 1974;1:1–6.

C.5. What is a fascia iliaca block (three-in-one block)?

The femoral, lateral femoral cutaneous, and obturator nerves can be blocked separately (**Fig. 47.5**). The three-in-one block is a

large-volume block, first described by Winnie et al., intended as an anterior approach to block all three nerves with one needle. The intention is to provide analgesia to the anterior and lateral thigh, as opposed to only the anterior thigh, by blocking the femoral and lateral cutaneous nerves, which lay together under the iliacus fascia, as they travel through the pelvis. The fascia iliaca block has been shown to provide good pain relief in elderly patients with hip fractures, in post-hip surgery patients, and in anterior thigh and knee surgery.

Anatomically, the nerves of the lumbar plexus run posterior to the iliacus fascia. The fascia iliaca is continuous with the posterior aspect of the inguinal ligament, passes behind the femoral vessels, and laterally attaches to the anterior superior iliac spine. It is covered by the fascia lata and forms the top of a fat-filled space called the lacuna musculorum (lateral to the lacuna vasorum; the femoral vessels sheath). Using the landmark-based technique, a line, mimicking the inguinal ligament, is drawn from the pubic bone to the anterior superior iliac spine. The puncture site is 0.5 cm caudal to a point at the lateral two-thirds of that line. The anesthetic is injected on the second "give" or loss of resistance as needle passes through the fascia lata and fascia iliaca, with pressure caudad to the needle.

Although the landmark-based technique is quick and easy to perform, complete sensory block of the anterior, medial, and lateral aspects of the thigh increased from 47% with loss of resistance technique to 82% using ultrasound guidance.

One technique to an ultrasound-guided fascia iliaca block utilizes placement of the ultrasound probe in the transverse position, similar to the standard ultrasound-guided femoral nerve block. Once the femoral artery is located, the hyperechoic femoral nerve is identified lateral to that with the fascia iliaca running above it (**Fig. 47.6**). The probe is moved laterally, tracing the fascia iliaca until the sartorius muscle is identified

(Fig. 47.7). The needle is passed in-plane under the fascia iliaca and local anesthetic injected while the distal femoral sheath is compressed. For the second technique, the probe is placed in the sagittal plane above the iliac bone, located where the sartorius muscle and the external oblique muscle come together above the iliacus (Fig. 47.8). Injecting the local anesthetic under the fascia iliaca with the needle in plane in a cephalad direction at this location theoretically results in a more proximal spread of the anesthetic in the direction of the lumbar plexus. Unfortunately, the obturator nerve is not blocked reliably using either approach.

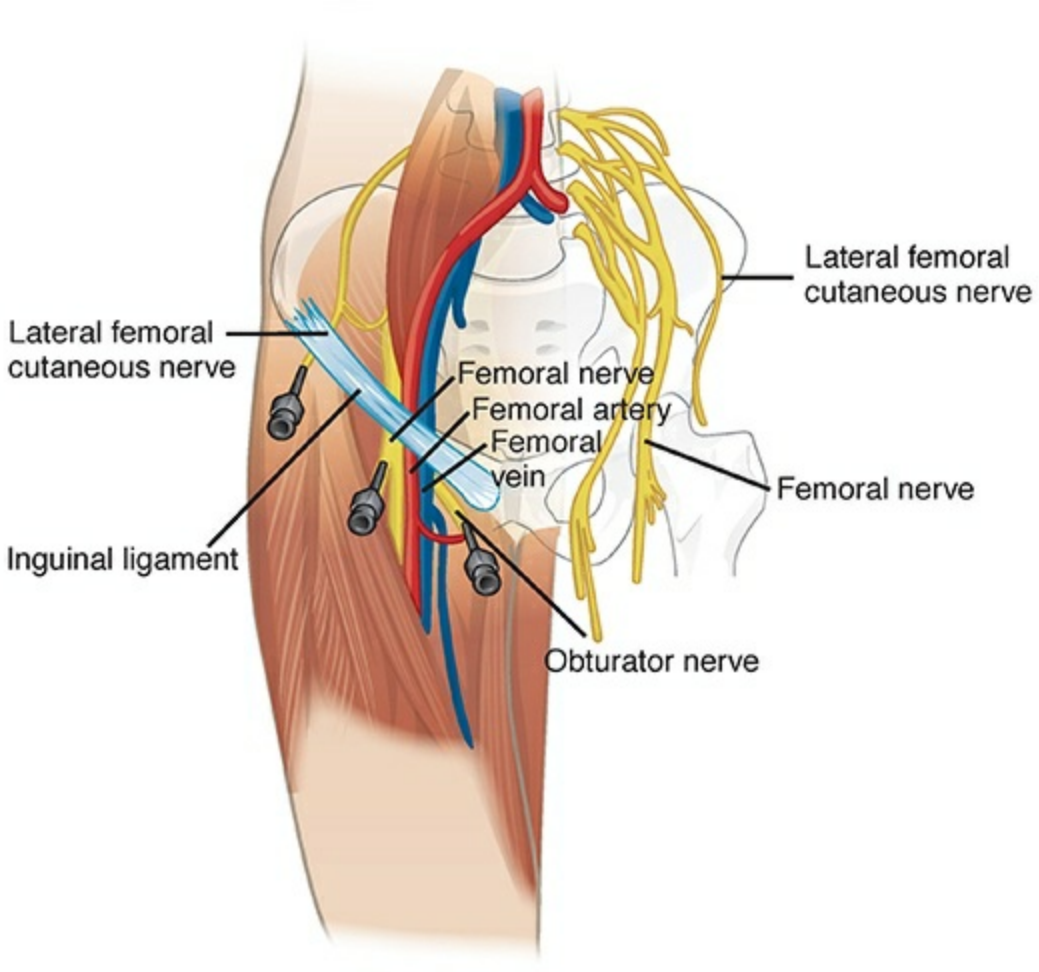

FIGURE 47.5. The femoral nerve block, lateral femoral cutaneous nerve block, and obturator nerve block.

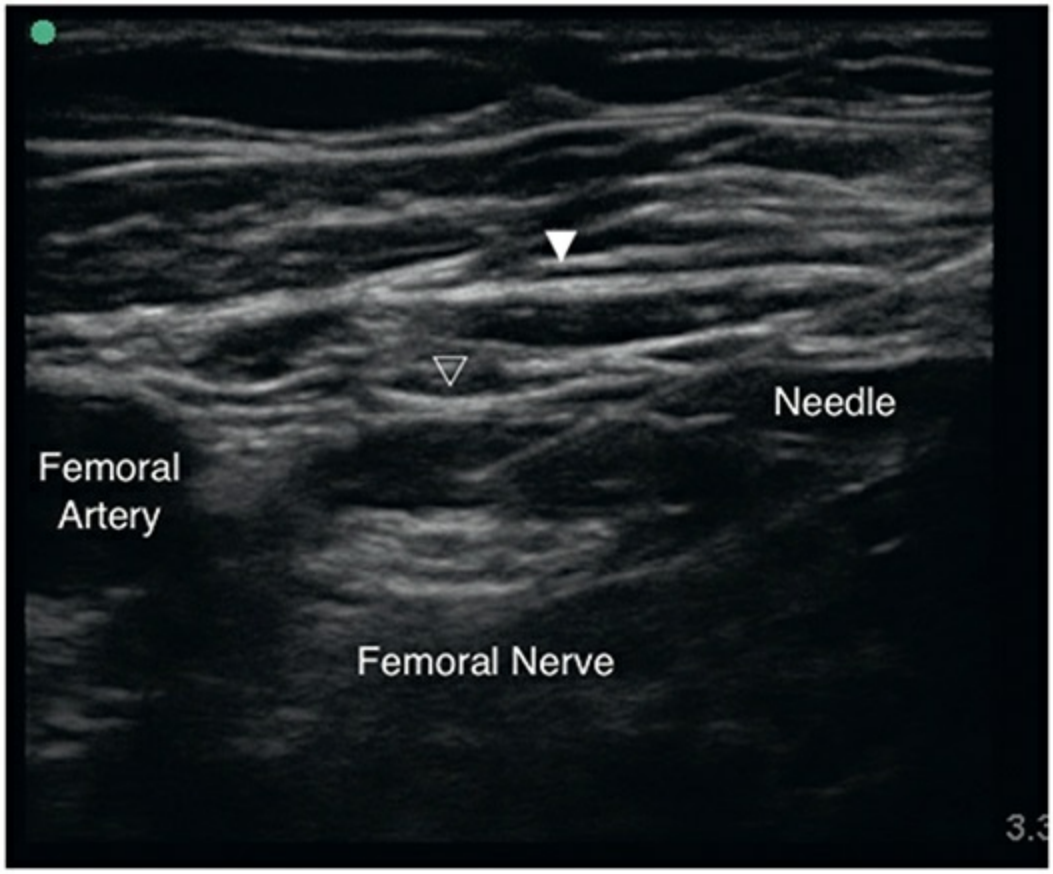

FIGURE 47.6. Perineural femoral nerve block. Fascia lata indicated by *solid triangle* and fascia iliaca by *blank triangle*.

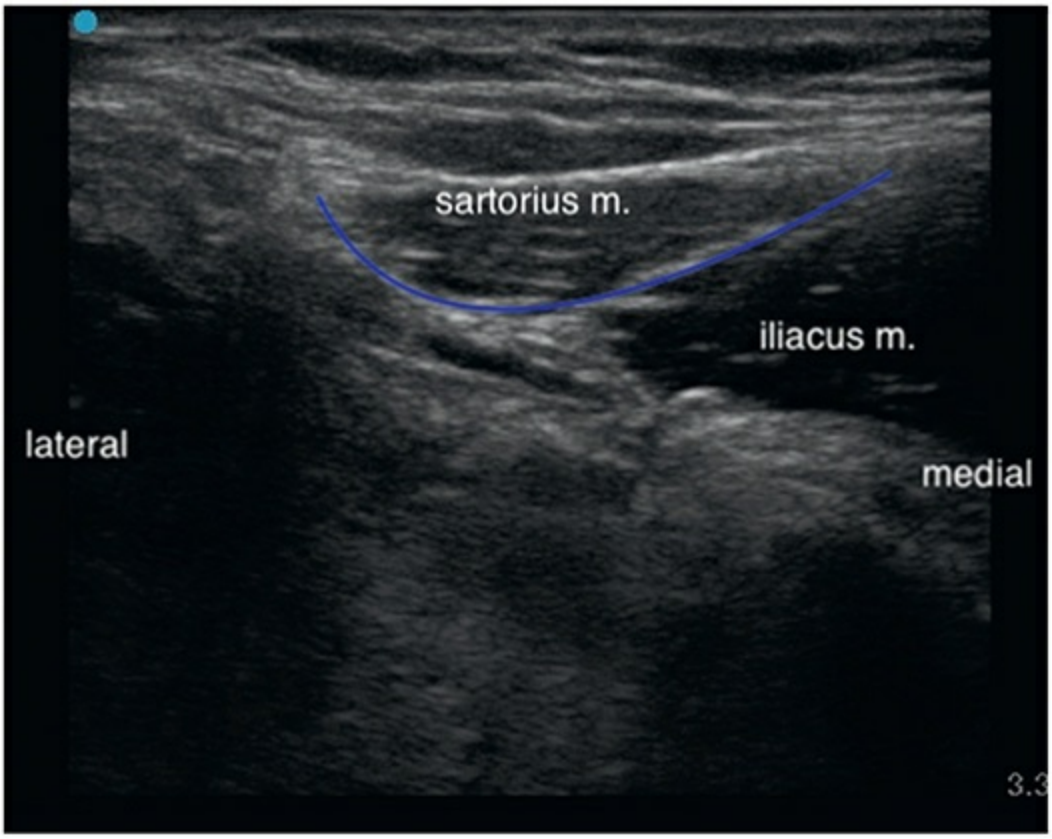

FIGURE 47.7. Fascia iliaca—infrainguinal fascia iliaca block, transverse approach Blue curved line indicates fascia iliaca.

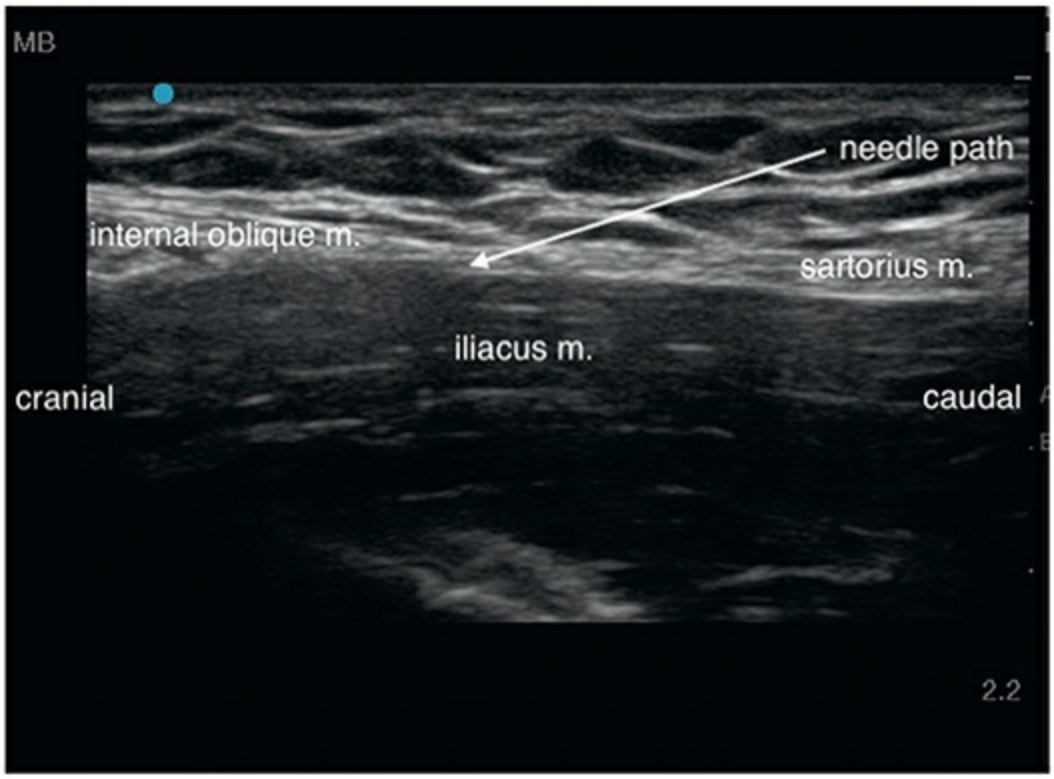

FIGURE 47.8. Suprainguinal fascia iliaca block, sagittal approach.

Dolan J, Williams A, Murney E, et al. Ultrasound guided fascia iliaca block: a comparison with the loss of resistance technique. *Reg Anesth Pain Med*. 2008;33(6):526–531.

Farag E, Mounir-Soliman L, eds. *Brown's Atlas of Regional Anesthesia*. 5th ed. Philadelphia, PA: Elsevier; 2017:97–102.

Hadzic A, ed. *Hadzic's Textbook of Regional Anesthesia and Acute Pain Management*. 2nd ed. New York: McGraw-Hill; 2017:602–607.

Kumar D, Hooda S, Kiran S, et al. Analgesic efficacy of ultrasound guided FICB in patients with hip fracture. *J Clin Diagn Res*. 2016;10(7):UC13–UC16.

Winnie AP, Ramamurthy S, Durrani Z. The inguinal paravascular technic of lumbar plexus anesthesia: the "3-in-1 block." *Anesth Analg*. 1973;52:989–996.

C.6. Describe the different ultrasound approaches to blocking the saphenous nerve above the knee.

The saphenous nerve is a sensory branch of the femoral nerve, which when blocked in combination with a sciatic nerve block, provides anesthesia for surgeries distal to the knee. Traditionally, this nerve was blocked via a subcutaneous wheel

of local anesthetics from the medial aspect of the tibial tuberosity to the anterior aspect of the tibia. The nerve lays lateral to the femoral artery while exiting the femoral triangle and then crosses over the roof of the adductor canal (subsartorial canal) and lays medial to the artery at the distal aspect of the adductor canal. The canal is bound anterolaterally by the vastus medialis muscle, anteriorly by the sartorius muscle, and posteromedially by the adductor magnus muscle. The saphenous nerve emerges from the adductor canal with the saphenous branch of the descending genicular artery and divides into the infrapatellar and sartorial branches. The sartorial branch courses through the fascia between the sartorius and gracilis muscles and emerges subcutaneously below the knee. Studies have proven ultrasound techniques to be quite reliable and effective in blocking this nerve, as the saphenous nerve emerges from the adductor canal. Just above the level of the knee, the nerve can be blocked between the sartorius and gracilis muscles in close proximity to the saphenous branch of the descending genicular artery. Krombach and Gray described blocking the saphenous nerve about 5 to 7 cm proximal to the popliteal crease, in the vastoadductor membrane (facial plane adjacent to the vastus medialis) deep to the sartorius muscle. Manickam et al. described blocking the saphenous nerve more proximally, in the distal adductor canal deep to the sartorius and anteromedial to the femoral artery (**Figs. 47.9** and **47.10**, **Video 47.1**).

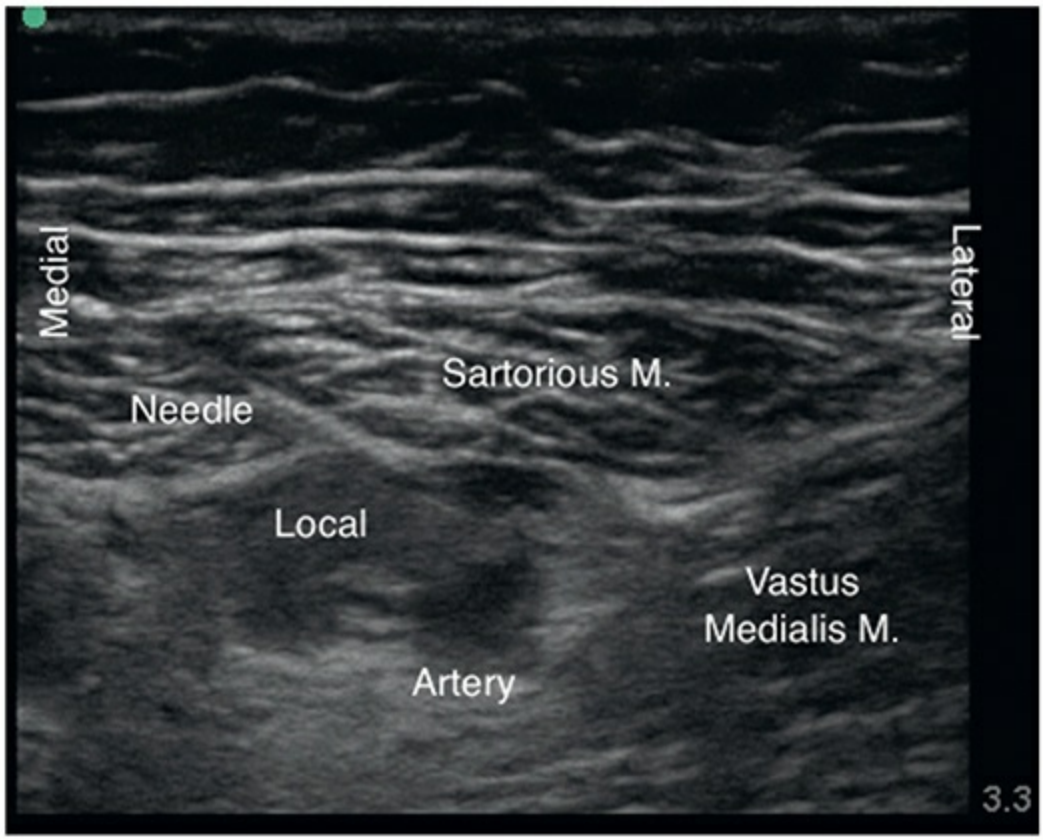

FIGURE 47.9. Post-periarterial saphenous nerve injection in the adductor canal.

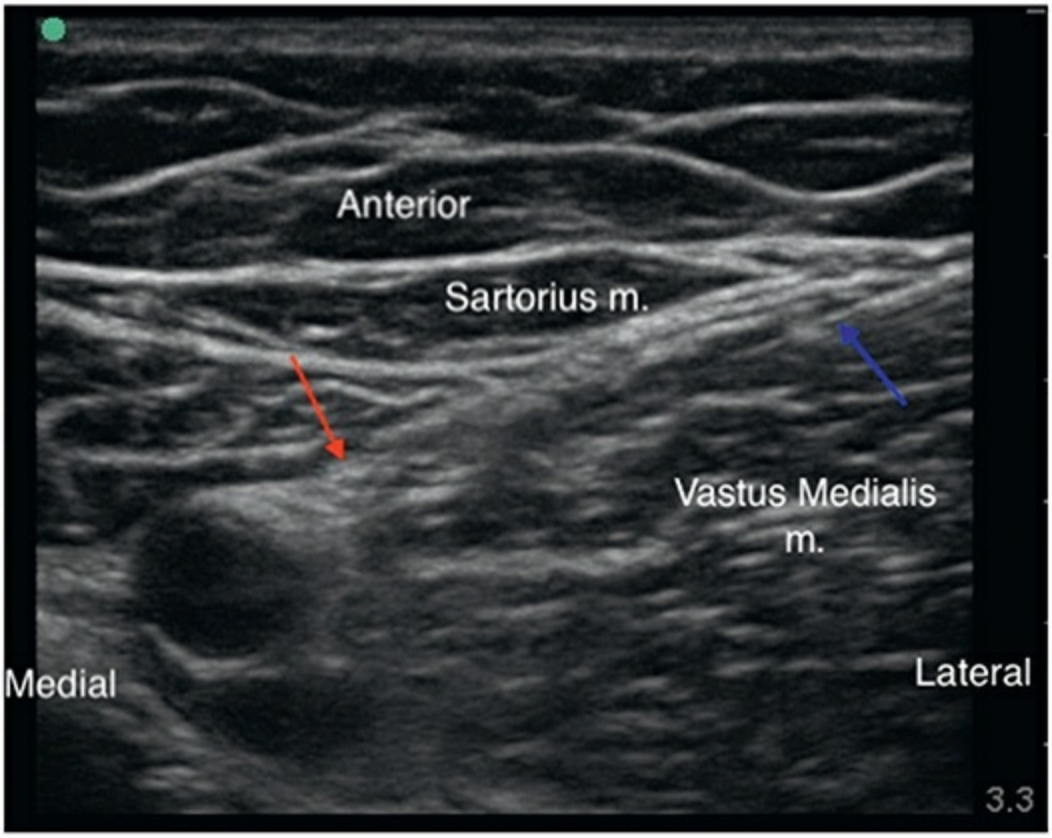

FIGURE 47.10. Saphenous nerve block: view of the lower adductor canal. Notice the sartorius muscle moving medially. Blue arrow indicates needle. *Red arrow* indicates saphenous nerve.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1450–1479.

Horn JL, Pitsch T, Salinas F, et al. Anatomic basis to the ultrasound-guided approach for saphenous nerve blockade. *Reg Anesth Pain Med*. 2009;34(5):486–489.

Krombach J, Gray AT. Sonography for saphenous nerve block near the adductor canal. *Reg Anesth Pain Med*. 2007;32(4):369–370.

Manickam B, Perlas A, Duggan E, et al. Feasibility and efficacy of ultrasound-guided block of the saphenous nerve in the adductor canal. *Reg Anesth Pain Med*. 2009;34(6):578–580.

Saranteas T, Anagnostis G, Paraskeuopoulos T, et al. Anatomy and clinical implications of the ultrasound-guided subsartorial saphenous nerve block. *Reg Anesth Pain Med*. 2011;36(4):399–402.

C.7. What benefits might a saphenous nerve block above the knee provide compared to a femoral nerve block?

Femoral and saphenous nerve blocks have been shown to

provide effective analgesia at the level of the knee and below. However, as a femoral nerve block provides analgesia to all the branches of the femoral nerve, it confers significant motor blockade to the quadriceps and has been associated with a small risk of falls during postoperative ambulation. Ideally, in cases where early ambulation and mobilization is desired, such as "fast-track" joint replacements, an analgesic block with motor preservation would be advantageous. Studies have shown that adductor canal saphenous nerve block provides equivalent analgesia compared to femoral block with improved quadriceps function in cases of knee arthroscopy, as well as ACL repair. In a group of healthy volunteers, Jaeger et al. demonstrated that a saphenous nerve block in the adductor canal reduced quadriceps strength 8% from baseline, whereas a femoral nerve block caused a 49% reduction from baseline. Although 100% could mobilize after a saphenous nerve block, only about 50% were mobile following a femoral nerve block. A possible basis for improved strength is that analgesia decreases centrally mediated inhibition of voluntary muscle contraction. Although a midthigh saphenous nerve block in the adductor canal will often spread to the nerve to the vastus medialis (sensory and motor), there would be less reduction in quadriceps muscle strength compared to a femoral nerve block.

Grevstad U, Mathiesen O, Valentiner LS, et al. Effect of adductor canal block versus femoral nerve block on quadriceps strength, mobilization, and pain after total knee arthroplasty: a randomized, blinded study. *Reg Anesth Pain Med*. 2015;40(1):3–10.

Jaeger P, Nielsen ZJ, Henningsen MH, et al. Adductor canal block versus femoral nerve block and quadriceps strength: a randomized, double-blind, placebo-controlled, crossover study in healthy volunteers. *Anesthesiology*. 2013;118:409–415.

Kim DH, Lin Y, Goytizolo EA, et al. Adductor canal block versus femoral nerve block for total knee arthroplasty: a prospective, randomized, controlled trial. *Anesthesiology*. 2014;120:540–550.

Xerogeanes JW, Premkumar A, Godfrey W, et al. Adductor canal vs. femoral nerve block in anterior cruciate ligament reconstruction: a randomized controlled trial. *Orthop J Sports Med*. 2017;5(7, suppl 6):2325967117S00277.

C.8. How would pain from a midthigh tourniquet dictate which peripheral nerve blocks to use in this patient? Describe the landmark technique of sciatic nerve block in the gluteal region. What is seen while performing an ultrasound technique to block the sciatic nerve?

A midthigh tourniquet will have implications in determining what blocks should be performed for lower extremity surgery. Although a tourniquet is used to decrease intraoperative blood loss, it occasionally has the unintended consequence of causing considerable pain in the thigh. The tourniquet is wrapped entirely around the leg and can affect both the femoral and sciatic nerves. Thus, it is important to block these nerves more proximal than at the adductor canal or the popliteal fossa. The mechanism of tourniquet pain is more complex than just secondary to pressure from the tourniquet and involves both unmyelinated C fibers and myelinated A fibers. The C fibers are more resistant to local anesthetic blockade, so when either neuraxial anesthesia or a regional block begins to wear off, or if they are incomplete to begin with, the C fibers will conduct resulting in the sensation of dull pain. This dull pain is experienced even with an “adequate” sensory block of the A fibers. C fibers are more readily blocked during general anesthesia, offering the lowest likelihood of tourniquet pain.

To perform a transgluteal sciatic nerve block with the landmark technique, the patient should be positioned in the lateral decubitus position with the leg to be blocked uppermost and flexed at the hip and knee. The landmarks are the greater trochanter and the PSIS. The distance between the greater

trochanter and the PSIS is measured, and the skin at 4 cm distal to the midpoint is marked as the insertion site. Alternatively, that point lies on a line from the greater trochanter to the sacral hiatus (**Fig. 47.11**). Once this site is located and the skin is prepped, the block needle is introduced at 90 degrees to the skin. Using a nerve stimulator, muscle twitches of the gluteal muscles are initially seen, and with further advancement, hamstring or calf twitches are seen. Ideally, the twitch remains at about 0.2 to 0.5 mA, indicating appropriate closeness to the nerve. When negative aspiration is confirmed, the local anesthetic of choice can then be injected.

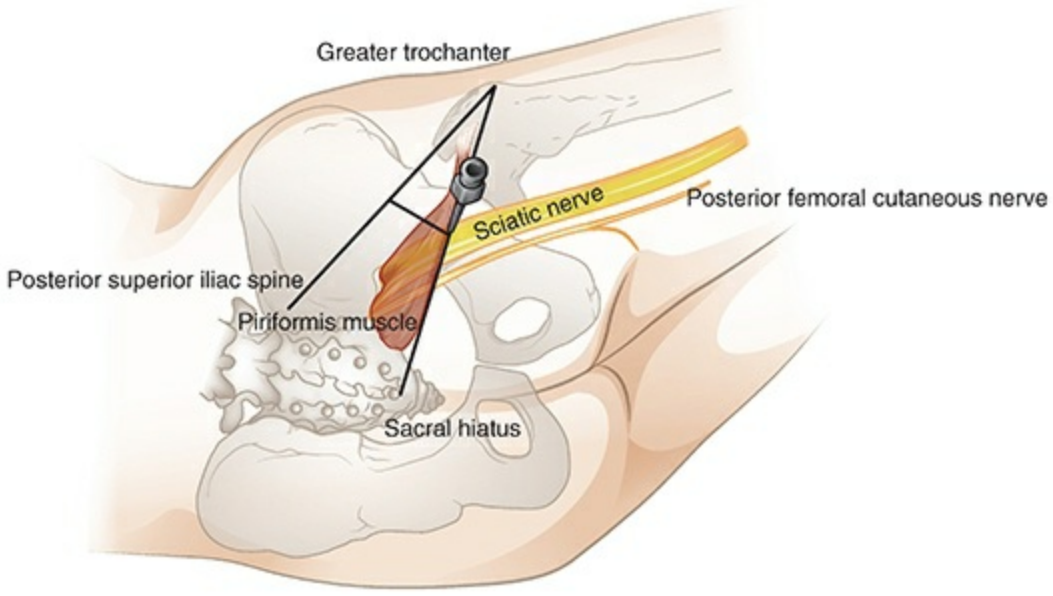

FIGURE 47.11. Sciatic nerve block, the Labat approach.

When utilizing an ultrasound-guided subgluteal approach, the nerve can be visualized between the ischial tuberosity and the greater trochanter. The patient is positioned either in the prone or lateral decubitus position; again, the leg and knee are flexed. Once the skin is cleaned, the curved transducer probe is placed over the skin. The nerve will be visualized between the two osseous structures, frequently described as being in a

"hammock" under the gluteus muscle. The local anesthetic solution will usually push the nerve away and actually improve the visualization of the nerve.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1450–1479.

Hadzic A, ed. *Hadzic's Textbook of Regional Anesthesia and Acute Pain Management*. 2nd ed. New York: McGraw-Hill; 2017:620–627, 1404–1417.

Sharma JP, Salhotra R. Tourniquets in orthopedic surgery. *Indian J Orthop*. 2012;46(4):377–383.

C.9. Why does a popliteal nerve block have a high failure rate if performed too proximate to the popliteal fossa when using a landmark/nerve stimulator technique? Describe how this can be avoided when using ultrasound-based popliteal block.

The landmark technique for performing a popliteal fossa block involves delineating the biceps femoris tendon, the semitendinosus and semimembranosus tendons, as well as the popliteal fossa crease. Needle insertion is at a point 7 cm above the popliteal crease at the midpoint between the lateral and medial tendons. Although this technique will work for a large majority of patients, a high failure rate does occur as a significant portion of the population has variant anatomy where the division of the sciatic nerve into the common peroneal nerve and the tibial nerve occurs more proximal to the level of the needle insertion point (**Fig. 47.12**). Thus, an incomplete blockade could occur if only one branch of the sciatic nerve is effectively blocked. The use of an ultrasound-guided technique allows for visualization of the nerve and the exact location of the division helping prevent such failure (**Fig. 47.13**, **Video 47.2**).

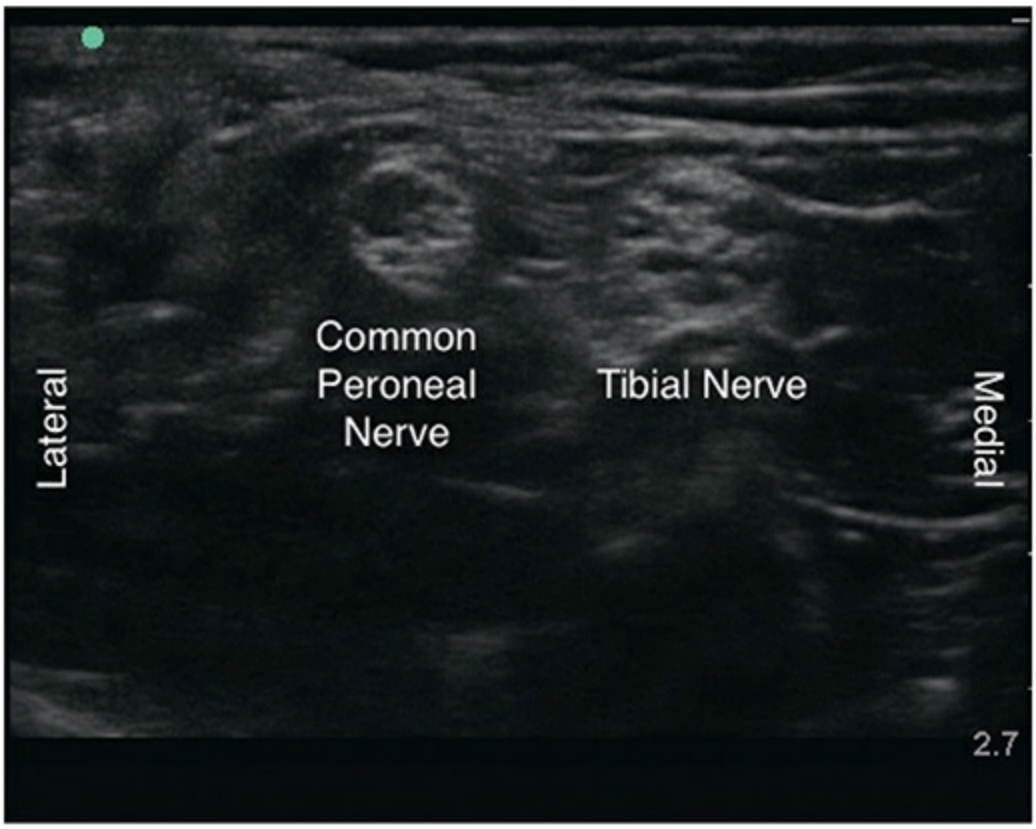

FIGURE 47.12. Popliteal fossa block showing local anesthetic surrounding nerves distal to nerve bifurcation.

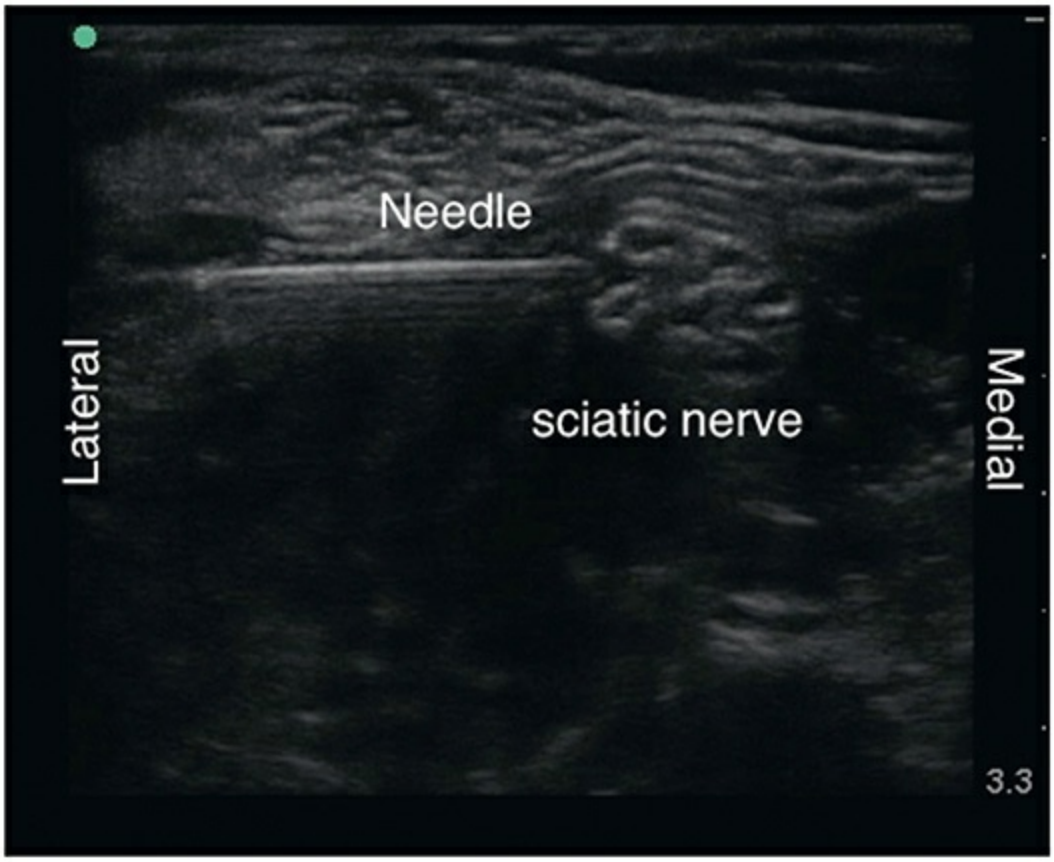

FIGURE 47.13. Popliteal fossa block just proximal to bifurcation.

Adibatti M, Sangeetha V. Study on variant anatomy of sciatic nerve. *J Clin Diagn Res*. 2014;8(8):ACO7–ACO9.

Hadzic A, ed. *Hadzic's Textbook of Regional Anesthesia and Acute Pain Management*. 2nd ed. New York: McGraw-Hill; 2017:1418–1426.

C.10. What is the IPACK block? In what situations would this block be useful?

IPACK stands for infiltration between the popliteal artery and the capsule of the knee. The IPACK block provides analgesia to the posterior compartment of the knee by anesthetizing the medial and lateral superior genicular nerves. It is typically performed under ultrasound guidance by first identifying the popliteal artery just proximal to the level of the femoral condyles (Fig. 47.14). The needle is placed between the popliteal artery and the femur in close proximity to the periosteum and 20 to 25 mL of local anesthetic is infiltrated in

the area and also as the needle is withdrawn (**Fig. 47.15**).

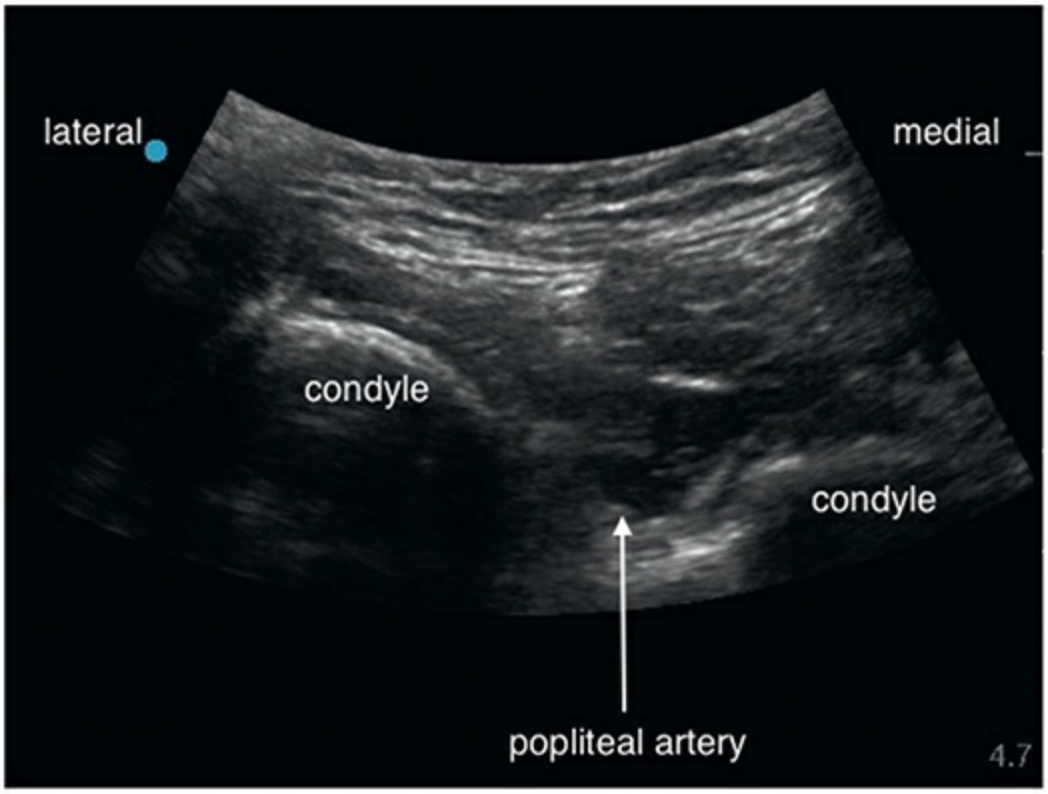

FIGURE 47.14. IPACK block—scanning at the level of the femoral condyles.

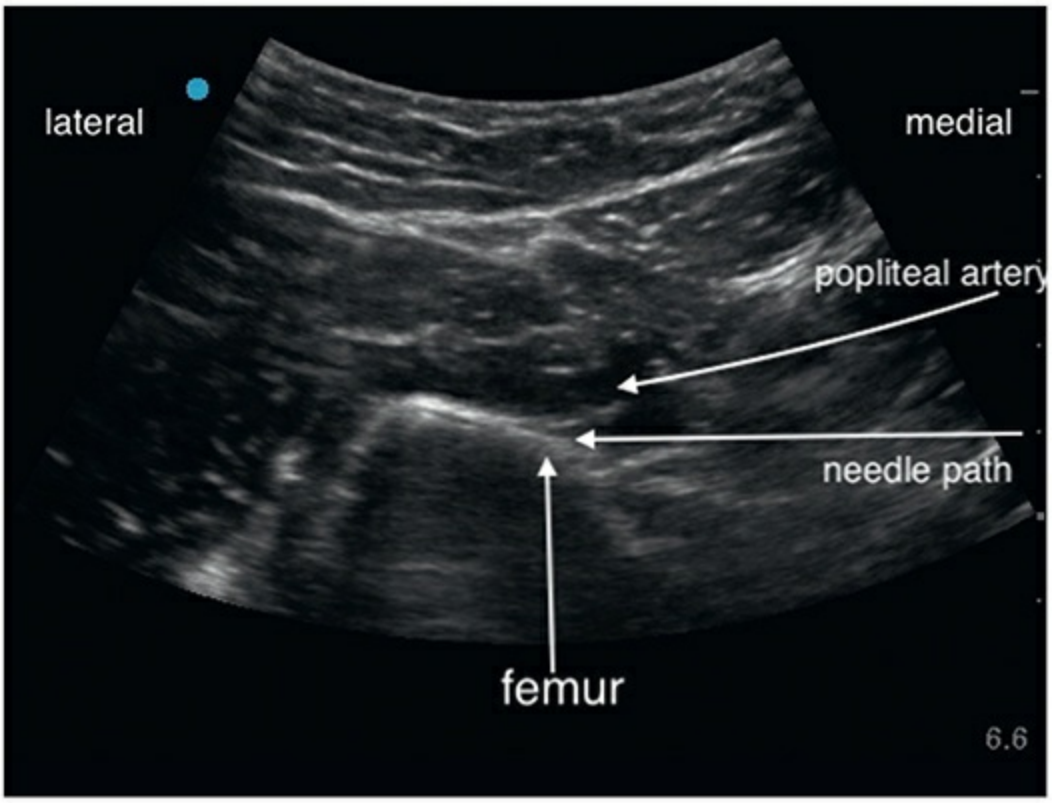

FIGURE 47.15. IPACK injection—location of IPACK injection between the popliteal artery and the femur, proximal to the femoral condyles.

The IPACK block is increasingly being used in conjunction with an adductor canal block to provide pain control after total knee arthroplasty (TKA) in the setting of "fast-track" recovery protocols. Although a sciatic block can also provide analgesia to the posterior knee, it is associated with significant motor block of the foot and ankle, delaying early mobilization after surgery and potentially masking a surgical injury to the peroneal nerve, which is not uncommon after TKA. Therefore, much like the adoption of the saphenous nerve block over the femoral nerve block, the IPACK block is being increasingly incorporated as a motor-sparing peripheral nerve block to enhance recovery after TKA. In a randomized trial of 86 patients undergoing TKA, Kim et al. demonstrated that the addition of the IPACK and adductor canal block significantly improved postoperative analgesia and reduced opioid consumption compared to periarticular injection

by the surgeon alone.

Kim DH, Beathe JC, Lin Y, et al. Addition of infiltration between the popliteal artery and the capsule of the posterior knee and adductor canal block to periarticular injection enhances postoperative pain control in total knee arthroplasty: a randomized controlled trial. *Anesth Analg*. 2019;129(2):526–535. doi:10.1213/ANE.0000000000003794.

Sinha SK, Abrams JH, Arumugam S, et al. Femoral nerve block with selective tibial nerve block provides effective analgesia without foot drop after total knee arthroplasty: a prospective, randomized, observer-blinded study. *Anesth Analg*. 2012;115(1):202–206.

D. Postoperative Pain Management

D.1. Describe compartment syndrome and how that risk would influence your postoperative plan for peripheral regional analgesia.

Compartment syndrome develops when there is an increase in pressure within a fixed compartment. Patients often have a collection of signs and symptoms including pain out of proportion to the injury, paresthesia, pallor, decreased sensation, weakness, and a late finding of paralysis. It is typically seen after trauma, especially long bone fractures, and specifically after any injury that increases the volume of a compartment of limited size. Tibial fractures are the most common cause, with an incidence of 1% to 10%. The pathophysiology has been described as cellular anoxia due to the inability of the blood flow in an injured area to meet the metabolic demands of local tissue. The resultant swelling and obstruction to venous outflow further decreases the arteriovenous gradient.

The use of regional anesthesia in patients at risk for compartment syndrome remains controversial. Theoretically, neuraxial blockade could prevent recognition of an acute compartment syndrome. Case reports have shown that signs and symptoms of acute compartment syndrome were present in

patients given high concentrations of local anesthetic for neuraxial analgesia but that the significance of the symptoms were not appropriately recognized. Other case reports have demonstrated that patients with dense motor and sensory blocks who are later diagnosed with acute compartment syndrome still reported severe pain in the distribution of the peripheral nerve block. A recent systematic review article concluded that regional anesthesia does not increase the risk of delayed diagnosis of compartment syndrome. Still, one should consider the risks of compartment syndrome, the exact location of the fracture, positioning during surgery, and the benefits of a regional anesthetic in this patient, taking into account his chronic pain issues.

Driscoll E, Maleki AH, Jahromi L, et al. Regional anesthesia or patient-controlled analgesia and compartment syndrome in orthopedic surgical procedures: a systematic review. *Local Reg Anesth*. 2016;9:65–81.

Elliot KG, Johnstone AJ. Diagnosing acute compartment syndrome. *J Bone Joint Surg Br*. 2003;85:625–632.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1158, 2146.

Kucera TJ, Boezaart AP. Regional anesthesia does not consistently block ischemic pain: two further cases and a review of the literature. *Pain Med*. 2014;15:316–319.

Mannion S, Capdevila X. Acute compartment syndrome and the role of regional anesthesia. *Int Anesthesiol Clin*. 2010;48(4):85–105.

D.2. How would the addition of dexamethasone to your local anesthetic influence the duration of the blocks placed in the OR?

The addition of dexamethasone to local anesthetic for peripheral nerve blockade has been shown to increase the duration of blockade. When dexamethasone is added to bupivacaine or ropivacaine 0.5%, the duration of sensory block increases from approximately 12 to 24 hours. There is some evidence that

giving an equivalent dose of intravascular dexamethasone concomitant to the block will prolong the duration of the sensory block to 24 hours. Recent meta-analysis has shown that perineural dexamethasone prolongs analgesia by 3.77 hours with a slight decrease of opioid consumption when compared with intravascular dexamethasone while providing a similar duration of prolonged motor blockade.

Chong MA, Berbenetz NM, Lin C, et al. Perineural versus intravenous dexamethasone as an adjuvant for peripheral nerve blocks: a systematic review and meta-analysis. *Reg Anesth Pain Med*. 2017;42(3):319–326.

De Oliveira GS Jr, Castro Alves LJ, Nader A, et al. Perineural dexamethasone to improve postoperative analgesia with peripheral nerve blocks: a meta-analysis of randomized control trials. *Pain Res Treat*. 2014;2014:179029.

Desmet M, Braems H, Reynvoet M, et al. I.V. and perineural dexamethasone are equivalent in increasing the analgesic duration of a single-shot interscalene block with ropivacaine for shoulder surgery: a prospective, randomized, placebo-controlled study. *Br J Anaesth*. 2013;111(3):445–452.

D.3. What is liposomal bupivacaine?

Liposomal bupivacaine is a slow-release form of the local anesthetic bupivacaine that has U.S. Food and Drug Administration (FDA) approval to be used for local infiltration and, most recently, for interscalene block to decrease postoperative pain. Each liposome has internal chambers with encapsulated bupivacaine that are released over an extended period of time. Some studies reported a duration of blockade of up to 72 hours as part of a peripheral or neuraxial technique, giving promise that this agent can be a potential substitute for the peripheral catheter. There has been evidence showing modest improvements in pain scores and patient satisfaction using liposomal bupivacaine compared to bupivacaine alone for major shoulder surgery.

Ilfeld BM. Liposome bupivacaine in peripheral nerve blocks and epidural injections to manage postoperative pain. *Expert Opin Pharmacother*.

2013;14(17):2421–2431.

Skolnik A, Gan T. New formulation of bupivacaine for the treatment of postoperative pain: liposomal bupivacaine and SABER-Bupivacaine. *Expert Opin Pharmacother*. 2014;15(11):1535–1542.

Vandepitte C, Kuroda M, Witvrouw R, et al. Addition of liposome bupivacaine to bupivacaine HCl versus bupivacaine HCL alone for interscalene brachial plexus block in patients having major shoulder surgery. *Reg Anesth Pain Med*. 2017;42(3):334–341.

D.4. What benefit would a peripheral nerve catheter provide over a long-acting local anesthetic? Are there any downsides?

Peripheral nerve catheters are a proven method for prolonging postoperative pain control with decreased intravenous or oral opioid use and hence their related side effects. They also have been shown to decrease the incidence and/or severity of chronic postsurgical pain syndromes. A peripheral nerve catheter gives patients the ability to have some control over their own pain management. As compared with long-lasting single-shot injections with additives, a catheter technique could provide analgesia beyond the first 24 hours, which is essentially the limit of duration of a single-shot block, aside from the use of liposomal bupivacaine. As compared to a long-lasting single-shot injection, peripheral catheters can be stopped and/or removed if needed. Peripheral nerve catheters are increasingly being used in the ambulatory and outpatient settings, with patients being discharged to home with an infusing peripheral nerve catheter in place. Large studies continue to show a low-risk profile with the use of at-home patient management of catheters. Some limitations to the placement of peripheral nerve catheters include the risk of infection, technical challenges inherent in their placement, time of placement, and the need for their management and supervision by anesthesiologists and other health care providers. Other risks of peripheral nerve catheters include damage to the nerve itself from direct contact

or nerve entrapment, damage to nearby structures, and intravascular placement and migration. Although these risks are recognized and need to be monitored, a recent comprehensive review article reports them to be exceedingly rare. Although there are no studies, at this time, directly comparing the use of peripheral nerve catheters to liposomal bupivacaine, the recent FDA approval of liposomal bupivacaine for interscalene block will add another dimension to the ongoing discussion regarding peripheral nerve catheters.

Ilfeld BM. Continuous peripheral nerve blocks: an update of the published evidence and comparison with novel, alternative analgesic modalities. *Anesth Analg*. 2017;124(1):308–335.

Merritt CK, Mariano ER, Kaye AD, et al. Peripheral nerve catheters and local anesthetic infiltration in perioperative analgesia. *Best Pract Res Clin Anaesthesiol*. 2014;28(1):41–57.

Vandepitte C, Kuroda M, Witvrouw R, et al. Addition of liposome bupivacaine to bupivacaine HCl versus bupivacaine HCL alone for interscalene brachial plexus block in patients having major shoulder surgery. *Reg Anesth Pain Med*. 2017;42(3):334–341.

D.5. You were able to perform a continuous spinal epidural (CSE) at L3–L4 and used 0.125% bupivacaine via epidural route for postoperative pain control. The patient reports that he is comfortable regarding both his back pain and his ankle pain. What benefit would continuing the patient's methadone confer in this case?

The use of chronic opioid regimens for patients suffering from chronic nonmalignant pain has increased dramatically over the past two decades. Acute postoperative pain control in patients who are taking maintenance opioids for addiction and dependence presents a challenge for health care providers. Studies have shown that these patients require opioid doses that are multiples of the doses needed by patients not exposed to

opioids chronically. Aside from tolerance to opioids, these patients often exhibit increased pain to surgical stimuli, when compared to an opioid-naive population. This may be secondary to increased anxiety and depression, the development of opioid-induced hyperalgesia, and changes in the endogenous opioid system. Multimodal analgesia, including regional techniques and nonopioid adjuvants, such as ketamine, nonsteroidal anti-inflammatory drugs, gabapentinoids and acetaminophen, greatly aid in controlling their pain postoperatively. Nonetheless, continuation of maintenance opioids (50% to 100%) is essential to avoid withdrawal symptoms. Approaches to maintaining opioid levels include continuation of the same preoperative opioid and route, changing the route of administration while continuing the same opioid, or using an equianalgesic conversion to a different opioid with a likely dose reduction secondary to lack of 100% cross tolerance. In addition, patients should generally receive their usual dose of opioids prior to surgery. Withdrawal from methadone may present 12 to 24 hours after the last doses, whereas withdrawal from medications such as morphine may fall within 6 to 18 hours. Withdrawal syndrome can present with agitation, diaphoresis, hypertension, diarrhea, nausea, emesis, abdominal cramps, and even seizures.

Hadi I, Morley-Forster PK, Dain S, et al. Brief review: perioperative management of the patient with chronic non-cancer pain. *Can J Anaesth*. 2006;53:1190–1199.

Mehta V, Langford R. Acute pain management for opioid dependent patients. *Anaesthesia*. 2006;61:269–276.

Richebé P, Beaulieu P. Perioperative pain management in the patient treated with opioids: continuing professional development. *Can J Anaesth*. 2009;56:969–981.

D.6. How can regional analgesia aid in fast-track postoperative care?

Fast-track programs are used to help decrease morbidity by

decreasing perioperative hospitalization. Both neuraxial and peripheral blockade can be utilized as an effective modality to aid in fast-track programs. Regional anesthesia can attenuate the inflammatory, endocrine, and metabolic responses to surgical stress and thus decrease perioperative complications. The blockade of the sympathetic response helps with improved blood flow, decreased thromboembolic events, and decreased blood loss. It also tempers the shivering response, which can potentially prolong postanesthetic care unit stays. Regional techniques can be used to minimize inhalational agents, muscle relaxants, and opioids with a resultant earlier awakening from general anesthesia or complete avoidance of general anesthesia. It improves immediate postoperative analgesia and has been shown to decrease the risk of infection. In addition, there is often earlier return of bowel function. Specifically, for lower extremity surgery, regional anesthesia can improve patient satisfaction with decreasing time to home readiness, opioid consumption, pain scores, time to ambulation, and postoperative nausea and vomiting. Regional anesthesia is the cornerstone of the new movement toward total joint replacement in the ambulatory setting.

Aasvang EK, Luna IE, Kehlet H. Challenges in postdischarge function and recovery: the case of fast-track hip and knee arthroplasty. *Br J Anaesth*. 2015;115(6):861–866.

Carli F, Kehlet H, Baldini G, et al. Evidence basis for regional anesthesia in multidisciplinary fast-track surgical care pathways. *Reg Anesth Pain Med*. 2011;36(1):63–72.

Memtsoudis SG, Sun X, Chiu YL, et al. Perioperative comparative effectiveness of anesthetic technique in orthopedic patients. *Anesthesiology*. 2013;118(5):1046–1058.

48 Complex Regional Pain Syndromes

Mohammad M. Piracha, Neel D. Mehta, Sudhir A. Diwan, and Vinod Malhotra

A 35-year-old woman complains of diffuse burning pain in the left arm and hand for the last 6 months. She recalls spraining her left wrist while playing volleyball. Her left hand feels colder than the right, and her fingertips are blue. She is a recently divorced high-profile executive.

A. Medical Disease and Differential Diagnosis

1. What is the differential diagnosis of pain in this patient?
2. What is complex regional pain syndrome (CRPS)?
3. What are the two types of CRPS?
4. What are the diagnostic criteria for CRPS? What is the incidence of this disease?
5. Define allodynia, hyperalgesia, hyperesthesia, and dysesthesia.
6. What are the stages of CRPS?
7. What are the possible etiologies of CRPS?
8. Explain the pathophysiology of the development of CRPS.
9. Define sympathetically maintained pain (SMP) and sympathetically independent pain (SIP).

10. How does CRPS differ from neuralgia?
11. What is central pain? How will you differentiate central pain from CRPS?
12. Is the social history of this patient relevant to the development of chronic pain syndrome?

B. Pain Management

1. How will you work up CRPS types I and II?
2. Describe the sympathetic nerve supply to the arm?
3. Where is the stellate ganglion located?
4. What are the anatomic landmarks used in the stellate ganglion block?
5. What are the clinical signs of stellate ganglion block?
6. What is Horner syndrome?
7. After a stellate ganglion block, this patient reports no significant change in the degree of pain despite developing Horner syndrome. Is the pain psychogenic in this patient?
8. What types of nerve fibers are interrupted in stellate ganglion block?
9. What is a differential block?
10. What are the two major classes of local anesthetics? Describe the major differences in their clinical pharmacology.
11. What factors determine the onset, potency, and duration of a local anesthetic block?
12. How does the addition of epinephrine to commercially available premixed solutions affect the efficacy of local anesthetics?
13. How will you treat this patient?
14. What is the pharmacologic management of CRPS?
15. What is the role of intravenous regional block (Bier method) in diagnosis and treatment of CRPS?
16. Compare and contrast the mechanism of actions of ketamine and methadone.

17. What roles does ketamine infusion play in the treatment of CRPS? Is there a guideline for ketamine infusion in treating CRPS?
18. What is neuromodulation? What is the role of spinal cord stimulation (SCS) in treating CRPS?
19. What is the role of surgical sympathectomy?
20. What role does intrathecal (IT) therapy play in managing CRPS?
21. If opioids are prescribed as treatment for CRPS patients, what is the Centers for Disease Control and Prevention (CDC) guideline of chronic opioid therapy?

C. Complications

1. What are the complications of stellate ganglion block?
2. What is the systemic toxicity of local anesthetics?
3. How do you treat the systemic toxicity of local anesthetic drugs?
4. What are the possible complications of SCS?
5. What are the possible complications of IT therapy?

A. Medical Disease and Differential Diagnosis

A.1. What is the differential diagnosis of pain in this patient?

Pain accompanied by burning and temperature change in this patient is most likely due to CRPS. The differential diagnosis may also include the following:

1. Peripheral neuropathy
2. Soft tissue injury
3. Vascular insufficiency (Raynaud disease)
4. Nerve entrapment syndrome (carpal tunnel syndrome)
5. Brachial plexopathy

Over the years, CRPS has been referred to as *reflex*

sympathetic dystrophy (RSD), causalgia, SMP, and chronic peripheral pain syndrome. The term *CRPS* was introduced in 1994 by the International Association for the Study of Pain subcommittee on taxonomy. It is subdivided into CRPS type I (formerly described as *RSD*) and CRPS type II (formerly described as *causalgia*).

Dutton K, Littlejohn G. Terminology, criteria, and definitions in complex regional pain syndrome: challenges and solutions. *J Pain Res*. 2015;8:871–877.

Stanton-Hicks MD. CRPS: what's in a name? Taxonomy, epidemiology, neurologic, immune and autoimmune considerations. *Reg Anesth Pain Med*. 2019;44:376–387.

A.2. What is complex regional pain syndrome (CRPS)?

CRPS is characterized by pain associated with sensory, autonomic, trophic, and motor abnormalities. CRPS is triggered by *noxious stimuli* (type I) or by *nerve injury* (type II). It is not limited to the distribution of a single peripheral nerve and is disproportionate to the inciting event.

RSD, causalgia, algodystrophy, Sudeck atrophy, and various other conditions are all grouped under CRPS. This diagnosis better describes the wide range of clinical signs and symptoms and the complexity of the pathophysiology responsible for the clinical picture.

Dutton K, Littlejohn G. Terminology, criteria, and definitions in complex regional pain syndrome: challenges and solutions. *J Pain Res*. 2015;8:871–877.

Stanton-Hicks MD. CRPS: what's in a name? Taxonomy, epidemiology, neurologic, immune and autoimmune considerations. *Reg Anesth Pain Med*. 2019;44:376–387.

A.3. What are the two types of CRPS?

CRPS-I is defined as a clinical syndrome triggered by a *noxious stimulus* that is not limited to the distribution of a single peripheral nerve; no nerve lesion can be identified. CRPS-II is

defined as a clinical syndrome that is due to a *nerve injury* and is mostly limited to the distribution of the injured nerve. The diagnostic criteria are the same for CRPS-I and II.

Marinus J, Moseley GL, Birklein F, et al. Clinical features and pathophysiology of complex regional pain syndrome. *Lancet Neurol*. 2011;10:637–648.

Stanton-Hicks MD, Burton AW, Bruehl SP, et al. An updated interdisciplinary clinical pathway for CRPS: report of an expert panel. *Pain Pract*. 2000;2(1):1–16.

A.4. What are the diagnostic criteria for CRPS? What is the incidence of this disease?

The diagnosis of CRPS can be made in the following context: a history of trauma to the affected area associated with pain that is disproportionate to the inciting event plus one or more of the following as defined by either the Orlando criteria or a modified version referred to as the Budapest criteria.

- Abnormal function of the sympathetic nervous system (vasomotor changes, skin color changes)
- Swelling
- Movement disorder
- Changes in tissue growth (dystrophy and atrophy)
- Sensory disturbances (hyperalgesia or allodynia)

The main features include pain that is continuous, burning in nature, independent of type and severity of injury, and not limited to a dermatomal distribution. Patients may complain of allodynia, dysesthesia, or hyperalgesia. Movement or stress exacerbates pain. Edema is usually present. Abnormal sudomotor activity, limb discoloration, and local temperature changes are common but inconsistent.

It affects between 200,000 and 1.2 million Americans. This syndrome may follow as many as 5% of all traumatic injuries with the arms being affected in approximately 60% of cases and the legs about 40%.

Ballantyne JC, Fishman SM, Rathmell JP, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2018:314–331.

Marinus J, Moseley GL, Birklein F, et al. Clinical features and pathophysiology of complex regional pain syndrome. *Lancet Neurol*. 2011;10:637–648.

A.5. Define allodynia, hyperalgesia, hyperesthesia, and dysesthesia.

- *Allodynia*: pain caused by a stimulus that normally does not provoke pain (i.e., touching with a cotton swab)
- *Hyperalgesia*: an increased response to a stimulus that is normally painful (i.e., increased response to pinprick)
- *Hyperesthesia*: increased sensitivity to a stimulus either due to a diminished threshold or an increased response to stimuli that are normally recognized. Hyperesthesia includes both allodynia and hyperalgesia.
- *Dysesthesia*: an abnormal sensation that is unpleasant to the patient. It may be either spontaneous or evoked (i.e., lumbar radiculopathy).

Ballantyne JC, Fishman SM, Rathmell JP, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2018:314–331.

A.6. What are the stages of CRPS?

Stage I

- Onset of severe pain limited to the site of injury
- Increased sensitivity of skin to touch and light pressure (hyperesthesia)
- Localized swelling
- Muscle cramps
- Stiffness and limited mobility

At the onset, the skin is usually warm, red, and dry; then it may change to blue (cyanotic) in appearance and become cold and sweaty.

- Increased sweating (hyperhidrosis)

- In mild cases, this stage lasts a few weeks and then subsides spontaneously or responds rapidly to treatment.

Stage II

- Pain becomes even more severe and more diffuse.
- Swelling tends to spread and it may change from a soft to hard (brawny) type.
- Hair may become coarse then scant; nails may grow faster and become brittle, cracked, and heavily grooved.
- Spotty wasting of bone (osteoporosis) occurs early but may become severe and diffuse.
- Muscle wasting begins.

Stage III

- Marked wasting of tissue (atrophic) eventually becomes irreversible.
- For many patients, the pain becomes intractable and may involve the entire limb.
- A small percentage of patients have developed generalized CRPS affecting the entire body.

Ballantyne JC, Fishman SM, Rathmell JP, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2018:314–331.

A.7. What are the possible etiologies of CRPS?

CRPS may follow relatively minor trauma with or without nerve injury. Causes leading to CRPS include the following:

- Injuries to peripheral tissues (e.g., fractures, dislocations, and postoperative state)
- Inflammatory conditions (e.g., fasciitis, tendonitis, bursitis, and arthritis)
- Immobilization as a result of injury or cast application
- Peripheral nerve injury resulting from direct compression or ischemia (e.g., brachial plexopathy, postherpetic neuralgia, and nerve root injury)

- Central nervous system insults (e.g., head injury, ischemia, and brain tumor)
- Spinal cord lesions
- Idiopathic

Ballantyne JC, Fishman SM, Rathmell JP, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2018:314–331.

A.8. Explain the pathophysiology of the development of CRPS.

Several hypotheses have been postulated, but none can explain all the findings and the varying responses to treatment in these patients. These hypotheses include the following:

- Abnormal discharges in sympathetic and nociceptive afferents produced by trauma
- Sensitization of peripheral sensory receptors produced by sympathetic hyperactivity
- Formation of ephapses (artificial synapses) after peripheral nerve injury
- Spontaneous neuronal ectopy at the site of demyelination or axonal injury
- Central reorganization of pain processing (central sensitization)

More than one sequence of events likely take place in a patient, giving rise to a mixed clinical picture. A dynamic change in the physiology and structure of central pain projecting neurons mediated through the *N*-methyl-D-aspartate (NMDA) receptor. Injury initiates and maintains a state of central sensitization in the central pain pathways, resulting in a lower threshold to fire pain transmission neurons and an increase in their receptive fields. This may involve disinhibition of spinal and trigeminal nociceptive neurons. This often precedes thermal and mechanical allodynia and spontaneous pain. Finally, the psychological component and neuromodulation cannot be

discernibly separated.

Benzon H, Rathmell JP, Wu CL, et al, eds. *Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby; 2013:346–360.

Marinus J, Moseley GL, Birklein F, et al. Clinical features and pathophysiology of complex regional pain syndrome. *Lancet Neurol*. 2011;10:637–648.

McMahon SB, Koltzenburg M, Tracey I, et al, eds. *Wall and Melzack's Textbook of Pain*. 6th ed. New York: Churchill Livingstone; 2013:961–977.

A.9. Define sympathetically maintained pain (SMP) and sympathetically independent pain (SIP).

The pain that is maintained by sympathetic innervation or circulating catecholamines is defined as SMP. It describes a pain mechanism, not a clinical syndrome. Therefore, by definition, patients with CRPS who report pain relief after a sympathetic block (e.g., stellate ganglion block) have SMP. Conversely, pain conditions that show features of sympathetic overactivity, yet fail to respond to sympathetic blocks, are described as SIP.

Ballantyne JC, Fishman SM, Rathmell JP, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2018:314–331.

A.10. How does CRPS differ from neuralgia?

The chronic pain seen in neuralgia is usually paroxysmal in nature and follows the distribution of nerve. The pain is sharp and shooting without associated vasomotor or sudomotor changes. The chronic pain syndrome of CRPS is a sustained, diffuse, burning pain that is independent of nerve distribution and is associated with vasomotor and sudomotor changes, edema, allodynia or hyperalgesia, and changes in skin color.

Benzon H, Rathmell JP, Wu CL, et al, eds. *Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby; 2013:346–360.

A.11. What is central pain? How will you differentiate central pain from CRPS?

Central pain is regional pain initiated or caused by a primary lesion or dysfunction in the central nervous system; it is usually associated with abnormal sensitivity to temperature and to noxious stimulus. Central pain, also referred to as *deafferentation pain*, is a difficult pain syndrome to treat because the pathophysiology is not well understood. Regional pain not relieved by peripheral nerve blocks, either sympathetic or somatic, is more likely to be central pain. Central pain may be associated with various neurologic symptoms and signs such as monoparesis, hemiparesis, or paraparesis. Central pain conditions typically include partial or complete loss of sensation, involvement of spinothalamic functions, and development of hypersensitivity in body parts that have loss normal somatosensory feedback as a result of a central nevous system lesion.

Abram SE, Haddox JD, eds. *The Pain Clinic Manual*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2000:253–259.

McMahon SB, Koltzenburg M, Tracey I, et al, eds. *Wall and Melzack's Textbook of Pain*. 6th ed. New York: Churchill Livingstone; 2013:990–1002.

A.12. Is the social history of this patient relevant to the development of chronic pain syndrome?

In patients with CRPS, the disproportionate pain and dysfunction and the absence of clear pathogenesis and pathophysiology have led to examination of potential psychological etiology. Also noted is the fact that as the CRPS progresses, patients' personality measures such as Minnesota Multiphasic Personality Inventory (MMPI) profiles tend to resemble those of patients experiencing chronic pain and psychological distress as evidenced by hypochondriasis, depression, and hysteria scales. Certainly, stress has been implicated in increasing sympathetic outflow. The literature suggests that the presence of psychological disorders,

particularly anxiety and depression, may predispose the patient to the development of CRPS. However, a large case-control study reported no differences in psychological variables between those with CRPS and those without CRPS after controlling for age, sex, and trauma. Furthermore, anxiety and stress can augment nociception, and therefore, antidepressive treatments can be useful.

de Mos M, Huygen FJ, Dieleman JP, et al. Medical history and the onset of complex regional pain syndrome (CRPS). *Pain*. 2008;139:458–466.

Marinus J, Moseley GL, Birklein F, et al. Clinical features and pathophysiology of complex regional pain syndrome. *Lancet Neurol*. 2011;10:637–648.

McMahon SB, Koltzenburg M, Tracey I, et al, eds. *Wall and Melzack's Textbook of Pain*. 6th ed. New York: Churchill Livingstone; 2013:990–1002.

B. Pain Management

B.1. How will you work up CRPS types I and II?

CRPS is diagnosed clinically with a detailed history and physical examination. Because it is a clinical diagnosis of exclusion, other specific conditions that could account for the degree of pain and dysfunction must be ruled out. Objective signs are variable but almost universally include loss of function of the affected part due to pain. Allodynia and hyperalgesia are extremely common. Change in temperature and sweating may vary depending on the stage of the disease. Several diagnostic studies may aid in the diagnosis of CRPS but are seldom pathognomonic.

A quantitative sweat test may show excessive sweating, and thermography may demonstrate abnormal heat regulation and disparity in temperature between affected and normal regions. Radiologic studies may reveal patchy osteoporosis in early stages. Triple-phase bone scintigraphy using technetium-99m

may show increased periarticular uptake in the affected extremity illustrated by unilateral hyperperfusion in the perfusion and blood pool phases. Negative triple-phase bone scan results do not rule out CRPS. Thermographic, radiologic, or scintigraphic findings can be nonspecific and should be correlated with the clinical findings. Positive diagnostic sympathetic blocks can confirm the sympathetically mediated component of CRPS.

McMahon SB, Koltzenburg M, Tracey I, et al, eds. *Wall and Melzack's Textbook of Pain*. 6th ed. New York: Churchill Livingstone; 2013:990–1002.

Stanton-Hicks MD. CRPS: what's in a name? Taxonomy, epidemiology, neurologic, immune and autoimmune considerations. *Reg Anesth Pain Med*. 2019;44:376–387.

B.2. Describe the sympathetic nerve supply to the arm?

The preganglionic sympathetic outflow to the upper extremity is derived from T2–T9. These fibers synapse with postganglionic neurons in the stellate ganglion. Therefore, a stellate ganglion block interrupts sympathetic outflow to the upper extremity.

Benzon H, Rathmell JP, Wu CL, et al, eds. *Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby; 2013:346–360.

B.3. Where is the stellate ganglion located?

The stellate ganglion is formed by the fusion of the inferior cervical and the first thoracic ganglia. It usually measures 2.5 cm × 1.5 cm × 0.5 cm and lies between the base of the transverse process of the seventh cervical vertebra and the neck of the first rib. It is situated behind the carotid sheath, ventral to the longus colli muscle, behind the vertebral artery, and lateral to the body of the vertebra. The vertebral, subclavian, inferior thyroid, and the first intercostal arteries are in close proximity to the ganglion and so is the recurrent laryngeal nerve. The left pleura is 1 to 2 cm below it, whereas the right pleura is in closer proximity.

Benzon H, Rathmell JP, Wu CL, et al, eds. *Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby; 2013:346–360.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2416.

B.4. What are the anatomic landmarks used in the stellate ganglion block?

The landmarks used in the stellate ganglion block are the jugular notch of the sternum, the sternocleidomastoid muscle, the cricoid cartilage, and Chassaignac tubercle. In a supine patient with the neck extended, a mark placed approximately 3.5 cm from the midline along the jugular notch and the same distance above the clavicle should overlie the transverse process of the seventh vertebra and the medial border of the sternocleidomastoid muscle. This marking is further confirmed by palpating the cricoid cartilage, which lies at the level of the sixth cervical vertebra, and the anterior tubercle on the vertebral transverse process, which is the most prominent tubercle in the neck (Chassaignac tubercle).

Benzon H, Rathmell JP, Wu CL, et al, eds. *Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby; 2013:346–360.

B.5. What are the clinical signs of stellate ganglion block?

A stellate ganglion block results in the following ipsilateral signs:

- *Eye*: ptosis, narrowing of the palpebral fissure, miosis, enophthalmos, conjunctival injection, and lacrimation
- *Face and neck*: anhidrosis, elevated local temperature, and nasal stuffiness
- *Arm*: increased temperature and plethysmographic evidence of improved cutaneous blood flow

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2416.

B.6. What is Horner syndrome?

Horner syndrome is a clinical entity characterized by ptosis, miosis, anhidrosis, and enophthalmos. It is usually seen with disease processes involving the cervical sympathetics and is the classic sign of a successful stellate ganglion block.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2416.

B.7. After a stellate ganglion block, this patient reports no significant change in the degree of pain despite developing Horner syndrome. Is the pain psychogenic in this patient?

Not necessarily. The Horner syndrome indicates only the interruption of sympathetic supply to the head and neck. Unless it is accompanied by objective changes in the arm, it does not indicate a sympathetic nerve block of the upper extremity. Furthermore, SMP will respond to sympathectomy, whereas SIP will not.

McMahon SB, Koltzenburg M, Tracey I, et al, eds. *Wall and Melzack's Textbook of Pain*. 6th ed. New York: Churchill Livingstone; 2013:990–1002.

B.8. What types of nerve fibers are interrupted in stellate ganglion block?

The stellate ganglion block results in interruption of the preganglionic, thinly myelinated type B fibers as well as the postganglionic, unmyelinated type C fibers.

Casale R, Glynn CJ, Buonocore M. Autonomic variations after stellate ganglion block: are they evidence of an autonomic afference? *Funct Neurol*. 1990;5:245–246.

B.9. What is a differential block?

The variable effects of local anesthetics on fibers performing different functions are termed as *differential block*. The

diagnostic distinction can be made by selectively blocking the function of these nerve fibers. The mechanism that results in a differential block is best explained by fiber size and myelination because these factors determine different sensitivities of nerve fibers to local anesthetics. By using different concentrations of local anesthetic, sympathetic and somatic fibers can be selectively blocked. A differential block may be helpful in differentiating somatic versus sympathetic pain and peripheral versus central pain.

Cousins MJ, Carr DB, Horlocker TT, et al, eds. *Cousins & Bridenbaugh's Neural Blockade: In Clinical Anesthesia and Pain Medicine*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:838–840.

B.10. What are the two major classes of local anesthetics? Describe the major differences in their clinical pharmacology.

The two major classes of clinically employed local anesthetics are esters and amides. The esters are hydrolyzed in the plasma by pseudocholinesterase; the amides are biotransformed in the liver. Although infrequent, local anesthetic toxicity is encountered more commonly in the ester group because of the para-aminobenzoic acid moiety. True allergic reactions to amides are rare and in most instances are caused by the preservatives in the solution. Each of the two groups of local anesthetics contains drugs with varying degrees of rate of onset, duration of neural blockade, potency, and toxicity.

Benzon H, Rathmell JP, Wu CL, et al, eds. *Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby; 2013:346–360.

B.11. What factors determine the onset, potency, and duration of a local anesthetic block?

- Onset correlates with pK_a.
- Potency correlates with lipid solubility.

- Duration correlates with degree of protein binding.

The commonly used local anesthetics are weakly basic tertiary amines that are lipid soluble and unstable in water. They are prepared as acidic salts because the ionized form, which is soluble in water, is stable. Therefore, the aqueous solution contains the ionized (cation) form of the local anesthetic in dissociation equilibrium with the unionized (free base) form depending on the pH of the medium.

$$\underset{\text{Cation}}{R{=}NH^{+}} \rightleftharpoons \underset{\text{Base}}{R{=}N} + H^{+}$$

When injected into the body, the relative rise in pH will allow the local anesthetic to convert to the uncharged base. The free base, being lipid soluble, will diffuse across the neural membrane and is responsible for neural blockade. With the exception of procaine and chloroprocaine, the commonly employed local anesthetics are highly protein bound and are therefore longer acting (**Table 48.1**).

TABLE 48.1 Physiochemical Properties of Commonly Used Local Anesthetics

Local Anesthetic	pK_a	Protein Binding (%)
Esters		
Procaine	8.9	5.8
Chloroprocaine	8.7	—
Tetracaine	8.5	75.6
Amides		
Lidocaine	7.9	64.3
Mepivacaine	7.6	77.5
Bupivacaine	8.1	95.6
Etidocaine	7.7	94.0

Benzon H, Rathmell JP, Wu CL, et al, eds. *Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby; 2013:346–360.

B.12. How does the addition of epinephrine to commercially available premixed solutions affect the efficacy of local anesthetics?

The addition of epinephrine to a local anesthetic increases the duration and intensity of a block. However, in commercially available premixed solutions containing epinephrine, antioxidants are added to preserve epinephrine, and the result is a lower buffered pH level of the solution. This lowering of the pH level can result in decreased efficacy of the local anesthetic. Best results are achieved by adding the desired concentration of epinephrine to the local anesthetic solution just before injection.

Benzon H, Rathmell JP, Wu CL, et al, eds. *Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby; 2013:346–360.

B.13. How will you treat this patient?

Early diagnosis and aggressive physical therapy with pharmacologic control of pain form the basis of the treatment of CRPS. Physical therapy is widely recommended and accepted as a first line of treatment. The treatment of CRPS will differ depending on whether the pain is SMP or SIP. A series of sympathetic blocks has been shown effective in treating SMP of CRPS. A multidisciplinary approach including physiotherapy and symptom-specific psychological treatments (e.g., biofeedback and hypnosis) may be beneficial. Many patients have a component of both SMP and SIP, and a combination of sympathectomy and analgesic treatment is recommended. However, no single treatment is consistently successful. Therefore, the treatment plan should be individualized.

McMahon SB, Koltzenburg M, Tracey I, et al, eds. *Wall and Melzack's Textbook of Pain*. 6th ed. New York: Churchill Livingstone; 2013:990–1002.

Stanton-Hicks MD. CRPS: what's in a name? Taxonomy, epidemiology, neurologic, immune and autoimmune considerations. *Reg Anesth Pain Med*. 2019;44:376–387.

B.14. What is the pharmacologic management of CRPS?

SMP of CRPS is treated with the drugs that deplete norepinephrine from the sympathetic nerve terminals. Oral sympatholytic agents include phenoxybenzamine, prazosin, and terazosin. Topical clonidine, a selective α_2-agonist, has been successfully used to treat SMP. Tricyclic antidepressants have been effective in approximately half the number of patients and have been recommended as first-line agents. Other drugs that have been successfully used to treat CRPS are anticonvulsants (e.g., gabapentin, pregabalin, carbamazepine, and topiramate), local anesthetics such as lidocaine and mexiletine, calcitonin, corticosteroids, and high-dose opioids. Anecdotal reports suggest that methadone (opioid with anti-NMDA receptor effect) has been more effective than other opioids. Long-term IT morphine has been reported to produce analgesic effects in CRPS. Nonsteroidal anti-inflammatory drugs have also been used successfully.

Abram SE, Haddox JD, eds. *The Pain Clinic Manual*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2000:177–184.

Becker WJ, Ablett DP, Harris CJ, et al. Long term treatment of intractable reflex sympathetic dystrophy with intrathecal morphine. *Can J Neurol Sci*. 1995;22:153–159.

B.15. What is the role of intravenous regional block (Bier method) in diagnosis and treatment of CRPS?

Intravenous regional block (Bier method) with guanethidine, reserpine, bretylium, and phentolamine has been used to achieve temporary sympatholytic effect and relieve SMP of CRPS. Intravenous guanethidine and reserpine have been reported to relieve pain in more than 50% of patients as compared with a control group in one study. However, guanethidine and reserpine are not commercially available in the United States. The combination of bretylium and lidocaine is more effective than

lidocaine alone. α-Adrenergic blockade with intravenous phentolamine is a sensitive test to identify patients with SMP. Phentolamine has been used as a predictor agent before more invasive sympathetic blocks.

Blanchard J, Ramamurthy S, Walsh N, et al. Intravenous regional sympatholysis: a double-blind comparison of guanethidine, reserpine, and normal saline. *J Pain Symptom Manage*. 1990;5:357–361.

Hord AH, Rooks MD, Stephens BO, et al. Intravenous regional bretylium and lidocaine for treatment of reflex sympathetic dystrophy: a randomized, double-blind study. *Anesth Analg*. 1992;74:818–821.

Raja SN, Treede RD, Davis KD, et al. Systemic alpha-adrenergic blockade with phentolamine: a diagnostic test for sympathetically maintained pain. *Anesthesiology*. 1991;74:691–698.

B.16. Compare and contrast the mechanism of actions of ketamine and methadone.

Methadone is a strong, long-acting opioid analgesic, whereas ketamine is a dissociative anesthetic. Methadone is used as an opioid but has mild NMDA receptor antagonist properties—the only strong opioid that has this quality. Ketamine is used in oral preparations, intravenous delivery systems, in skin preparations, and other delivery methods including being compounded in various percentages. These medications can block NMDA glutamate receptors and decrease the windup pain and central sensitization typical of chronic intractable pain. Windup causes an amplification of the incoming pain signal at the level of second-degree neurons in the dorsal horn of the spinal cord. By blocking these receptors, not only is windup pain decreased but also tolerance to opioid medications can also be decreased. Ketamine has the added effect of blocking sodium channels.

Benzon H, Rathmell JP, Wu CL, et al, eds. *Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby; 2013:346–360.

Chizh BA. Low dose ketamine: a therapeutic and research tool to explore N-methyl-D-aspartate (NMDA) receptor-mediated plasticity in pain pathways. *J*

Psychopharmacol. 2007;21(3):259–271.

B.17. What roles does ketamine infusion play in the treatment of CRPS? Is there a guideline for ketamine infusion in treating CRPS?

Although ketamine may have more than one mechanism of action, the basis for using it to treat CRPS may reside in its strong ability to block NMDA receptors. Ketamine is the only potent NMDA-blocking drug currently available for clinical use. An appropriately prolonged infusion of ketamine appears to maintain a level of ketamine in the central nervous system long enough to reverse the effects of the sensitization process and associated pain.

Currently, three methods of ketamine administration have been used for treatment including an outpatient low-dose ketamine administration; a low-dose awake inpatient technique; and a ketamine "coma" technique, which is a controversial treatment not currently allowed in the United States. Although studies are continuing, ketamine therapy has been shown to be effective for relief of pain CRPS-I; to date, no adverse cognitive effects of extended ketamine infusion treatment have occurred. Side effects, however, can occur in the high-dose setting; the infusion can be associated with significant risks including chronic catheterization, the need for parenteral nutrition, and endotracheal intubation. The outpatient therapy requires the patient to return for a 10-day period of time and often losses effectiveness after 6 to 12 weeks.

The guideline currently available for ketamine infusion is mainly focused on chronic neuropathic pain. Although there is moderate evidence showing ketamine infusion can provide effective short-term relief of CRPS-I pain, there is no consensus on the role of ketamine infusion in long-term management of the disease.

Cohen SP, Bhatia A, Buvanendran A, et al. Consensus guidelines on the use of intravenous ketamine infusions for chronic pain from the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, and the American Society of Anesthesiologists. *Reg Anesth Pain Med*. 2018;43:521–546.

Goldberg ME, Torjman MC, Schwartzman RJ, et al. Pharmacodynamic profiles of ketamine (R)- and (S)- with 5-day inpatient infusion for the treatment of complex regional pain syndrome. *Pain Physician*. 2010;13(4):379–387.

Kiefer RT, Rohr P, Ploppa A, et al. Complete recovery from intractable complex regional pain syndrome, CRPS-type I, following anesthetic ketamine and midazolam. *Pain Pract*. 2007;7:147–150.

Zhao J, Wang Y, Wang D. The effect of ketamine infusion in the treatment of complex regional pain syndrome: a systemic review and meta-analysis. *Curr Pain Headache Rep*. 2018;22:12.

B.18. What is neuromodulation? What is the role of spinal cord stimulation (SCS) in treating CRPS?

Neuromodulation, per International Neuromodulation Society definition, is "the alteration of nerve activity through the delivery of electrical stimulation or chemical agents to targeted sites of the body." Randomized controlled studies support the efficacy of SCS in treating pain of CRPS, and SCS has been shown to be superior to conventional medication management. Neurostimulation Appropriateness Consensus Committee (NACC) guidelines suggest the use of SCS for treating both CRPS-I and CRPS-II (evidence I, recommend strength A).

While the effectiveness and efficiency of different SCS stimulation modes are being investigated, dorsal root ganglion (DRG) stimulation has also significantly improved the management of CRPS and been proven to be noninferior in managing pain of CRPS, with less paresthesia in undesired body locations. Peripheral nerve stimulation (PNS) has also been reported to successfully achieve analgesia in CRPS patients. PNS would require that the injured nerve(s) would need to be known and identifiable for targeted stimulation but offers a

smaller and less invasive option for patients.

Deer TR, Krames E, Mekhail N, et al. The appropriate use of neurostimulation: new and evolving neurostimulation therapies and applicable treatment for chronic pain and selected disease states. Neuromodulation Appropriateness Consensus Committee. *Neuromodulation*. 2014;17:599–615.

Deer TR, Mekhail N, Provenzano D, et al. The appropriate use of neurostimulation of the spinal cord and peripheral nervous system for the treatment of chronic pain and ischemic diseases: the Neuromodulation Appropriateness Consensus Committee. *Neuromodulation*. 2014;17:515–550.

Deer TR, Pope JE, Lamer TJ, et al. The Neuromodulation Appropriateness Consensus Committee on best practices for dorsal root ganglion stimulation. *Neuromodulation*. 2019;22(1):1–35.

Herschkowitz D, Kubias J. Wireless peripheral nerve stimulation for complex regional pain syndrome type I of the upper extremity: a case illustration introducing a novel technology. *Scand J Pain*. 2018;18:555–560.

Sokal P, Harat M, Zieliński P, et al. Tibial nerve stimulation with a miniature, wireless stimulator in chronic peripheral neuropathic pain. *J Pain Res*. 2017;10:613–619.

B.19. What is the role of surgical sympathectomy?

Surgical, chemical, or radiofrequency sympathectomy produces short-term pain relief, but long-term results are poor and inconsistent. Delayed failure of sympathectomy may be due to regeneration of ipsilateral nerves or reinnervation from the contralateral sympathetic nerves.

Kumar K, Nath RK, Toth C. Spinal cord stimulation is effective in the management of reflex sympathetic dystrophy. *Neurosurgery*. 1997;40(3):503–508.

Rocco AG. Radiofrequency lumbar sympatholysis. The evolution of a technique for managing sympathetically maintained pain. *Reg Anesth*. 1995;20(1):3–12.

B.20. What role does intrathecal (IT) therapy play in managing CRPS?

As a form of neuraxial analgesia, IT therapy bypasses first-pass metabolism and the blood–brain barrier, allowing lower effective doses and decreased systemic adverse effects. It is

usually achieved through an IT drug delivery system/device and should be considered only as a salvage approach after failing high doses of systemic opioids.

Polyanalgesic Consensus Conference (PACC) guidelines recommend both morphine (evidence level IIIB) and ziconotide (evidence level IA) as first-line IT monotherapy for either cancer- or non–cancer-related chronic pain, including CRPS; however, each of the medication has their own limitation and thus require monitoring. PACC guidelines recommend trialing before a permanent device is placed and that the pros and cons of the therapy must be thoroughly discussed with patients before initiating the treatment.

Deer TR, Pope JE, Hanes MC, et al. Intrathecal therapy for chronic pain: a review of morphine and ziconotide as firstline options. *Pain Med*. 2019;20(4):784–798.

Deer TR, Pope JE, Hayerk SM, et al. The Polyanalgesic Consensus Conference (PACC): recommendations on intrathecal drug infusion systems best practices and guidelines. *Neuromodulation*. 2017;20:96–132.

B.21. If opioids are prescribed as treatment for CRPS patients, what is the Centers for Disease Control and Prevention (CDC) guideline of chronic opioid therapy?

In 2016, CDC has published a guideline to address the (1) timing, (2) strategies, and (3) risk–benefit assessment of prescribing opioids for chronic pain other than cancer treatment, palliative care, or end-of-life care. Other resources including checklist, fact sheets, and mobile application are also available.

CDC guidelines also recommend thoroughly discussing risks and benefits with patients before starting therapy, initiating therapy with immediate-release opioids, and reevaluating benefits and harms frequently. Last but not least, offer treatment for opioid use disorder when aberrant behavior of opioid use is

perceived.

Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. *MMWR Recomm Rep*. 2016;65:1–49.

C. Complications

C.1 What are the complications of stellate ganglion block?

Although complications appear infrequently, the more common complications of stellate ganglion block are as follows:

- Intra-arterial injection: seizure and hematoma
- Recurrent laryngeal nerve paralysis: hoarseness of voice
- Brachial plexus block: motor weakness
- Accidental epidural or subarachnoid injection
- Esophageal injury
- Pneumothorax: respiratory distress

To avoid complications, aspiration of the needle should be performed before, during, and after administration of local anesthetics to look for (1) air, (2) blood, and (3) cerebrospinal fluid.

Benzon H, Rathmell JP, Wu CL, et al, eds. *Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby; 2013:346–360.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2416.

C.2 What is the systemic toxicity of local anesthetics?

The systemic toxic effects of local anesthetics are related to drug levels in blood, and they are manifested mainly in the central nervous system and the cardiovascular system. As a rule, the central nervous system effects precede the cardiovascular toxic manifestations.

Central Nervous System Effects

Central nervous system effects include light-headedness,

dizziness, tinnitus, visual disturbances, drowsiness, disorientation, slurred speech, muscle twitching, generalized grand mal seizures, and electroencephalographic changes. The blood levels of local anesthetics associated with central nervous system changes in humans are as follows:

- Procaine: 20 μg per mL
- Lidocaine, mepivacaine, and prilocaine: 5 to 10 μg per mL
- Tetracaine, bupivacaine, and etidocaine: 1.5 to 4 μg per mL
- Lowering the $Paco_2$ by hyperventilation decreases the convulsive threshold dose of a local anesthetic drug.

Cardiovascular Effects

Ventricular arrhythmias are reported with intravenous bupivacaine only. Cardiac resuscitation is extremely difficult in patients with bupivacaine-induced cardiac arrhythmias. Ropivacaine is less toxic than bupivacaine but more toxic than lidocaine. The mechanism of enhanced cardiotoxicity in pregnant patients is not well understood; nevertheless, 0.75% bupivacaine is no longer recommended in pregnant patients in the United States (**Table 48.2**).

TABLE 48.2 Cardiovascular Effects of Lidocaine

Blood Level Lidocaine (μg per mL)	Electrocardiographic Changes	Hemodynamic Effects
<5	—	—
5–10	↑ PR interval	↓ Myocardial contraction
	↑ QRS duration	↓ Cardiac output
	Sinus bradycardia	Vasodilatation
>10	↑ PR interval	↓ Myocardial contraction
	↑ QRS duration	↓ Cardiac output
	Sinus bradycardia	Circulatory collapse
	Atrioventricular block	
	Asystole	

↑, increase; ↓, decrease.

Benzon H, Rathmell JP, Wu CL, et al, eds. *Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby; 2013:346–360.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:865–891.

C.3 How do you treat the systemic toxicity of local anesthetic drugs?

The principles of treatment include the following:

- Secure and maintain the airway.
- Ensure adequate oxygenation and ventilation.
- Treat hypotension and bradycardia promptly.

For patients in cardiac arrest or with severe, refractory arrhythmias, intravenous fat emulsions should be given. The suggested bolus dose is 1.5 mL per kg of 20% fat emulsion (Intralipid) over 1 minute followed by a continuous infusion at 0.25 mL/kg/min. If there is no clinical improvement, the bolus dose should be repeated and the infusion should be increased to 0.5 mL/kg/min. The infusion should be continued for at least 10 minutes after hemodynamic stability is restored but discontinued within an hour.

- Perform immediate cardiopulmonary resuscitation for profound cardiovascular collapse.
- Perform electrical cardioversion for ventricular tachycardia or fibrillation.
- Control seizures with the following:
  - Diazepam, 0.1 to 0.2 mg per kg, intravenously
  - Thiopental sodium, 1 to 2 mg per kg, intravenously

Benzon H, Rathmell JP, Wu CL, et al, eds. *Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby; 2013:346–360.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:883–887.

C.4 What are the possible complications of SCS?

Epidural SCS is a simple procedure and carries low morbidity. The majority of complications are associated with the implants involving electron fracture or lead migration, which are correctable. Other more serious complications include epidural hematoma, epidural abscess, permanent neurologic deficits, or serious spinal cord injury; however, the risk of these adverse events are less than spine surgery.

Deer TR, Krames E, Mekhail N, et al. The appropriate use of neurostimulation: new and evolving neurostimulation therapies and applicable treatment for chronic pain and selected disease states. Neuromodulation Appropriateness Consensus Committee. *Neuromodulation*. 2014;17:599–615.

Deer TR, Mekhail N, Provenzano D, et al. The appropriate use of neurostimulation of the spinal cord and peripheral nervous system for the treatment of chronic pain and ischemic diseases: the Neuromodulation Appropriateness Consensus Committee. *Neuromodulation*. 2014;17:515–550.

Deer TR, Pope JE, Lamer TJ, et al. The Neuromodulation Appropriateness Consensus Committee on best practices for dorsal root ganglion stimulation. *Neuromodulation*. 2019;22(1):1–35.

C.5. What are the possible complications of IT therapy?

Based on the characteristics, there are five classes of potential IT therapy complications, including mechanical system, pharmacologic, surgical, patient-specific, and refill complications. The severity of the results can range from local hygroma to life-threatening anaphylaxis, respiratory depression, or arrest. It is also worth noting that ziconotide may cause neuropsychiatric adverse effect and is contraindicated in patients with preexisting history of psychosis or suicidal ideation.

Bottros MM, Christo PJ. Current perspectives on intrathecal drug delivery. *J Pain Res*. 2014;7:615–626.

Deer TR, Pope JE, Hanes MC, et al. Intrathecal therapy for chronic pain: a review of morphine and ziconotide as firstline options. *Pain Med*. 2019;20(4):784–798.

49 Cancer Pain

Shakil Ahmed and Sudhir A. Diwan

A 44-year old man was referred to the pain clinic for evaluation and management of abdominal pain. He was recently diagnosed with adenocarcinoma of the pancreas with retroperitoneal lymph nodes in the paraaortic region. His pain is localized in the epigastric region and is worse during the night and decreased during the day. He is taking sustained-release morphine sulfate (MS Contin), 100 mg orally every 8 hours, and immediate-release morphine sulfate, 30 mg orally every 3 hours as needed, for breakthrough pain. The patient reports inadequate pain control, nausea, vomiting, and constipation.

A. Medical Disease and Differential Diagnosis

1. What is the definition of pain?
2. How significant is the problem of pain in patients with cancer?
3. What are the components of cancer pain?
4. How does the pain contribute to the suffering of patients with cancer?
5. How do psychological factors affect pain in patients with cancer?
6. What are the causes of pain in patients with cancer?
7. How do you classify pain in patients with cancer?
8. What are the characteristics of pancreatic cancer pain?

9. How do you assess pain in patients with cancer?
10. What is the differential diagnosis of abdominal pain?

B. Pharmacologic Treatment of Pain

1. What is the World Health Organization stepladder approach for cancer pain management?
2. What class of drugs does morphine sulfate belongs to?
3. What is the difference between morphine and synthetic opioids?
4. How does mixed opioid agonist/antagonist differ from opioid agonist?
5. Describe the role of methadone in the management of cancer pain.
6. What are the advantages and disadvantages of methadone?
7. What is the mechanism of action of opioids?
8. What are the side effects of opioid therapy?
9. Define tolerance and physical dependence.
10. How would you treat the side effects of opioid therapy?
11. What is tramadol? Is it an opioid?
12. When would you consider adjuvant analgesics as part of the treatment plan?
13. The patient and his family are worried about addiction. How would you approach this problem?
14. Describe different routes of opioid administration.
15. Describe advantages and complications of patient-controlled analgesia (PCA). What is minimum effective analgesic concentration (MEAC)?
16. What is meperidine? How is it different from other opioids?
17. What is rotation of opioids? When would you consider rotation of opioids?

C. Invasive Therapy

1. Describe the role of peripheral nerve blocks in cancer pain management.

2. Describe the role of celiac plexus block in cancer pain management.
3. What are the complications of celiac plexus block?
4. Would you consider neuraxial opioid infusion in this patient? Discuss complications of this procedure.
5. Which medications can be used intrathecally? What is ziconotide?
6. What is a Personal Therapy Manager (PTM), and what role does it play in neuraxial pain relief?
7. Would you consider neuraxial neurolysis in this patient to manage his pain? Discuss advantages and disadvantages of these blocks.
8. Which neuroablative procedures can be considered in the terminal stage of pancreatic cancer?
9. Describe the role of radiation therapy in cancer pain.

D. Nonpharmacologic Management

1. What are the various nonpharmacologic techniques of cancer pain management?
2. What physical modalities have been successfully tried in cancer pain management?
3. Describe the role of neuromodulation in cancer pain management.
4. What psychological techniques have been promoted for comfort care and pain relief?
5. What are distraction and reframing techniques? What is the role of hypnosis in cancer pain?

A. Medical Disease and Differential Diagnosis

A.1. What is the definition of pain?

According to the International Association for the Study of Pain, pain is defined as “an unpleasant, sensory and emotional

experience associated with actual or potential tissue damage or described in terms of such damage."

Williams and Craig proposed another definition in light of the new understanding of pain, "Pain is a distressing experience associated with actual or potential tissue damage with sensory, emotional, cognitive and social components."

Anand KJS, Craig KD. New perspectives on the definition of pain. *Pain*. 1996;67:3–6.

Merskey H, Bogduk N, eds. *Classification of Chronic Pain: Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms*. 2nd ed. Seattle, WA: IASP Press; 1994:210.

Williams AC, Craig KD. Updating the definition of pain. *Pain*. 2016;157(11):2420–2423.

A.2. How significant is the problem of pain in patients with cancer?

There are 1,762,450 new patients with cancer annually in 2019. Cancer causes 606,880 deaths per year, making it the second leading cause of death in the United States. Thirty percent of the patients with cancer have pain at the time of diagnosis, and 65% to 85% of patients with cancer have pain at advanced stages. Thirty-six percent have pain severe enough to impair their ability to function.

Vainio and Auvinen studied 1,840 patients with advanced cancer and found 24% with no pain, 24% with mild pain, 30% with moderate pain, and 21% with severe pain.

Van den Beuken-van Everdingen and colleagues showed in a pooled meta-analysis of 52 studies that more than one-third of cancer patients graded their pain as moderate or severe. Pooled prevalence of pain was >50% in all cancer types including gastrointestinal, lung, breast, and urogenital, with the highest prevalence in head/neck cancer patients (70%).

Daut and Cleeland found pain to be an early symptom of cancer in 48% to 50% of patients with cancer of breasts, ovary,

prostate, colon, and rectum and in 20% of patients with uterus and cervical cancer.

American Cancer Society. *Cancer Facts & Figures 2014*. Atlanta, GA: American Cancer Society; 2014.

Bruera E, Kim HN. Cancer pain. *JAMA*. 2003;290:2476–2479.

Daut RL, Cleeland CS. The prevalence and severity of pain in cancer. *Cancer*. 1982;50:1913–1918.

Vainio A, Auvinen A. Prevalence of symptoms among patients with advanced cancer: an international collaborative study. *J Pain Symptom Manage*. 1996;12(1):3–10.

van den Beuken-van Everdingen M, de Rijke J, Kessels A, et al. Prevalence of pain in patients with cancer: a systematic review of the past 40 years. *Ann Oncol*. 2007;18(9):1437–1449.

A.3. What are the components of cancer pain?

The components of cancer pain are sensory, affective, and psychological.

The sensory components could be nociceptive pain elicited by activation of sensory nerve endings, by mechanical, chemical, radioactive, or thermal energy. It is often associated with ongoing tissue damage and may be of somatic or visceral origin. Somatic pain may be superficial, well localized, sharp, pricking, burning or deep diffused, dull, and aching. Visceral pain is usually diffuse, referred to body surface, and has a sickening quality to it.

Neuropathic pain is due to pathologic change in the discharge properties of the neurons because of invasion, compression, or damage caused by various cancer treatment modalities. It is typically described as burning, lancinating, painful numbness, or itching sensations. Phantom pain is a pain referred to the amputated part of the body. Psychological pain is usually due to fear, anxiety, depression, existential questions, anger, social and financial issues, social support, and the impact the pain has on the family and caregivers. Most cancer patients report more than

one site of pain.

Ballantyne JH, Fishman SM, Rathmell JPC, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2018:599–620.

Sela RA, Bruera E, Conner-Spady B, et al. Sensory and affective dimensions of advanced cancer pain. *Psychooncology*. 2002;11:23–34.

A.4. How does the pain contribute to the suffering of patients with cancer?

Sustained pain on its own can create complex, enduring, unpleasant emotional suffering by its ability to create awareness of the perceived threat to one's life. It causes helplessness in the face of the inevitability of demise as well as exhaustion of hope. Patients with cancer usually identify pain as an indicator of disease progression. Suffering may be attributable to many factors besides physical complaints. Psychological factors include financial issues, lack of social support, loss of job or social position in society, loss of independence, effect on family and friends, social isolation, and fear of death.

A.5. How do psychological factors affect pain in patients with cancer?

The ultimate perception of pain depends on the nociceptive stimulus and psychological fear, anger, anxiety, or depression. Twenty-five percent of patients with cancer meet criteria for major depressive syndromes at some point in their illness, with an overall prevalence of 53% in hospitalized patients with cancer. Psychological factors may significantly exacerbate pain. The psychological suffering is associated with the disease and the imminence of death.

Symptoms usually include anxiety, restlessness and irritability, sleep disorders, obsessive thinking, slowness in motor responses, and hopelessness. Psychological suffering is most typically manifested in depression, which most of the

patients suffer during the initial stages of the disease, when the disease metastasize, and when they are in a particularly poor condition. These factors affect overall pain behavior and suffering. General deterioration causes them to withdraw into their home or the hospital. Also, a meta-analysis of studies showed that depression predicts mortality, but not progression, in cancer patients.

Ballantyne JH, Fishman SM, Rathmell JPC, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2018:599–620.

Satin JR, Linden W, Phillips MJ. Depression as a predictor of disease progression and mortality in cancer patients: a meta-analysis. *Cancer*. 2009;115(22):5349–5361.

Speigel D, Giese-Davis J. Depression and cancer: mechanisms and disease progression. *Biol Psychiatry*. 2003;54:269–282.

A.6. What are the causes of pain in patients with cancer?

Pain in patients with cancer may be due to (1) presence and progression of the tumor itself, for example, bone involvement, viscus obstruction, and nerve compression; (2) indirect effect of the tumor, for example, metabolic imbalance, infection, and venous or lymphatic obstruction; (3) consequence of cancer treatment, such as chemotherapy, radiation therapy, or surgery; or (4) unrelated mechanisms such as migraine and myofascial pain.

Localized invasion of peripancreatic structures most commonly causes back pain, which stems from tumor invasion of the splanchnic plexus, common bile duct obstruction, retroperitoneum, or pancreatitis. This pain is described as severe, gnawing, epigastric, upper abdominal radiating to the middle of the back, worse on lying down and improved with upright position.

Grond and colleagues found in a prospective study of 2,266 patients with cancer that 30% had one pain syndrome, 39% had two pain syndromes, 31% had three pain syndromes, 85% by the

cancer itself (bone, 35%; soft tissue, 45%; and visceral, 34%), and 17% by anticancer treatment.

The bone cancer pain has both nociceptive and neuropathic components, which evolve with disease progression. The tumor and associated cells release factors that sensitize and activate bone nociceptors, injure the sensory nerve fibers, and release growth factors that drive ectopic sprouting of nerve fibers and neuroma formation, all of which can contribute to peripheral and central sensitization.

Ballantyne JH, Fishman SM, Rathmell JPC, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2018:599–620.

Grond S, Zech D, Diefenbach C, et al. Assessment of cancer pain: a prospective evaluation in 2266 cancer patients referred to a pain service. *Pain*. 1996;64:107–114.

Mantyh PW. Bone cancer pain: from mechanism to therapy. *Curr Opin Support Palliat Care*. 2014;8(2):83–90.

A.7. How do you classify pin in patients with cancer?

Pain, in patients with cancer, may be classified on the basis of the following:

- Chronicity: acute or chronic
- Intensity and severity: visual analog score, numeric pain score; and verbal: mild, moderate, severe, or worst possible pain
- Pathophysiology and mechanism: nociceptive or neuropathic, tumor infiltration of nerves, infiltration of soft tissue or hollow organs, serosa, solid organ necrosis, and destruction of bone
- Individual type and stage of disease: pancreatic, ovarian, prostatic, breast, or lung
- Pattern of pain: incidental pain related to an event or activity; spontaneous pain unrelated to an event or activity and end-of-dose failure
- Pain syndromes: tumor invasion of bone, nerves, spinal cord,

viscera, blood vessels, postsurgical, and postchemotherapy and postradiation therapy pain

The pancreatic carcinoma usually presents with vague symptoms of anorexia, weight loss, abdominal discomfort, new-onset diabetes mellitus, or thrombophlebitis. The vague nature of symptoms may result in delay of diagnosis.

Boland EG, Mulvey MR, Bennett MI. Classification of neuropathic pain in cancer patients. *Curr Opin Support Palliat Care*. 2015;9(2):112–115.

Caraceni A, Weinstein S. Classification of cancer pain syndromes. *Oncology (Williston Park)*. 2001;15:1627–1640.

Fainsinger RL, Nekolaichuk CL, Lawlor PG, et al. A multicenter study of the revised Edmonton Staging System for classifying cancer pain in advanced cancer patients. *J Pain Symptom Manage*. 2005;29(3):224–237.

Ochoa JL. Neuropathic pain: redefinition and a grading system for clinical and research purposes. *Neurology*. 2009;72(14):1282–1283.

A.8. What are the characteristics of pancreatic cancer pain?

Pancreatic cancer affects 12 or 13 patients per 100,000 in the Western world, men more than women, and Blacks more than Whites. In 2019, an estimated 56,770 adults (29,940 men and 26,830 women) in the United States will be diagnosed with pancreatic cancer. If the cancer is detected at an early stage when surgical removal of the tumor is possible, the 5-year survival rate is 37.4%. About 10% of people are diagnosed at this stage. If the cancer has spread to surrounding tissues or organs, the 5-year survival rate is 12%. For the 53% of people who are diagnosed after the cancer has spread to a distant part of the body, the 5-year survival rate is 3%.

About 30% to 60% of patients present with pain, and 80% of the patients with advanced cancer complain of pain. Patients complain of diffuse epigastric pain radiating to the back that is increased on lying down and improved on sitting. About 90% of pancreatic tumors are of the adenocarcinoma type. Cancer in the

head of the pancreas usually invades the stomach, duodenum, gall bladder, and peritoneum, whereas tumors in the body spreads to liver, spleen, lymph nodes, and left adrenal gland. A study of 42 Japanese patients on clinical characteristics of Japanese patients with epithelioid hemangioendothelioma showed tumor size >3.0 cm is an independent indicator of a poor prognosis in epithelioid hemangioendothelioma. The presence of symptoms at the time of diagnosis and high Ki-67 index implies poor survival.

Howlader N, Noone AM, Krapcho M, et al, eds. *SEER Cancer Statistics Review (CSR), 1975–2016*. Bethesda, MD: National Cancer Institute; 2019.

Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. *CA Cancer J Clin*. 2019;69(1):7–34.

A.9. How do you assess pain in patients with cancer?

A stepwise approach is required for the assessment of pain. It includes history, physical examination, and data collection ending with clinical diagnosis. It helps the clinician achieve goals of providing pain relief. Assessment involves identifying features of pain, such as location, intensity, quality, timing, exacerbating/relieving factors, response to previous analgesics, and disease-modifying treatments; effects of pain on daily activities and psychological state; associated symptoms; complete physical examination; and laboratory data and imaging.

Ballantyne JH, Fishman SM, Rathmell JPC, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2018:599–620.

A.10. What is the differential diagnosis of abdominal pain?

Although abdominal pain could arise from different structures within the peritoneal cavity, the retroperitoneal organs can cause similar pain syndromes. Location and radiation of the pain can give important clues to make the diagnosis. Retroperitoneal

structures present with dull or sharp back pain that is increased on lying down and relieved on sitting hunched up. Abdominal tumors are frequently characterized by colicky pain associated with nausea that is worse after eating. Abdominal pain may be referred to distant areas like shoulder, neck, or back depending on the organ involved. Tumors of the small bowel or large bowel may present with symptoms of obstruction (e.g., abdominal distention, nausea, and bilious vomiting) or hematemesis or melena. Other common causes of abdominal pain include omental metastasis, volvulus of intestine, infectious peritonitis, radiation enteritis, and peritoneal carcinomatosis. Mesenteric ischemia presents with diffuse pain that is increased with meals and weight loss.

Nonmalignant causes of abdominal pain such as appendicitis, cholecystitis, and pancreatitis can occur in patients with cancer coincidentally and may complicate the diagnostic process. Opioid analgesics may not be used in these patients because they may exacerbate symptoms of colicky pain (due to spasm of sphincter of Oddi), nausea, vomiting, paralytic ileus, and constipation.

Ballantyne JH, Fishman SM, Rathmell JPC, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2018:599–620.

B. Pharmacologic Treatment of Pain

B.1. What is the World Health Organization stepladder approach for cancer pain management?

The World Health Organization advocated a stepladder approach to manage cancer pain exclusively with oral medications depending on the pain intensity and, to some extent, the pain mechanism (**Fig. 49.1**).

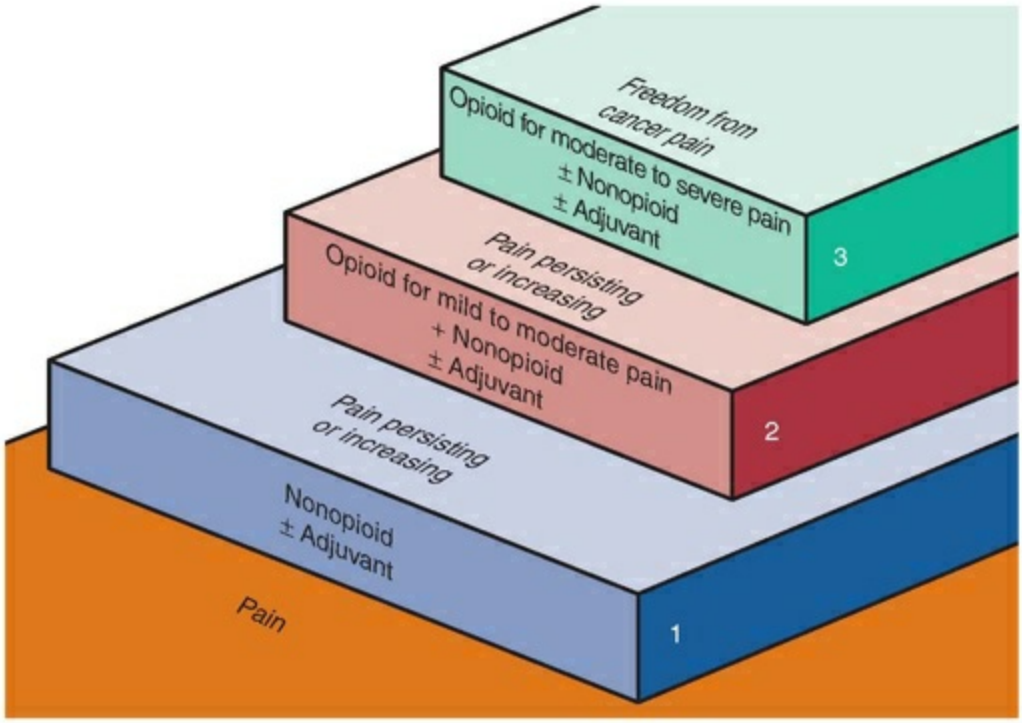

FIGURE 49.1. World Health Organization–advocated stepladder approach to management of cancer pain.

Step 1. Manage the pain by nonopioid medications with or without adjuvants.
Step 2. If pain is persisting or increasing, add weak opioids to nonopioid analgesics and adjuvants.
Step 3. Strong opioids are used with nonopioid analgesics and adjuvants until the patient achieves complete analgesia.

Noninvasive routes of drug delivery should be maintained as long as possible because of its simplicity, convenience, and cost. A fourth step has been added for patients who still have significant pain despite maximum medical management. At this point, interventional procedures including neuromodulation, drug delivery systems, and/or neurolysis should be employed.

Cuomo A, Bimonte S, Forte CA, et al. Multimodal approaches and tailored therapies for pain management: the trolley analgesic model. *J Pain Res*. 2019;12:711–714.

Mercadante S. Management of cancer pain. *Intern Emerg Med*. 2010;5(suppl

1):S31–S35.

Pazdur R, Wagman L, Camphausen KA, et al, eds. *Cancer Management: A Multidisciplinary Approach. Medical, Surgical, & Radiation Oncology*. 13th ed. Philadelphia, PA: FA Davis; 2010:731–746.

B.2. What class of drugs does morphine sulfate belongs to?

Morphine is classified as a μ-receptor opioid agonist because of its high specificity for activation of μ-receptors. An ideal opioid agonist would have a high specificity for receptors producing desirable effects (analgesia and minimal or no specificity for other receptors that cause side effects). Opioids are unique in producing analgesia without loss of consciousness.

Brunton LB, Hilal-Dandan R, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 13th ed. New York: McGraw-Hill; 2018:368–372.

B.3. What is the difference between morphine and synthetic opioids?

Morphine is the principal phenanthrene alkaloid present in opium. It is highly ionized and water soluble. The most active molecule of morphine is the levorotatory isomer of stereochemical structure. The synthetic opiates contain the phenanthrene nucleus of morphine and are manufactured by synthesis, rather than chemical modification. Clinically, histamine release by morphine differentiates it from the synthetic opioids. This may cause urticaria, allergic reactions, and hemodynamic instability, particularly in volume-depleted patients.

Ballantyne JH, Fishman SM, Rathmell JPC, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2018:599–620.

B.4. How does mixed opioid agonist/antagonist differ from opioid agonist?

The mixed-action opioids bind to μ-receptors, where they are partial agonists or competitive antagonists. Antagonistic properties of these drugs can attenuate the efficacy of subsequently administered opioid agonists and cause withdrawal symptoms in patients already receiving opioid agonists. The advantages of these drugs include low potential for respiratory depression and physical dependence. A dysphoric reaction is very common with mixed-action opioids. Their use is limited because of a ceiling effect whereby progressive escalation in doses does not increase analgesia as with opioid agonists.

Ballantyne JH, Fishman SM, Rathmell JPC, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2018:599–620.

Brunton LB, Hilal-Dandan R, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 13th ed. New York: McGraw-Hill; 2018:368–377.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier Saunders; 2019:680–741.

B.5. Describe the role of methadone in the management of cancer pain.

The efficient oral and rectal absorption with prolonged duration of analgesic action of methadone makes it a highly effective and attractive oral drug for cancer pain management.

Methadone is a synthetic opiate drug with a unique agonist/antagonist action. Methadone is a μ-receptor agonist and an *N*-methyl-d-aspartate (NMDA) receptor antagonist. Activation of NMDA receptors is involved in the development of hypersensitivity and central sensitization in neuropathic pain and tolerance to opioids. Because of the antagonistic effect at the NMDA receptor site, methadone is very effective in neuropathic pain secondary to cancer-related pathology and therapeutic interventions. The same antagonistic action of methadone minimizes the development of tolerance to opioids.

Alford DP, Compton P, Samet JH. Acute pain management for patients receiving maintenance methadone or buprenorphine therapy. *Ann Intern Med*. 2006;144:127–134.

Brunton LB, Hilal-Dandan R, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 13th ed. New York: McGraw-Hill; 2018:368–374.

Gropper MA, Eriksson LI, Fleisher LA, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier Saunders; 2019:680–741.

Manfredi PL, Gonzalez GR, Cheville AL, et al. Methadone analgesia in cancer pain patients on chronic methadone maintenance therapy. *J Pain Symptom Manage*. 2001;21:169–174.

B.6. What are the advantages and disadvantages of methadone?

Methadone has several advantages including oral and rectal absorption with bioavailability to 95%, high potency, high lipid solubility, low cost, and no active metabolites. Methadone has a long half-life, and its analgesic effect lasts 6 to 8 hours. However, methadone has been used for a long time for heroin abusers as detoxification and maintenance; it carries a social stigma, which can interfere with adequate pain management. Methadone has an irregular elimination half-life with inter individual variation between 20 and 60 hours. Because of that, the cumulative effect of methadone causes sedation, makes titration difficult, and has led to the concept of individualization of methadone dosing.

Ballantyne JH, Fishman SM, Rathmell JPC, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2019:687–792.

Brunton LB, Chabner B, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 13th ed. New York: McGraw-Hill; 2018:368–374.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier Saunders; 2019:680–741.

B.7. What is the mechanism of action of opioids?

Opioids act as agonists at stereospecific opioid receptors that are

normally activated by endogenous ligands known as endorphins in brainstem and spinal cord. Binding of opioid to the receptor inhibits adenylate cyclase activity and causes hyperpolarization of neurons, which results in suppression of spontaneous discharge and evoked potential. Opioids also interfere with transmembrane transport of calcium ion and interfere with the release of neurotransmitters like acetylcholine, dopamine, norepinephrine, and substance P. Inhibition of acetylcholine release from nerve endings is the basis of analgesic activity of opioids.

Ballantyne JC, Fishman SM, Rathmell JP, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2019:1333–1343.

Brunton LB, Chabner B, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 13th ed. New York: McGraw-Hill; 2018:355–377.

Gropper MA, Cohen NH, Eriksson L, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier Saunders; 2019:680–741.

B.8. What are the side effects of opioid therapy?

The opioid-related side effects occur because of opioid receptor pharmacodynamics, metabolites, or both. Sedation and respiratory depression are due to μ-receptor activation. Tolerance to these side effects is developed within a very short period of treatment. The dysphoric reaction is due to activation of κ-receptors. Psychotomimetic and depersonalization reactions are due to activation of σ-receptors. Nausea and vomiting are caused by direct stimulation of the chemoreceptor trigger zone. Increased intrabiliary pressure is due to spasm of the sphincter of Oddi. Other side effects commonly observed are constipation, pruritus, and myoclonus. Almost all side effects diminish with time, except constipation and myoclonus. Patients with cancer who develop constipation secondary to opioid therapy are required to be on a regular bowel regimen to avoid subsequent serious consequences. In patients with compromised renal

function, metabolites of morphine (M3G, M6G) cause excessive sedation and metabolites of meperidine (normeperidine) lower the seizure threshold. The most commonly reported adverse events in the MERITO study of 159 cancer patients were somnolence (24% of patients), constipation (22%), vomiting (13%), nausea (10%), and confusion (7%).

Ballantyne JC, Fishman SM, Rathmell JP, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2019:1333–1335.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier Saunders; 2019:680–741.

B.9. Define tolerance and physical dependence.

Tolerance occurs with the development of the need to gradually escalate the dose to achieve the same pain control, and it can develop in 2 to 3 weeks. Tolerance does not indicate abuse or addiction, it is commonly associated with increasing pain or disease progression. Physical dependence develops after chronic use of opioids, and it is characterized by development of withdrawal syndrome after administration of an opioid antagonist or abrupt discontinuation of the medication. The potential for tolerance is an agonistic effect of opioids.

Canfield MC, Keller CE, Frydrych LM, et al. Prescription opioid use among patients seeking treatment for opioid dependence. *J Addict Med*. 2010; 4:108–113.

Fishman SM, Ballantyne JC, Rathmell JP, eds. *Bonica's Management of Pain*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009:418–423.

B.10. How would you treat the side effects of opioid therapy?

Oversedation and respiratory depression are treated with a specific μ-receptor antagonist, naloxone, as well as supplemental oxygen. Naloxone, in a 1 to 4 μg per kg intravenous bolus, promptly reverses sedation, respiratory depression, and analgesia. Continuous intravenous infusion at the rate of 2 to 4

μg/kg/hr will reverse only side effects without reversing analgesia. Nausea and vomiting should be managed by antiemetics. Constipation should be treated with a regular bowel regimen of laxatives and stool softener. Peripherally acting μ-opioid receptor antagonists (PAMORA; methylnaltrexone, naloxegol, naldemedine) and a chloride channel activator (lubiprostone) improve opiate-induced bowel dysfunction without reversing analgesia. Generalized pruritus may respond to one or more doses of antihistamine; however, pruritus may not be related to histamine release.

Cherny N, Ripamonti C, Pereira J, et al. Strategies to manage the adverse effects of oral morphine: an evidence-based report. *J Clin Oncol*. 2001;19:2542–2554.

De Conno F, Ripamonti C, Fagnoni E, et al. The MERITO Study: a multicentre trial of the analgesic effect and tolerability of normal-release oral morphine during 'titration phase' in patients with cancer pain. *Palliat Med*. 2008;22(3):214–221.

Slatkin N, Thomas J, Lipman AG, et al. Methylnaltrexone for treatment of opioid-induced constipation in advanced illness patients. *J Support Oncol*. 2009;7:39–46.

Viscusi ER. Clinical overview and considerations for the management of opioid-induced constipation in patients with chronic noncancer pain. *Clin J Pain*. 2019;35(2):174–188.

B.11. What is tramadol? Is it an opioid?

Tramadol (Ultram) is a nonopioid synthetic analgesic with weak μ-receptor agonistic activity and is thought to exert its analgesic effects by inhibition of reuptake of norepinephrine and serotonin. It should be started at 50 to 100 mg every 6 to 8 hours. It may exhibit μ-receptor–related clinical side effects like respiratory depression and constipation. Prolonged use may lead to physical and psychological dependence. Tramadol was placed into schedule IV of controlled substances effective August 18, 2014.

Tapentadol is a centrally acting pain reliever, with agonist

activity at the μ-receptor and inhibition of norepinephrine reuptake. Compared to oxycodone IR, tapentadol showed a reduction in gastrointestinal side effects, specifically nausea, constipation, and vomiting. Tapentadol should be administered first in the 50-mg strength and can be increased to 100 mg every 4 to 6 hours as needed. Of note, it too can also cause respiratory depression because it shows μ-opioid agonist activity and is a controlled substance.

Both tramadol and tapentadol can cause life-threatening serotonin syndrome with the use of other serotonin-norepinephrine uptake inhibitors, selective serotonin reuptake inhibitors, tricyclic antidepressants, or monoamine oxidase inhibitors and, therefore, should be used with caution in patients on these medications.

There is limited, very low quality, evidence from randomized controlled trials that tramadol produced pain relief in some adults with pain due to cancer and no evidence at all for children.

Brunton LB, Hilal-Dandan R, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 13th ed. New York: McGraw-Hill; 2018:696–697.

Drug Enforcement Administration, U.S. Department of Justice. Schedule of controlled substances: placement of tramadol into schedule IV. Final rule. *Fed Regist*. 2014;79(127):37623–37630.

Grond S, Sablotzki A. Clinical pharmacology of tramadol. *Clin Pharmacokinet*. 2004;43:879–923.

B.12. When would you consider adjuvant analgesics as part of the treatment plan?

In cancer pain management, adjuvant drugs are considered to enhance pain relief. The adjuvant analgesics are a heterogeneous group of medications originally developed for purposes other than pain relief. These drugs may become necessary in the multimodal approach to treat pain, the adverse effects of

analgesic medications, or to treat concomitant psychological disturbances such as insomnia, anxiety, depression, and psychosis. The most useful adjuvants used clinically to manage cancer pain are as follows:

- Corticosteroids
- Tricyclic antidepressants (e.g., amitriptyline)
- Anticonvulsants (e.g., gabapentin)
- Amphetamines
- *N*-methyl-D-asparate (NMDA) receptor antagonists (e.g., methadone, ketamine)
- α_2-Agonists (e.g., clonidine)
- Antihistaminics
- Phenothiazines

Ballantyne JC, Fishman SM, Rathmell JP, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2018:1682–1710.

Haywood A, Good P, Khan S, et al. Corticosteroids for the management of cancer-related pain in adults. *Cochrane Database Syst Rev*. 2015; (4):CD010756.

Oosterling A, te Boveldt N, Verhagen C, et al. Neuropathic pain components in patients with cancer: prevalence, treatment, and interference with daily activities. *Pain Pract*. 2016;16(4):413–421. doi:10.1111/papr.12291.

B.13. The patient and his family are worried about addiction. How would you approach this problem?

Unfortunately at times, it becomes difficult to differentiate between drug abuse and the deterioration in physical or psychosocial functioning caused by the disease and its treatment. For example, questionable drug-related behaviors would be difficult to recognize in a patient who develops social withdrawal or cognitive changes following brain irradiation for metastases.

Addiction is defined as a persistent pattern of dysfunctional use of opioids that may involve adverse consequences associated with continued use, loss of control over use of opioids,

compulsive use of drug, craving for the drug, and a typical drug-seeking behavior. Patients with chronic pain who are using opioids are not at higher risk of addiction than the general population. The goals of treatment including palliation of pain and improvement in the patient's quality of life must be clearly defined and explained to the patient and his relatives. At no time should patients with cancer pain be undertreated because of the fear of addiction. The patient and his family should be educated about the common misconception that addiction is a common outcome of opioid therapy.

Opioid analgesic therapy must be tailored to carefully monitor all patients in order to minimize misuse and abuse and every patient is potentially at some degree of risk for opioid misuse. This is affected by patient's disease progression, tolerance, changes in pain quality, mental health, comorbidities, other drug therapies, and changes in the patient's lifestyle.

Berger A, Shuster JL Jr, Von Roenn JH, eds. *Principles and Practice of Palliative Care and Supportive Oncology*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007:593–603.

Heit HA. Addiction, physical dependence, and tolerance: precise definitions to help clinicians evaluate and treat chronic pain patients. *J Pain Palliat Care Pharmacother*. 2003;17:15–29.

Pergolizzi JV, Gharibo C, Passik S, et al. Dynamic risk factors in the misuse of opioid analgesics. *J Psychosom Res*. 2012;72(6):443–451.

B.14. Describe different routes of opioid administration.

Oral medications should be used as the first-line approach in most patients with cancer pain who are receiving opioid analgesics. **Table 49.1** outlines the routes of opioid administration and available opioid preparations.

TABLE 49.1 Routes of Opioid Administration

Route of Administration	Available Opioid Preparation
Oral	Morphine

	Hydromorphone (Dilaudid) Methadone (Dolophine) Oxycodone, hydrocodone Codeine, meperidine Levorphanol
Rectal	Suppositories containing morphine Hydromorphone, oxycodone
Transdermal	Fentanyl patch
Sublingual	Fentanyl, methadone, buprenorphine
Intramuscular/subcutaneous	Morphine, hydromorphone, methadone Meperidine, levorphanol
Intravenous	Morphine, meperidine, methadone, fentanyl Hydromorphone, oxymorphone
Epidural/intrathecal	Morphine, methadone, hydromorphone Fentanyl, sufentanil, meperidine

The rectal or transdermal route should be chosen before considering invasive therapy for cancer pain. The sublingual route is limited by the inability to deliver large doses.

The intramuscular route is not preferred for long-term administration because it requires repeated painful injections and offers no pharmacodynamic advantages. Intravenous administration provides quick onset and is ideal for painful crises in patients with cancer as PCA.

The equianalgesic doses of opioids used orally and parenterally are listed in **Table 49.2**.

TABLE 49.2 Opioids Used Orally or Parenterally to Treat Cancer Pain

	Equianalgesic Dose (mg)[a]	
Drug	**Oral**	**Parental**
Morphine	30	10
Hydromorphone	6	2
Oxycodone	20–30	NA
Methadone	10[b]	10[b]
Levorphanol	2–3[b]	2[b]
Codeine	130[c]	75

NA, not available in the United States.

[a]Suggested doses are guidelines only. Doses are based on chronic opioid use.

[b]Particular care with titration is recommended because doses may need to be reduced significantly when steady-state levels are reached after 2 to 3 days.

[c]Codeine doses greater than 65 mg may be associated with significant constipation.

Brunton LB, Hilal-Dandan R, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 13th ed. New York: McGraw-Hill; 2018:377–379.

Knotkova H, Fine PG, Portenoy RK. Opioid rotation: the science and the limitations of the equianalgesic dose table. *J Pain Symptom Manage*. 2009;38(3):426–439.

Mercadante S. The patient with difficult cancer pain. *Cancers (Basel)*. 2019;11(4):E565. doi: 0.3390/cancers11040565.

Quigley C. Opioid switching to improve pain relief and drug tolerability. *Cochrane Database Syst Rev*. 2004;(3):CD004847. doi:10.1002/14651858.CD004847.

B.15. Describe advantages and complications of patient-controlled analgesia (PCA). What is minimum effective analgesic concentration (MEAC)?

Intravenous PCA is very advantageous for patients with chronic cancer pain because it allows patients to self-administer medication and find their own comfort zone between side effects and pain control within limits set by the physician. The PCA device is a computerized, programmable, lightweight, battery-operated portable pump with the capability of storage and retrieval of data by the microprocessor. The pump is programmed for three modes of drug delivery: (1) continuous per hour rate infusion only, which is preset by the physician and the patient has no control over it; (2) continuous with boluses for breakthrough pain, boluses controlled by the patient; and (3) boluses with lockout time in minutes set by the physician and the patient can control his or her own requirement. If required, the physician or nurse can deliver extra boluses. Intermittent rescue doses for breakthrough pain, along with continuous

infusion, decrease the total requirement of opioids. Only rescue-dose delivery mode is safer because patients will not take medication if there is no pain. However, continuous-delivery mode carries risks of oversedation and respiratory depression. The initial cost of the drug-delivery device and training of the health care provider could be expensive. PCA can also be provided by subcutaneous, epidural, or intrathecal route.

MEAC is the minimum effective analgesic concentration of the opioid that is the lower level of the therapeutic window.

Functional impairment of excretory organs is common in the elderly, half-life of the active drug and metabolites is increased in the elderly and in patients with renal dysfunctions except buprenorphine, therefore doses be reduced, a longer time interval be used between doses, and creatinine clearance be monitored except for buprenorphine.

Ballantyne JC, Fishman SM, Rathmell JP, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2018:537–679.

Brunton LB, Hilal-Dandan R, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 13th ed. New York: McGraw-Hill; 2017:566–578.

Mercadante S. The patient with difficult cancer pain. *Cancers (Basel)*. 2019;11(4):E565.

Pergolizzi J, Böger RH, Budd K, et al. Opioids and the management of chronic severe pain in the elderly: consensus statement of an international expert panel with focus on the six clinically most often used World Health Organization step III opioids (buprenorphine, fentanyl, hydromorphone, methadone, morphine, oxycodone). *Pain Pract*. 2008;8(4):287–313.

B.16. What is meperidine? How is it different from other opioids?

Meperidine is a synthetic opioid that pharmacologically resembles morphine. Meperidine is not an ideal drug for chronic pain because of its short duration of action and its high potential for abuse. The by-product normeperidine is exclusively excreted via the kidney with an elimination half-life of 36 to 40 hours. In

patients with compromised renal function, by-product accumulation has been associated with central nervous system toxicity, including myoclonus, tremulousness, hallucinations, and seizures. Meperidine possesses anticholinergic activity similar to atropine, causing mydriasis, orthostatic hypotension, and tachycardia. Compared with other opioids, meperidine very rarely causes pruritus when given neuraxially. It is extremely effective in the treatment of postoperative shivering. Meperidine also demonstrates local anesthetic actions. It is contraindicated in patients who are receiving monoamine oxidase inhibitors because of the risk of a potentially fatal syndrome characterized by hyperthermia, rigidity, and seizures.

Brunton LB, Hilal-Dandan R, Knollman B. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 13th ed. New York: McGraw-Hill; 2018:372–373.

B.17. What is rotation of opioids? When would you consider rotation of opioids?

The sequential trial of changing one opioid to another when either treatment-limiting toxicity or poor responsiveness develops has become known as *opioid rotation*. The variable response from opioid to opioid in an individual has led to this approach; changing to an alternative opioid may yield a far better balance between side effects and analgesia.

For those patients in whom pain control is inadequate and who have intolerable side effects, different strategies are implemented to improve analgesia. Opioid rotation is a simple strategy that almost all physicians can implement. Depending on equianalgesic potency ratio guidelines, switch is made to other opioids such as methadone or transdermal fentanyl patch. This should be done under close supervision and preferably in an inpatient environment.

Afsharimani B, Kindl K, Good P, et al. Pharmacological options for the

management of refractory cancer pain-what is the evidence? *Support Care Cancer*. 2015;23(5):1473–1481.

Ballantyne JC, Fishman SM, Rathmell JP, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2018:537–679.

Knotkova H, Fine PG, Portenoy RK. Opioid rotation: the science and the limitations of the equianalgesic dose table. *J Pain Symptom Manage*. 2009;38(3):426–439.

Kotlinska-Lemieszek A. Rotation, partial rotation (semi-switch), combining opioids, and titration. Does "opioid plus opioid" strategy make a step forward on our way to improving the outcome of pain treatment? *J Pain Symptom Manage*. 2010;40(1):e10–e12.

C. Invasive Therapy

C.1. Describe the role of peripheral nerve blocks in cancer pain management.

Some patients experience inadequate pain despite control, maximal medical management, or because of intolerable side effects. Interventional techniques may significantly reduce the level of pain allowing a significant decrease in analgesic requirement. Interventional therapies that can be considered depending on the location and distribution of the thoracic or abdominal pain and the involvement of viscera are the following:

- Intercostal nerve blocks
- Intrapleural blockade
- Splanchnic nerve blocks
- Celiac plexus block
- Hypogastric plexus block
- Thoracic and lumbar paravertebral blocks
- Rectus abdominis block
- Transversus abdominis plane (TAP block)
- Iliac crest block
- Ilioinguinal and iliohypogastric nerve block
- Cave of Retzius (space between urinary bladder and

symphysis pubis) block

The most useful blocks for the upper abdomen and thorax are intercostal nerve blocks and celiac plexus blocks and splanchnic nerve block and superior hypogastric and ganglion impair blocks for the lower abdomen, pelvic, and perineal pain. Thoracic and lumbar paravertebral blocks are performed to obtain spinal nerve segmental analgesia. The intercostal and thoracic paravertebral nerve blocks carry the risk of pneumothorax due to proximity of the pleura and lung. The peripheral nerve blocks are performed at anatomic sites away from the central neuraxis.

Patients with pancreatic cancer who was not tolerating opioids or not receiving adequate analgesia may benefit from a neurolytic celiac plexus block.

Neuraxial infusion of epidural and intrathecal analgesics reduces the doses of drugs required to provide adequate analgesia thereby reducing the adverse effects of systemic administration. It also benefits the patients with intolerable sedation, confusion, and/or inadequate pain control with systemic opioid administration or patients who have pain from a variety of anatomic locations.

Percutaneous kyphoplasty and vertebroplasty might be helpful for painful spinal metastases or in cases of vertebral compression fractures in, for example, multiple myeloma.

Neurodestructive procedures may be used for visceral pain from abdominal or pelvic malignancy.

Neurostimulation procedures have been useful for painful chemotherapy induced peripheral neuropathies, neuralgias, and complex regional pain syndrome.

Interventions are not appropriate if technical expertise is not available.

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de Leon-Casasola OA. Current developments in opioid therapy for management of cancer pain. *Clin J Pain*. 2008;24(suppl 10):S3–S7.

Swarm RA, Abernethy AP, Anghelescu DL, et al. Adult cancer pain. *J Natl Compr Canc Netw*. 2013;11(8):992–1022.

Thapa D, Rastogi V, Ahuja V. Cancer pain management-current status. *J Anaesthesiol Clin Pharmacol*. 2011;27(2):162–168.

Waldman SD, ed. *Atlas of Interventional Pain Management*. 4th ed. Philadelphia, PA: Elsevier; 2015:360–446.

C.2. Describe the role of celiac plexus block in cancer pain management.

Diagnostic celiac plexus block with a local anesthetic is performed to precisely differentiate sympathetically maintained pain and localize retroperitoneal or upper abdominal pain. A positive result of the diagnostic block is an indication for more definitive neurolysis in chronic cancer and nonmalignant pain. Success rates of celiac plexus neurolysis are lower in patients suffering from chronic nonmalignant abdominal pain than in those suffering from abdominal pain due to neoplasms involving the upper abdominal viscera. Neurolysis of celiac plexus with alcohol or phenol is performed under fluoroscopic guidance or computed tomography–guided technique and strict sterile condition by using a single- or two-needle periaortic technique, single-needle transaortic technique, single-needle anterior technique, or endoscopic ultrasound (EUS)-guided technique. Individual skills of the treating physician, available facilities, patient's general condition, and extent of the spread of tumor should be considered in determining the type of technique to use.

Computed tomography (CT) guidance provides better visibility of tumor, lymph nodes, and the celiac plexus.

Pain physicians for celiac plexus neurolysis commonly use 40 to 50 mL of 50% to 70% alcohol or 6% to 10% phenol. Smaller volumes are recommended for absolute alcohol and higher concentration of phenol. Neurolysis with phenol is less painful because of its local anesthetic action, whereas alcohol neurolysis

is very painful and should be blocked with pretreatment with local anesthetics.

A Cochrane review from 1990 to 2010 to determine the efficacy and safety of celiac plexus neurolysis in reducing pancreatic cancer pain found that there is minimal statistical evidence for the superiority of pain relief over analgesic therapy; however, because celiac plexus block causes fewer adverse effects than opioids, it is important to consider for patients.

Arcidiacono PG, Calori G, Carrara S, et al. Celiac plexus block for pancreatic cancer pain in adults. *Cochrane Database Syst Rev*. 2011;(3):CD007519.

de Leon-Casasola OA. *Cancer Pain: Pharmacological, Interventional and Palliative Care Approaches*. Philadelphia, PA: Saunders; 2006:401–416.

Rosland JH, Geitung JT. CT guided neurolytic blockade of the coeliac plexus in patients with advanced and intractably painful pancreatic cancer. *Scand J Pain*. 2018;18(2):247–251.

Waldman SD, ed. *Atlas of Interventional Pain Management*. 4th ed. Philadelphia, PA: Elsevier; 2015:360–446.

C.3. What are the complications of celiac plexus block?

Serious complications should rarely occur in the hands of a skilled clinician. Hypotension and increased gastrointestinal motility are the most common complications of this block. Neurologic complications include subarachnoid or epidural injection and lumbar nerve root injury, causing long-lasting paresthesia. A potentially severe complication can occur as a result of accidental injection into the nutrient artery of the spinal cord (artery of Adamkiewicz), causing paraplegia. Injury to the kidney may cause temporary hematuria that may not need any treatment. Other complications have been reported due to proximity of other vital structures include pneumothorax, chylothorax, intradiscal injection, retroperitoneal hematoma, and failure to ejaculate.

Ballantyne JC, Fishman SM, Rathmell JP, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2019:717–719.

C.4. Would you consider neuraxial opioid infusion in this patient? Discuss complications of this procedure.

In properly selected patients, epidural, intrathecal (subarachnoid), or intraventricular infusions of opioids have the advantage of producing profound analgesia without motor, sensory, or autonomic blockade. These routes are considered to deliver preservative-free medications when pain is not well controlled by noninvasive (oral, subcutaneous, or intravenous) routes and escalation of doses is limited by intolerable side effects. The potency ratio of oral to epidural morphine is 1:30 and that from oral to intrathecal morphine is 1:300. The decrease in the size of dose from oral to intrathecal greatly reduces the side effects and improves pain control and quality of life. The PCA technique can also be employed for epidural routes. Programmable intrathecal pumps can deliver medications at the prescribed dose. Fixed or flexible doses of morphine can deliver via the intrathecal pumps. Recently approved patient-controlled device allows patient-activated doses via the intrathecal pump (Personal Therapy Manager or PTM, Medtronic Neurological, Minneapolis, MN). Morphine is the most commonly used drug. Other opiates, local anesthetics, ziconotide, α_2-agonists, etc can be used as recommended by the Polyanalgesic Consensus panel.

These routes require a skilled experienced clinician, meticulous technique, and family and facility support in which close monitoring and follow-ups can be done. These procedures are reversible but involve an initial expense for specialized care and operating room costs. Intraspinal opioids may produce the same side effects of nausea, mental clouding, and sedation as in oral and parenteral dosing. Infection (e.g., meningitis and epidural abscess) and hematoma are potentially devastating complications that can cause permanent neurologic deficit if not dealt with in a timely basis. Pruritus and urinary retention are

more common than with oral or parenteral administration.

Deer TR, Pope JE, Hayek SM, et al. The Polyanalgesic Consensus Conference (PACC): recommendations on intrathecal drug infusion systems best practices and guidelines. *Neuromodulation*. 2017;20(2):96–132.

Stearns L, Boortz-Marx R, Du Pen S, et al. Intrathecal drug delivery for the management of cancer pain: a multidisciplinary consensus of best clinical practices. *J Support Oncol*. 2005;3:399–408.

C.5. Which medications can be used intrathecally? What is ziconotide?

Morphine is the most commonly used drug; other opiates such as hydromorphone, fentanyl, and sufentanil can be used intrathecally. In addition, local anesthetics, α-agonist such as clonidine, and baclofen can be used as recommended by the Polyanalgesic Consensus panel.

Recently, Prialt (ziconotide), a synthetic equivalent of a naturally occurring peptide found in marine snails, has been shown to be effective in pain relief when used intrathecally. It is a selective voltage-gated calcium channel blocker that inhibits release of pyroglutamate, calcitonin, and substance P in the brain and spinal cord. Side effects include dizziness, nausea, confusion, and psychosis, and therefore, patients trailed on ziconotide should be monitored for cognitive impairment, hallucinations, or changes in mood and consciousness.

Only morphine, baclofen, and ziconotide has been approved by the U.S. Food and Drug Administration (FDA).

Bhatia G, Lau ME, Koury KM, et al. Intrathecal drug delivery (ITDD) systems for cancer pain. *F1000Res*. 2014;2:96.

Deer TR, Pope JE, Hayek SM, et al. The Polyanalgesic Consensus Conference (PACC): recommendations on intrathecal drug infusion systems best practices and guidelines. *Neuromodulation*. 2017;20(2):96–132.

Stearns L, Boortz-Marx R, Du Pen S, et al. Intrathecal drug delivery for the management of cancer pain: a multidisciplinary consensus of best clinical practices. *J Support Oncol*. 2005;3:399–408.

Williams J, Day M, Heavner J. Ziconotide: an update and review. *Expert Opin Pharmacother*. 2008;9:1575–1583.

C.6. What is a Personal Therapy Manager (PTM), and what role does it play in neuraxial pain relief?

Increasingly being used is a patient-controlled device that allows patient-activated doses via the intrathecal pump (PTM, Medtronics Neurological, Minneapolis, MN). The PTM enables the patient to activate delivery of physician-programmed supplemental doses of intrathecal medication. This is especially useful for patients experiencing intermittent pain of carrying intensity that cannot be adequately managed with a simple continuous infusion, have an unpredictable need for varying doses of drug, or experience inadequate pain relief or intolerable side effects from supplemental systemic breakthrough pain medications. Nevertheless, risk of sedation, respiratory depression, and other adverse effects are just as possible as when taking oral opiate supplementation, and therefore, caution and careful programming should be ensured. Also see section C.4.

de Leon-Casasola OA. *Cancer Pain: Pharmacological, Interventional and Palliative Care Approaches*. Philadelphia, PA: Saunders; 2006:417–429.

Ilias W, le Polain B, Buchser E, et al. Patient-controlled analgesia in chronic pain patients: experience with a new device designed to be used with implanted programmable pumps. *Pain Pract*. 2008;8(3):164–170.

Rauck R, Cherry D, Boyer MF, et al. Long-term intrathecal opioid therapy with a patient-activated, implanted delivery system for the treatment of refractory cancer pain. *J Pain*. 2003;4:441–447.

Stearns L, Boortz-Marx R, Du Pen S, et al. Intrathecal drug delivery for the management of cancer pain: a multidisciplinary consensus of best clinical practices. *J Support Oncol*. 2005;3:399–408.

C.7. Would you consider neuraxial neurolysis in this patient to manage his pain? Discuss advantages and disadvantages of these blocks.

Due to physical separation of motor and sensory nerve roots in the spinal canal and intrathecal space, chemical neurolytic procedures allow sensory blockade without loss of motor functions. Inadequate pain control with intolerable side effects makes this patient an ideal candidate for neuraxial neurolysis; however, complications of the procedure should be weighed against benefits. Epidural or intrathecal (subarachnoid) neurolytic blocks are considered for severe intractable pain from advanced cancer as an adjuvant to relieve pain and suffering and improve quality of life. These blocks are primarily effective in relieving pain of somatic origin and less effective for visceral and neuropathic pain.

In selected patients in whom pain relief is not achieved by less invasive measures, these blocks can provide rapid analgesia and allow dosage (and side effects) reduction of systemic drugs. However, risks of postural hypotension, bowel and bladder incontinence, and motor and sensory deficit in the lower extremities cannot be overemphasized. These blocks are irreversible and require a skilled clinician to perform the procedure.

de Leon-Casasola OA. *Cancer Pain: Pharmacological, Interventional and Palliative Care Approaches*. Philadelphia, PA: Saunders; 2006:501–507.

McHugh ME, Miller-Saultz D, Wuhrman E, et al. Interventional pain management in the palliative care patient. *Int J Palliat Nurs*. 2012;18(9):426–428, 430–433.

C.8. Which neuroablative procedures can be considered in the terminal stage of pancreatic cancer?

Based on the location and type of pain (somatic, visceral, deafferentation), the general condition of the patient, the stage of tumor and metastasis, the life expectancy, and the expertise available, the following neurosurgical procedures could be considered:

- Peripheral neurectomy
- Dorsal rhizotomy
- Anterolateral cordotomy (spinal tractotomy)
- Commissural myelotomy
- Hypophysectomy

Ballantyne JC, Fishman SM, Rathmell JP, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2019:1698–1707.

C.9. Describe the role of radiation therapy in cancer pain.

Radiation therapy can be curative or palliative to relieve pain from metastasis and symptoms from local extension of the disease. Radiation therapy is complementary to chemotherapy, surgery, and analgesic drug therapies to enhance the effectiveness of pain control. Radiating therapy can palliate when disease can not be controlled. Along with therapeutic effectiveness of radiation treatment, the absence of complete specificity for disease may exacerbate or even cause new pain. It is most commonly used for bone metastasis. The radiation dosage should be administered in the fewest fractions possible to promote pain control during and after treatment.

Johnstone C, Lutz ST. The role of hypofractionated radiation in the management of non-osseous metastatic or uncontrolled local cancer. *Ann Palliat Med*. 2014;3(4):291–303. doi:10.3978/j.issn.2224-5820.2014.10.01.

McQuay HJ, Collins SL, Carroll D, et al. Radiotherapy for the palliation of painful bone metastases. *Cochrane Database Syst Rev*. 2000;(2):CD001793.

D. Nonpharmacologic Management

D.1. What are the various nonpharmacologic techniques of cancer pain management?

Eisenberg and colleagues demonstrated that cancer and other chronic pain syndromes like AIDS and arthritis may get benefit from alternative modalities. Practicing physical activity and

sport during cancer modifies fatigue and quality of life and reduces symptoms of depression.

The common therapies offered are as follows:

- Physical therapy and physical modalities
- Physical activity and sport
- Relaxation and massage
- Chiropractic manipulation
- Spiritual healing
- Biofeedback and hypnosis
- Magnetic and low-power laser therapy
- Transcutaneous electrical nerve stimulation (TENS)
- Homeopathy
- Acupuncture
- Prayer

Bouillet T, Bigard X, Brami C, et al. Role of physical activity and sport in oncology: scientific commission of the National Federation Sport and Cancer CAMI. *Crit Rev Oncol Hematol*. 2015;94:74–86.

Bradley LA, McKendree-Smith NL, Cianfrini LR. Cognitive-behavioral therapy interventions for pain associated with chronic illness: evidence for their effectiveness. *Semin Pain Med*. 2003;1:44–54.

Eisenberg DM, Kessler RC, Foster C, et al. Unconventional medicine in the United States. Prevalence, costs, and patterns of use. *N Engl J Med.* 1993;328:246–252.

Pinell XA, Kirkpatrick SH, Hawkins K, et al. Manipulative therapy of secondary lymphedema in the presence of locoregional tumors. *Cancer*. 2008;112(4):950–954.

D.2. What physical modalities have been successfully tried in cancer pain management?

Physical modalities may be useful in conjunction with conventional systemic and interventional treatments used to control cancer-related pain, especially in patients with movement-associated pain. Physical modalities may help decrease stiffness, increase blood flow to the part, help relax the patient, and reduce the dose of analgesics. They include

cutaneous stimulation, superficial heat and cold therapy, massage, vibration, and pressure. Cold therapy (cryotherapy) causes vasoconstriction, reduces inflammation, and decreases muscle spasm. Superficial application of heat (thermotherapy) acts through conduction or convection to increase blood flow to the skin and superficial organs. Heat also decreases joint stiffness and increases muscle flexibility. Physical therapy and exercise help to strengthen weak muscles, mobilize stiff joints, and restore coordination. Exercise may reduce pain by 25%. Weight-bearing exercises are avoided if an impending fracture is suspected.

Benzon H, Rathmell J, Wu CL, et al, eds. *Raj's Practical Management of Pain*. 4th ed. St. Louis, MO: Mosby; 2008:418–426.

Bouillet T, Bigard X, Brami C, et al. Role of physical activity and sport in oncology: scientific commission of the National Federation Sport and Cancer CAMI. *Crit Rev Oncol Hematol*. 2015;94:74–86.

Cheville AL, Basford JR. Role of rehabilitation medicine and physical agents in the treatment of cancer-associated pain. *J Clin Oncol*. 2014;32(16):1691–1702.

D.3. Describe the role of neuromodulation in cancer pain management.

Neuromodulation techniques like spinal cord stimulation and deep brain stimulation have not been popular in cancer pain management because of incompatibility with magnetic resonance imaging (MRI). But this therapy is now being used more frequently since the availability of the MRI compatible spinal cord stimulator systems. Neuromodulation techniques have variable outcome results with success rates between 18% and 80% depending on the study cited. Much of the literature is about chronic nonmalignant pain syndromes. The consensus among most pain physicians is that neuropathic pain syndromes are more effectively treated as spinal cord syndromes than as nociceptive pain syndromes.

TENS and acupuncture are believed to activate endogenous pain-relieving pathways. Low-voltage stimulation to large myelinated peripheral nerves via cutaneous electrodes may significantly reduce pain. Spinal cord stimulation appears to be a promising therapy for intractable cancer pain and can offer relief of neuropathic pain, which is present in 15% to 40% of cancer pain patients. Recently, high-frequency spinal cord stimulation, burst stimulation and dorsal root ganglion, and MRI compatible spinal cord stimulation systems may increase the role of this therapy in cancer patient. Studies have shown significant pain relief in postthoracotomy pain, back pain, leg pain, groin pain, and testicular pain related to carcinoma. Based on the evidence, motor cortex stimulation should be abandoned.

Burchiel KJ, Raslan AM. Contemporary concepts of pain surgery. *J Neurosurg,* 2019;130(4):1039–1049.

Yakovlev AE, Resch BE. Spinal cord stimulation for cancer-related low back pain. *Am J Hosp Palliat Care*. 2012;29:93–97.

Yakovlev AE, Resch BE, Karasev SA. Treatment of cancer-related chest wall pain using spinal cord stimulation. *Am J Hosp Palliat Care*. 2010;27:552–556.

D.4. What psychological techniques have been promoted for comfort care and pain relief?

Psychological distress impacts pain. Depression, anxiety, anger, and mood disturbances have been correlated with higher levels of perceived cancer pain. Also, there has been increase in the number of people surviving with cancer, as result of advances in cancer treatment, who are suffering from intractable pain. Psychological interventions are an important part of a multimodal approach to pain management in patients with cancer. Some techniques that are used are relaxation, biofeedback, hypnosis, imagery, and cognitive-behavioral therapy. They help patients gain a sense of control over pain. Cognitive and behavioral techniques are designed to influence

the interpretation of events and bodily sensations. Cognitive techniques help patients think differently about their pain and its management. Behavioral techniques help patients develop skills to cope with pain and help modify their reactions to pain. Patients who undergo psychotherapy report less pain. Relaxation therapy is a well-established modality in managing cancer pain. Several variations of relaxation strategies and techniques have been widely practiced in patients suffering from advanced cancer and have proven effective. Relaxation strategies like deep breathing, muscle relaxation, and imagery are recommended for the promotion of comfort and relief of pain in hospitalized patients.

Relaxation and imagery are used to achieve a state of mental and physical relaxation, thereby relieving anxiety and muscle tension.

Patients with higher levels of social support have reported lower intensity of cancer pain.

These interventions have medium-size effects on both pain severity and interference per meta-analysis by Gorin. Therefore, quality controlled psychosocial interventions should be part of a multimodal approach to managing pain in cancer patients.

Byker GL, Leskuski D. Nonpharmacological management of pain. In: Berger A, Shuster J, Von Roenn J, eds. *Principles and Practice of Palliative Care and Supportive Oncology*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2013:42–54.

Eccleston C, Morley SJ, Williams AC. Psychological approaches to chronic pain management: evidence and challenges. *Br J Anaesth*. 2013;111(1):59–63.

National Institutes of Health. *National Institutes of Health State-of-the-Science Conference Statement: Symptom Management in Cancer: Pain, Depression, and Fatigue*. Bethesda, MD: National Institute of Health; 2002.

Sheinfeld Gorin S, Krebs P, Badr H, et al. Meta-analysis of psychosocial interventions to reduce pain in patients with cancer. *J Clin Oncol*. 2012;30(5):539–547.

D.5. What are distraction and reframing techniques?

What is the role of hypnosis in cancer pain?

Distraction and reframing techniques encourage focused attention on stimuli other than pain. This involves singing, talking, praying, and watching television. Reframing helps monitor and evaluate negative thoughts and images while encouraging positive thoughts and behavior.

Hypnosis by a skilled person decreases pain and anxiety in patients who have difficulty managing their pain. It also increases coping skills. This technique allows heightened awareness and focused concentration to manipulate perception of pain and has been effective in the management of cancer-related pain syndromes.

Devine EC. Meta-analysis of the effect of psychoeducational interventions on pain in adults with cancer. *Oncol Nurs Forum*. 2003;30:75–89.

Ong AD, Zautra AJ, Reid MC. Chronic pain and the adaptive significance of positive emotions. *Am Psychol*. 2015;70(3):283–284.

Sheinfeld Gorin S, Krebs P, Badr H, et al. Meta-analysis of psychosocial interventions to reduce pain in patients with cancer. *J Clin Oncol*. 2012;30(5):539–547.

50 Low Back Pain and Sciatica

David Y. Wang

A 57-year-old former factory worker was injured on the job 8 years ago. He experienced severe low back and right leg pain after lifting a heavy piece of equipment and was found to have a herniated L4–L5 intervertebral disc with compression of the right L5 nerve root. He underwent a lumbar laminectomy and decompression surgery; nevertheless, he has continued to complain of back pain and right sciatica.

A. Medical Disease and Differential Diagnosis

1. How great an issue is low back pain in the general population?
2. What is the prevalence of low back pain?
3. What is the societal cost of low back pain?
4. What causes low back pain?
5. What are the risk factors for low back pain?
6. What are the potential sources of pain in the spine?
7. What is the anatomy of the intervertebral discs? What is the mechanism of pain from herniated discs?
8. What is the anatomy of the spinal facets? How do the facet joints cause pain?
9. What are the important findings through history and physical examination?

10. What are the appropriate diagnostic studies for low back pain?
11. What is the differential diagnosis of low back pain?
12. What are the causes of persistent back pain after multiple spine surgeries?

B. Management of Low Back Pain and Sciatica

1. What are the noninterventional treatments available?
2. What traditional interventional treatments are available and how should they be used?
3. What are some of the recent safety improvements recommended for lumbar epidural steroid injection?
4. What are some of other approaches in minimally invasive interventions?
5. What are the concerns about magnetic resonance imaging (MRI) safety in patients with a spinal cord stimulator (SCS)?
6. When should surgery be considered?
7. What surgical options are available for the treatment of disc disease?

A. Medical Disease and Differential Diagnosis

A.1. How great an issue is low back pain in the general population?

Disorders of the lumbosacral spine cause pain, disability, suffering, public health issues, and socioeconomic issues. Most adults will experience several episodes of low back pain during their lifetime. It is estimated that 80% of workers will lose work time because of this complaint. On the basis of primary diagnosis only, a National Ambulatory Medical Care Survey from 1989 to 1990 ranked low back pain as the fifth most frequent reason for adults to visit an office-based medical practice. In 2010, low back pain was ranked third behind only ischemic heart disease and chronic obstructive pulmonary

disease in causing poor health and mortality burden in United States. Lower back pain has been ranked the highest in terms of causing disability and fifth in the overall burden per the Global Burden of Disease 2010 study.

Hart LG, Deyo RA, Cherkin DC. Physician office visits for low back pain. Frequency, clinical evaluation, and treatment patterns from a U.S. national survey. *Spine (Phila Pa 1976)*. 1995;20:11–19.

Hoy D, March L, Brooks P, et al. The global burden of low back pain: estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis*. 2014;73:968–974.

National Institute of Neurological Disorders and Stroke. *Low Back Pain Fact Sheet*. Bethesda, MD: National Institute of Neurological Disorders and Stroke; 2014:1–50. NIH publication 15-5161.

A.2. What is the prevalence of low back pain?

A global review of the prevalence of low back pain in the adult general population has shown its point prevalence to be approximately 12%, with a 1-month prevalence of 23%, a 1-year prevalence of 38%, and a lifetime prevalence of approximately 40%. Furthermore, as the population ages over the coming decades, the number of individuals with low back pain is likely to increase substantially. Low back pain usually begins in early life, with the highest frequency of symptoms occurring between ages 35 and 55 years. Of all adults in industrialized societies, 60% to 80% are affected at some point in their lives. Work absence and symptom duration increase with aging. An acute episode of low back pain usually resolves within 6 weeks. More persistent pain lasting beyond 3 to 6 months occurred in only 5% to 10% of patients with back pain. The U.S. Agency for Health Care Policy and Research reported that 90% of patients with acute low back pain recover their usual activity tolerance within 4 weeks of injury. The remaining 10% of patients who do not recover with time or routine therapy go on to develop chronic symptoms and secondary problems. At 1 year, the

incidence of acute back pain converting to chronic back pain is 20%. Recurrences of low back pain are also common, with the percentage of subsequent low back pain episodes ranging from 20% to 44% within 1 year for working populations to lifetime recurrences of up to 85%.

Freburger JK, Holmes GM, Agans RP, et al. The rising prevalence of chronic low back pain. *Arch Intern Med*. 2009;169:251–258.

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Jackson T, Thomas S, Stabile V, et al. Prevalence of chronic pain in low-income and middle-income countries: a systematic review and meta-analysis. *Lancet*. 2015;385(suppl 2):S10.

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Rubin DI. Epidemiology and risk factors for spine pain. *Neurol Clin*. 2007;25:353–371.

A.3. What is the societal cost of low back pain?

The costs of low back pain include functional impairment, activity limitations, reduced quality of life, disability, underemployment, reduced work productivity, and direct medical cost. It appears that the societal perception of disability has changed dramatically over time. This has resulted in an increased rate and cost of disability and overutilization of medical care, including surgical treatments. Back pain in workers 40 to 65 years of age costs employers an estimated $7.4 billion per year. Duke University Medical Center researchers found that patients suffering from back pain consume more than $90 billion annually in health care expenses, with approximately $26 billion of that amount directly attributable to treating the back pain. Their results demonstrate the enormous economic impact of back pain. The total $90 billion spent in 1998 represented 1% of the U.S. gross domestic product (GDP), and

the $26 billion in direct back pain costs accounted for 2.5% of all health care expenditures for that year. These data came from the Medical Expenditure Panel Survey (MEPS) in 1998. The team found that 25.9 million adults reported back pain in 1998, with 172.7 million reporting no back pain. The figures do not include information about back pain in nursing home patients, who in the 1977 research accounted for about 20% of medical costs. As a result, the costs of care for back pain almost certainly top $100 billion annually. A study in the *Journal of the American Medical Association* found that chronic pain conditions, including arthritis, back problems, and other ailments, drain $61.2 billion a year from the U.S. economy. Back pain accounted for about a quarter of the lost or unproductive work and is second only to headaches as the most frequent pain complaint of workers. The annual cost to U.S. employers is $100 billion for spine-related disabilities.

Dagenais S, Caro J, Haldeman S. A systemic review of low back pain cost of illness studies in the United States and internationally. *Spine J*. 2008;8:8–20.

Katz JN. Lumbar disc disorders and low-back pain: socioeconomic factors and consequences. *J Bone Joint Surg Am*. 2006;88(suppl 2):21–24.

Luo X, Pietrobon R, Sun SX, et al. Estimates and patterns of direct health care expenditures among individuals with back pain in the United States. *Spine (Phila Pa 1976)*. 2004;29(1):79–86.

Ricci JA, Stewart WF, Chee E, et al. Back pain exacerbations and lost productive time cost in United States workers. *Spine (Phila Pa 1976)*. 2006;31:3052–3060.

Stewart WF, Ricci JA, Chee E, et al. Lost productive time and cost due to common pain conditions in the US workforce. *JAMA*. 2003;290(18):2443–2454.

A.4. What causes low back pain?

Majority of low back pain is mechanical in nature caused by injury, compression, tears, and bone and disc degeneration. Common causes include the following:

- Sprains and strains

- Intervertebral disc degeneration/internal disc disruption (IDD)
- Herniated disc (bulge, protrusion, extrusion, sequestration of disc)
- Radiculopathy
- Spondylosis/facet joint arthrosis
- Spondylolisthesis
- Traumatic injury
- Spinal stenosis/foraminal stenosis/lateral recess stenosis
- Skeletal irregularity (scoliosis, kyphosis)
- Compression fracture/end plate fracture
- Cluneal nerves entrapment (superior and middle cluneal nerves)
- Sacroiliac joint dysfunction
- Other underlying conditions
  - Infections
  - Tumors
  - Abdominal aortic aneurysms
  - Kidney stones
  - Endometriosis
  - Fibromyalgia

National Institute of Neurological Disorders and Stroke. *Low Back Pain Fact Sheet*. Bethesda, MD: National Institute of Neurological Disorders and Stroke; 2014:1–50. NIH publication 15-5161.

Shobeiri E, Khalatbari MR, Taheri MS, et al. Magnetic resonance imaging characteristics of patients with low back pain and those with sciatica. *Singapore Med J*. 2009;50(1):87–93.

A.5. What are the risk factors for low back pain?

Traditional beliefs suggested that heavy physical jobs required high-energy demand and significant stress and strain on the spine, whereas light jobs required low-energy demand. Many low-energy jobs, however, are static, which is an inherent risk factor for low back pain. Low back pain, degenerative disc disease, and disc herniation are associated with the following:

- Repetitive heavy lifting
- Static work posture (sitting or standing)
- Frequent twisting and bending
- Vibration (operation of motor vehicle or industrial device)
- The common vibration of construction vehicles and industrial devices ranging in frequency from 3.5 to 8.9 Hz.
- Low-frequency vibration, especially around 5 Hz, in conjunction with a prolonged seated position is associated with spine problems.
- The potential for damage to the disc through mechanical resonance is analogous to the high notes of an opera soprano shattering a wine glass.
- Fatigue of the abdominal and paraspinal muscles has been demonstrated when subjected to 30 minutes of vibration. In the absence of this support, the spine is further susceptible to injury.
- A meta-analysis of 17 studies revealed that whole-body vibration is associated with an increased risk of low back pain, sciatica, and lumbar intervertebral disc disorders.
- Cigarette smoking is linked to low back pain, sciatica, and lumbar disc herniation. In an animal model, cigarette smoking significantly affects the vasculature outside the intervertebral disc, where the most pronounced effect is the reduction of solute-exchange capacity, cellular uptake, and metabolism within the disc.
- Cross-country skiing. In a study of skiing and spinal trauma, the diagonal body position required for cross-country skiing was the most common back pain–inducing stance, whereas no skier experienced back pain when only downhill skiing.

The “oxidative stress hypothesis of aging” theory proposed that enhancement of oxygen consumption resulting from increased physical activity may accelerate disc degeneration. On the other hand, strenuous exercises may contribute to positive

nutritional effect by facilitating the transport of small solutes into and out of the disc. Generally, it is believed that people who are physically fit or who maintain a balanced exercise program appear to have a lower risk for chronic low back pain and a more rapid recovery after an episode of acute back pain.

Ballantyne JC, Fishman SM, Rathmell JP, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2018:1643–1645.

Frymoyer JW, Pope MH, Clements JH, et al. Risk factors in low-back pain. An epidemiological survey. *J Bone Joint Surg Am*. 1983;65:213–218.

Wilder DG, Woodworth BB, Frymoyer JW, et al. Vibration and the human spine. *Spine (Phila Pa 1976)*. 1982;7:243–254.

A.6. What are the potential sources of pain in the spine?

In order to more easily identify the various sources of pain, the spine may be divided into three compartments: anterior, middle, and posterior.

The anterior compartment consists of the vertebral body and intervertebral disc. The anterior unit is bound together by cephalocaudal ligaments: anterior longitudinal ligament and posterior longitudinal ligament (PLL). The anterior longitudinal ligament is anatomically much broader and stronger than the PLL. The PLL is intact throughout the length of the vertebral column until it reaches the lumbar vertebrae. From L1, it becomes progressively narrower until at L5–S1 it is only half of its original width. This anatomic feature contributes to an inherent structural weakness in the lumbar spine. Hence, the lower lumbar spine is the region subjected to the greatest static stress and most spinal movement resulting in the greatest kinetic strain.

The middle (neuraxial) compartment contains all of the structures within the bony and ligamentous boundaries of the spinal canal. This includes the PLL, epidural space, meninges, spinal cord, dorsal and ventral nerve roots, root sleeves, dorsal

root ganglia, and ligamentum flavum.

The posterior compartment contains the facet joints, laminae, vertebral arches, and structures posterior to the plane of the transverse processes and innervated by the dorsal rami of the spinal nerves. The ligaments are extremely important in stabilizing the vertebral column. The ligamentum flavum (yellow ligament), which connects the laminae of adjacent vertebrae, is the thickest and strongest ligament in the lumbar region. It can contribute to spinal stenosis by folding inward during an upright posture, extension of the back, and hypertrophying.

The sinuvertebral nerve (also known as recurrent meningeal nerve) originates lateral to the neural foramina and enters the spinal canal anterior to the dorsal root ganglion (DRG). It is a branch of the somatic ventral nerve root and the sympathetic grey ramus communicans. This specific nerve, the nerve of Luschka, innervates the outer one-third of the disc annulus, PLL, epidural membranes, and dura at the segmental level of origin and adjacent levels. Therefore, it has the ability to transmit pain messages from a problematic disc to the brain. It is important to note that central low back pain, with or without referred pain to the buttocks, may derive from the irritation of the outer part of the annulus fibrosis or the PLL.

In summary, the potential sources of low back and radicular pain include the bony structure of vertebrae, muscles attached to the spine and hips, fasciae, ligaments, discs, facet joints, meninges, vessels, nerve roots, DRG, and nerves in the surrounding areas.

The natural wear and tear on the discs and facet joints results in microtrauma and degeneration. This can induce the release of neurohumoral mediators such as phospholipase A_2, serotonin, H^+, substance P, prostaglandin E_2, and so on, to produce

inflammation of the nerve roots or meninges and to sensitize local nociceptors. Furthermore, it has been theorized that material from the nucleus pulposus, sheltered from the immune system by the presence of the annulus fibrosus, might act as a foreign protein and trigger an autoimmune reaction. The demonstration of an activated immunocompetent cellular response at the epidural interface of the herniation of the nucleus pulposus supports the concept of the immunogenic capacity of the nucleus pulposus. Tissue injury or inflammation can cause a barrage of nociceptive input into the spinal cord. This may lead to a phenomenon called *central sensitization* or *windup* of neurons in the dorsal horn of the spinal cord. The release of excitatory amino acids and neuropeptides in the dorsal horn is thought to be the mechanism underlying the phenomenon of central sensitization. At the cellular level, there is an increase in spontaneous discharge and an expansion of neural receptive fields of wide-dynamic-range (WDR) neurons located in Rexed lamina V of the spinal cord. Clinically, this is characterized by the sensation of pain when exposed to nonnoxious stimuli (allodynia), a significantly increased response to painful input (hyperalgesia), and an increased response to repetitive stimulation (hyperpathia).

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Kang JD, Georgescu HI, McIntyre-Larkin L, et al. Herniated lumbar intervertebral discs spontaneously produce matrix metalloproteinases, nitric oxide, interleukin-6, and prostaglandin E2. *Spine (Phila Pa 1976)*. 1996;21:271–277.

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Saal JS. The role of inflammation in lumbar pain. *Spine (Phila Pa 1976)*. 1995;20:1821–1827.

A.7. What is the anatomy of the intervertebral discs? What is the mechanism of pain from herniated discs?

The intervertebral disc is a ring-like structure composed of a centrally located well-hydrated pliable proteoglycan matrix, the nucleus pulposus, which comprises two-thirds of the surface area of the disc. Surrounding the nucleus is a fibrocartilaginous ring composed predominantly of type I collagen, the annulus fibrosus, which makes up the remaining one-third of the surface area of the disc. The annulus fibrosus is stronger anteriorly but often defective posteriorly. As a self-contained fluid system, the disc absorbs shock, permits transient compression, and allows movement. It provides a cushion between the vertebral bodies and allows for greater flexibility.

As the disc ages, the number of viable cells in the nucleus pulposus decreases, and the proportion of cells that exhibit necrosis changes from 2% in infancy to 50% in young adults and 80% in the elderly. The water content in the young disc is 80% to 90% in the nucleus pulposus. With aging, the discs tend to dehydrate, losing up to 70% of their water content. As the nucleus pulposus further dehydrates, it becomes more fibrous and less compliant. A disc will usually herniate under strain and pressure. When overstressed, it will protrude along in the path of least resistance, usually posterolaterally. This can cause direct mechanical pressure on the nerve roots resulting in radiculopathy.

In the healthy back, only the outer third of the annulus fibrosus is innervated. In the degenerative or disrupted disc, small unmyelinated nerve fibers grow into the inner third of the annulus fibrosus and even into the nucleus pulposus. IDD is a condition characterized by a degenerated nucleus pulposus with radial fissures extending into the peripheral annulus fibrosus.

Upon rupture of the disc, the release of irritative material near the meninges can induce radiculitis and symptoms of radiculopathy without actual herniated disc material compressing the nerve roots. Under such circumstances, significant disc herniation might not be visualized on MRI or computed tomography (CT) scan. In brief, the proposed mechanisms of radiculopathy include direct pressure on nerve fibers as a result of compression injury and indirect impact through impairment of microcirculation, chemical irritation and inflammation, immune reaction, edema formation secondary to permeability changes of the intraneural capillaries, and impairment of the nutritional transport to the nerve root.

Compression of the nerve roots is dependent on the effective space available within the neural foramina, the osseous structures surrounding the neural foramina, and the tethering effects of the intraspinal and extraspinal ligaments. Posterolateral disc herniations can impinge on the lumbar dorsal root, which then initiates electrical discharges for as long as 25 minutes after the mechanical stimulus has been removed. Radiculopathy can be produced by either biochemical or mechanic stimulation of a swollen, stretched, or compressed nerve root. Approximately 3% to 12% of all lumbar disc herniations occur laterally and extend into or beyond the foraminal zone; in this setting, the patients will complain of sudden and severe radicular pain, often with dysesthesia. On the other hand, discogenic pain resulting from a central disc bulge or herniation stimulates several lumbar tissues such as the outer layer of the annulus fibrosus or PLL. Clinically, this is manifested as central low back pain without any radicular symptoms.

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Stafford MA, Peng P, Hill DA. Sciatica: a review of history, epidemiology, pathogenesis, and the role of epidural steroid injection in management. *Br J Anaesth*. 2007;99(4):461–473.

Takebayashi T, Cavanaugh JM, Cüneyt Ozaktay A, et al. Effect of nucleus pulposus on the neural activity of dorsal root ganglion. *Spine (Phila PA 1976)*. 2001;26:940–945.

A.8. What is the anatomy of the spinal facets? How do the facet joints cause pain?

The facet, or zygapophysial, joints consist of two arthrodial joints superiorly and inferiorly, each lined with synovium, lubricated by synovial fluid, and contained within a joint capsule. These synovial joints enhance spinal stability and flexibility. In the upper part of the lumbar spine (L1–L3), the facet planes lie in a generally vertical sagittal plane and permit flexion and extension but prevent lateral flexion or bending in the lordotic curve. The lumbosacral facet joints at the level of L5–S1 depart the farthest from the sagittal plane, allowing some rotation of the lower part of the lumbar spine. With slight forward flexion, the facets of the other lumbar vertebrae separate and permit a modest degree of lateral movement and rotation. Facet loading, if of a repetitive nature, may play a role in the degeneration of the facet joint. After repeated wear and tear, these joints are susceptible to osteoarthritis and associated synovial cyst formation. Hypertrophic facet joints or cysts can encroach on the spinal canal or the intervertebral foramina and contribute to the development of central spinal, lateral recess, or foraminal stenosis.

5th ed. Philadelphia, PA: Wolters Kluwer; 2018:1260.

Devlin VJ, ed. *Spine Secret Plus*. 2nd ed. St. Louis, MO: Elsevier Mosby; 2012:332–336.

Hsu KY, Zucherman JF, Shea WJ, et al. Lumbar intraspinal synovial and ganglion cyst (facet cyst). Ten-year experience in evaluation and treatment. *Spine (Phila Pa 1976)*. 1995;20:80–89.

A.9. What are the important findings through history and physical examination?

A problem-focused pain history should include onset, location, intensity (e.g., pain scale 0 to 10), characteristics (achy, spasmodic, stabbing, burning, shooting, etc.), and duration plus aggravating and alleviating factors. The essential purpose in the initial evaluation is to differentiate patients with serious underlying pathology from those with mild problems.

Patients with a disc problem will usually experience an exacerbation of their symptoms with spinal flexion, which increases intradisc pressure. By contrast, in the setting of spinal stenosis, standing or walking exacerbates back and leg pain, whereas some forward flexion may alleviate these symptoms. In moderate-to-severe spinal stenosis, extension of the spine may cause radicular pain.

Patients with compression fractures typically present with severe back pain, often intense with minimal lateral rotation or with flexion and relieved by rest. A history of bladder, bowel, or sexual dysfunction may indicate compression of the cauda equina or conus medullaris. Unlike sciatica, often with its unilateral nerve root involvement, patients with cauda equina syndrome usually have bilateral involvement. Although motor function may be normal and pain uncommon in those with conus lesions, patients often demonstrate abnormalities of sensation in a saddle distribution, feeling touch or dysesthesia, but neither pain nor temperature. Causes of these symptoms may be a fracture of L1 or L2, tumor, large central disc herniations, or

intramedullary cysts affecting the conus. These disorders are considered surgical emergencies and require aggressive evaluation and prompt surgical consultation.

The physical examination should include Lasègue sign (the straight leg raising test), Braggard (Bragard) test (dorsiflexion of the ankle with elevation of the leg), and the crossover test. These clinical tests are considered positive when sciatica is reproduced with elevation of the leg between 30 and 60 degrees. If testing the uninvolved leg produces contralateral symptoms, disc disease should be considered. A positive crossover sign occurs when straight leg raising of the patient's contralateral leg elicits pain on the affected side. It is usually a strong indication of nerve root irritation or compression. Extension of the knee while in a seated position, also known as *distracted straight leg raise*, can test sciatic nerve tension too. The patient with significant nerve root irritation tends to complain of increased pain or lean backward to reduce tension on the nerve. The differential diagnosis of spinal shock, upper motor neuron lesions, and lower neuron lesions is shown in **Table 50.1**. The nerve root signs are shown in **Table 50.2**.

TABLE 50.1 Differentiating Spinal Shock, Upper Motor Neuron Lesions, and Lower Motor Neuron Lesions

Disease State	Deep Tendon Reflex	Pathologic Reflex/Plantar Response	Superficial Reflex (Normal)
Spinal shock	Absent	Absent	Absent
Upper motor neuron disease	Increased; rarely may be decreased in the acute setting	Positive/extensor Babinski sign + Oppenheim sign +	Decreased or absent For example, cremasteric reflex −
Lower motor neuron disease	Decreased	Negative/flexor	Present (but L1–L2 lesion will have cremasteric reflex −)

+, positive; −, negative.

TABLE 50.2 Nerve Root Signs

Root Level	Reflex Decrease	Sensory Defect	Motor Weakness
L4	Knee jerk	Anterior thigh, knee, and shin	"Single squat and rise test"; quadriceps (mostly L4)
L5	No easily elicited reflex	Lateral leg and middle dorsal foot	"Heel walk test"; dorsiflexion of foot and toes (L5 and some L4); especially big toe, extensor hallucis longus (EHL)
S1	Ankle jerk	Posterior calf and sole	"Toe walk test"; gastrocnemius/soleus; "toe flexors"

Benzon HT, Rathmell JP, Wu CL, et al, eds. *Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby Elsevier; 2014:151–161.

Waldman SD, ed. *Pain Management*. Philadelphia, PA: Saunders Elsevier; 2007:762–764.

A.10. What are the appropriate diagnostic studies for low back pain?

In the absence of signs of serious medical disease, there is no need for special studies because 90% of patients will recover spontaneously within 4 weeks of the onset of pain. Waiting 4 weeks before considering special tests allows these patients to recover spontaneously and avoid unneeded procedures. When pain persists beyond 4 to 6 weeks (or shorter if it is severe), plain radiographs (x-ray) of the spine should be considered. Pertinent findings include the height of the intervertebral spaces and vertebral bodies, and bony changes in the end plates. With oblique views, the facet joint space and any spondylolysis can be revealed. The lateral view can help estimate the severity of spondylolisthesis. If there is symptom of vague flank pain with or without hematuria, which renal colic pain often begins as, a kidney, ureter, and bladder (KUB x-ray, similar to abdomen x-ray) radiography can help to identify stones. A CT scan can show a herniated disc or fragment in the spinal canal. It can help to identify early epidural hematoma. With contrast, it can help

further differentiate tumors, abscesses, and granuloma in the central nervous system. MRI provides excellent anatomic definition of the disc and its hydration status; it can also show the anatomy of the surrounding soft tissues. MRI with intravenous gadolinium is indicated for distinguishing between a recurrent disc herniation and recent postoperative scar tissue. It is particularly useful when distinguishing intrinsic from extramedullary or epidural spinal cord lesions. When MRI is contraindicated, a myelogram may reveal a filling defect at the level of posterior bulging discs. The myelogram in conjunction with a CT scan enables axial imaging of the spinal cord and subarachnoid space. A bone scan is helpful in the diagnosis of bone or bony fractures that may not be visible by radiography or CT scan, or whenever metastatic disease is suspected.

Ballantyne JC, Fishman SM, Rathmell JP, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2018:1265–1267.

Benzon HT, Rathmell JP, Wu CL, et al, eds. *Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby Elsevier; 2014:185–242.

Mekhail NA, Moufawad S. Discography and discogenic pain. *Tech Regional Anesth Pain Manage*. 2000;4:126–131.

A.11. What is the differential diagnosis of low back pain?

In general, there are numerous diagnostic labels used to describe low back pain, for example, lumbosacral sprain, lumbar discogenic syndrome, mechanical low back pain, spinal stenosis, spondylosis, spondylolisthesis, osteoarthritis/facet joint syndrome, myofascial pain syndrome, unstable low back, discitis, and failed back surgery syndrome (FBSS). Each of these labels suggests its own underlying pathology. It is also helpful to review causes of low back pain that are described at section A4.

Acute lumbosacral sprain, by far the most common cause of new-onset low back pain, is often only associated with the

presence of postural back pain. It frequently results from reflex muscle spasms secondary to local irritation of structures in the back. When muscle spasms occur, the normal anatomy may be disturbed and undue force applied to surrounding tissues and structures.

Clinically, the following five tests are not uncommonly requested by spinal surgeons for further differential diagnosis. Discography/discogram/discomanometry (discometry) is a specialized diagnostic test specifically indicated to help diagnose discogenic pain. The presence of pain fibers in the outer third of the annulus fibrosus may explain back pain in some individuals with an annulus tear or IDD. The test involves an intradiscal puncture and instillation of contrast into the disc nucleus. It provides direct confirmation of nuclear morphology and the integrity of the vertebral end plate and annulus. Selective nerve root block with local anesthetic is performed to determine if a specific spinal nerve is the source of pain. Either facet joint block (intra-articular injection) or medial branches block may help differentiate between axial discogenic pain and facet joint pain syndrome. Sacroiliac joint injection can help to rule out pain resulting from sacroiliac joint dysfunction. Electromyography (EMG) and nerve conduction studies (NCS) can help diagnose neuromuscular abnormalities/disorders. In every case, a careful history, physical examination, and the appropriate diagnostic studies will help elucidate the "pain generator."

Ballantyne JC, Fishman SM, Rathmell JP, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2018:1260–1262, 1265–1267.

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Benzon HT, Rathmell JP, Wu CL, et al, eds. *Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby Elsevier; 2014:312–327.

Schwarzer AC, Aprill CN, Bogduk N. The sacroiliac joint in chronic low back pain. *Spine (Phila Pa 1976)*. 1995;20:31–37.

A.12. What are the causes of persistent back pain after multiple spine surgeries?

Persistent back or leg pain after one or more spinal surgeries is called FBSS or *postlaminectomy syndrome*. The aforementioned implies persistent radicular symptoms or neuropathic complaints after previous surgery (most commonly in the lumbar spine). Usually, the cause is a combination of both nociceptive and neuropathic pain. Over time, a strong psychological component can develop with progressive disability as treatments fail. Approximately 37,500 patients are diagnosed with this syndrome annually in the United States.

When pain persists or recurs in a patient after spinal surgery, the most common causes are those of foraminal stenosis, discogenic disorder and recurrent disc herniation. Epidural fibrosis and scarring are less common. Patients with this condition often report constant dull, aching, poorly localized low back pain with intermittent sharp episodes. They may also report pain or abnormal sensations with neuropathic characteristics such as burning, shooting, throbbing, stabbing, or pulling. The exact source of these complaints is unclear, although the scar tissue or arachnoiditis is frequently implicated. When reoperation is performed for the purpose of neurolysis only, a transient improvement of sciatica may be seen, but it usually recurs within the first postoperative year. Success rates for reoperating on patients with FBSS have been highly variable, ranging from 25% to 80%. These patients are perhaps the most challenging of all. They deserve a comprehensive multidisciplinary evaluation, including orthopedic and neurosurgical consultations. Furthermore, surgical intervention should be avoided in the absence of a clear indication. Repeated imaging studies add to the health care expenses and

interventions that may not have a great therapeutic yield.

Ballantyne JC, Fishman SM, Rathmell JP, eds. *Bonica's Management of Pain*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2018:1290–1292.

Benzon HT, Rathmell JP, Wu CL, et al, eds. *Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby Elsevier; 2014:312–327.

Petraglia WF III, Farber SH, Thomas SM, et al. Increasing rates of imaging in failed back surgery syndrome (FBSS) patients: a 10 year perspective. *Neurosurgery*. 2015;62(suppl 1):200–201.

B. Management of Low Back Pain and Sciatica

B.1. What are the noninterventional treatments available?

The cornerstone of treatment for low back pain and mild sciatica caused by a herniated lumbar disc is conservative care, which includes bed rest, medications, and physical therapy. Patients whose symptoms fail to respond to conservative care may require more invasive treatment.

Evidence of both clinical and epidemiologic data suggests that the longer the back pain and work loss persist, the less likely there will be improvement of the pain. The chance for return to work is even lower. Improved early management and greater access to primary care services should greatly reduce the number of patients with a simple backache requiring a referral to a hospital. An early return to activity seems to be associated with a better outcome than does prolonged bed rest (greater than 4 days).

Treatment varies depending on the cause of pain. In December 1994, the Agency for Health Care Policy and Research announced the following guidelines for the care of acute low back problems:

- A brief period of rest
- Over-the-counter pain relievers

- Trunk-strengthening exercises
- A single spinal manipulation

In order to avoid reinjury, an incremental, gradually increasing regimen of aerobic exercise (up to 30 minutes daily) can usually be started within the first 2 weeks of symptom onset. Such activities have been found to stress the back no more than sitting on the side of the bed for an equal period of time. The combination of aerobics for general fitness with some specific training to improve the strength and endurance of the back muscles is often beneficial.

The role of medications in the treatment of low back pain is to control pain, facilitate rehabilitation, restore normal sleep patterns, and improve mood and motivation. Nonsteroidal anti-inflammatory drugs are an essential part of the treatment of patients with inflammatory back pain, such as that associated with spondylitis. Other medications that have been shown to be useful include tricyclic antidepressants and anticonvulsants. Muscle relaxants are often used to decrease muscle spasms and assist in promoting rest for patients with severe pain. These are usually indicated for short-term treatment and acute relief. Short-term therapy with opioid analgesics may be needed to promote rest as well as maintain activity in the acute phase of low back pain. Long-term use of these medications is generally discouraged. When recovery does not occur within 4 to 6 weeks and no additional pathology is detected, physical therapy is indicated. Patients should be encouraged to increase activities. Patients limited by back symptoms can minimize the stress of lifting by keeping any lifted object close to the body at the level of the navel. However, activities such as twisting, bending, and reaching while lifting, also increase stress on lumbar disc or back. Those are well-demonstrated by Dr. Alf Nachemson's studies, which are summarized by his classical drawings of different body positions over pressure (L3–L4 intradiscal

pressure) bar graphs. His pioneering disc pressure measurements are still quoted extensively in many textbooks.

Prolonged sitting may aggravate back symptoms in discogenic pain patients because of the progressive increase in pressure at specific points in the abnormal disc. Body weight optimization and a program that teaches good posture and body mechanics are very important. Neuromuscular reconditioning must be included to ensure a function-specific, task-oriented program. The exercise training is designed as a step-by-step program to improve a patient's function and optimize neutral spine posture. These programs include stabilization training to attain adequate dynamic control of their lumbar spine forces and eliminate repetitive injury. Soft tissue flexibility, joint mobility, abdominal muscle strengthening, and aerobic exercise are also important factors. Spinal manipulation is controversial and is neither recommended in patients with radiculopathy pain nor is it wise in those for whom a diagnosis has not been established.

Benzon HT, Rathmell JP, Wu CL, et al, eds. *Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby Elsevier; 2014:312–327.

Cherkin DC, Deyo RA, Battie M, et al. A comparison of physical therapy, chiropractic manipulation, and provision of an educational booklet for the treatment of patients with low back pain. *N Engl J Med*. 1998;339:1021–1029.

Nachemson A. The load on lumbar disks in different positions of the body. *Clin Orthop Relat Res*. 1966;45:107–122.

B.2. What traditional interventional treatments are available and how should they be used?

Common traditional interventional treatment includes the following:

- Trigger point injection
- Traditional epidural steroid injection (interlaminar or caudal approach)
- Transforaminal epidural steroid injection (transforaminal approach)

- Facet joint intra-articular block or medial branch block
- Sacroiliac joint injection

Interventional techniques such as trigger point injections and local infiltration are used to provide pain relief of short duration, especially in acute phase, so that other activities and physical therapy that might otherwise be severely limited by pain may be pursued.

Corticosteroids play an important role against inflammation and reduction of edema. Steroids injected into the epidural space have been used for treating low back pain and radiculopathy for many decades. Despite widespread use, the results of epidural steroid injection are still in question because studies evaluating the response to this therapy have been small, poorly controlled, and lacking good long-term follow-up. Published studies of the effectiveness of epidural steroid injections have varied from 18% to 90%. Epidural steroid injections can be performed through the interlaminar route, the caudal canal, or the intervertebral foramina. The spread of solution in both caudal and interlaminar injection is less controllable because of inconsistent lateral flow into the ventral compartment. This renders the medication less effective as it is diverted away from the compartment, depending on the tightness of the lateral recess (e.g., lateral recess stenosis) and the size of the dural sac. In normal volunteers, the transforaminal method showed good ventral flow, whereas the interlaminar approach showed predominantly dorsal flow, which was far from the usual site of impingement.

Patients who suffer from lumbar facet arthropathy may have symptoms, including band-like low back pain and associated hip, groin, or thigh pain. Pain rarely radiates below the knee in this condition. Blockade of the medial branch of the dorsal ramus of the spinal nerve or intra-articular injections of the lumbar facets are effective in short-term alleviation of this type

of pain. Radiofrequency ablation (RFA) procedures use radiofrequency energy to disrupt nerve function. When it is applied to medial branch nerves, the transmission of pain signal from problematic facet joints can be limited or reduced for several months (greater than 6 months).

Among back pain patients, 15% to 30% were found to have pain arising from the sacroiliac joint. The joint is innervated by L5–S2 ventrally and L5–S4 dorsally. Liliang et al. demonstrated that 40% and Depalma et al. found that 43% of postlumbar fusion patients had pain that was derived from sacroiliac joint. In addition, Ha et al. reported that 75% of postlumbar fusion patients showed sacroiliac joint degenerative changes on CT scan at 5 years follow-up. The sacroiliac joint block serves as a diagnostic procedure to determine if the sacroiliac joint is the source of the patient's pain.

Benzon HT, Rathmell JP, Wu CL, et al, eds. *Practical Management of Pain*. 5th ed. St. Louis, MO: Mosby Elsevier; 2014:312–327.

DePalma MJ, Ketchum JM, Saullo TR. Etiology of chronic low back pain in patients having undergone lumbar fusion. *Pain Med.* 2011;12(5):732–739.

Ha KY, Lee JS, Kim KW. Degeneration of sacroiliac joint after instrumented lumbar or lumbosacral fusion: a prospective cohort study over five-year follow-up. *Spine (Phila Pa 1976)*. 2008;33(11):1192–1198.

Liliang PC, Lu K, Liang CL, et al. Sacroiliac joint pain after lumbar and lumbosacral fusion: findings using dual sacroiliac joint blocks. *Pain Med.* 2011;12(4):565–570.

Manchikanti L, Hirsch JA, Falco F JE, et al. Management of lumbar zygapophysial (facet) joint pain. *World J Orthop*. 2016;7(5):315–337.

Manchikanti L, Singh V, Kloth D, et al. Interventional techniques in the management of chronic pain: part 2.0. *Pain Physician*. 2001;4:24–96.

Thawrani DP, Agabegi SS, Asghar F. Diagnosing sacroiliac joint pain. *J Am Acad Orthop Surg*. 2019;27:85–93.

Zhai J, Zhang L, Li M, et al. Epidural injection with or without steroid in managing chronic low back and lower extremity pain: a meta-analysis of ten randomized controlled trials. *Int J Clin Exp Med*. 2015;8(6):8304–8316.

B.3. What are some of the recent safety improvements recommended for lumbar epidural steroid injection?

The working group (expert working group with facilitation from the U.S. Food and Drug Administration [FDA] Safe Use Initiative [SUI]) and the advising national organizations (representatives from leading specialty societies) unanimously agreed that epidural injections of steroid were rarely associated with serious complications due to injuries of the central nervous system. They agreed that transforaminal injections are associated with a risk of catastrophic neurovascular complications and that particulate steroids appear to be inordinately represented in case reports of these complications. Clinical considerations improving technical aspects of the procedures included use of appropriate image-guided views (**Figs. 50.1** and **50.2**), injection of contrast under the real-time fluoroscopy, review of prior imaging studies, use of face mask and sterile gloves, use of extension tubing, and avoidance of heavy sedation. Although digital subtraction imaging (DSI) may help to detect vascular uptake (**Fig. 50.3**), the sensitivity was demonstrated to be 60% in one study as compared to aspiration sensitivity of 20%.

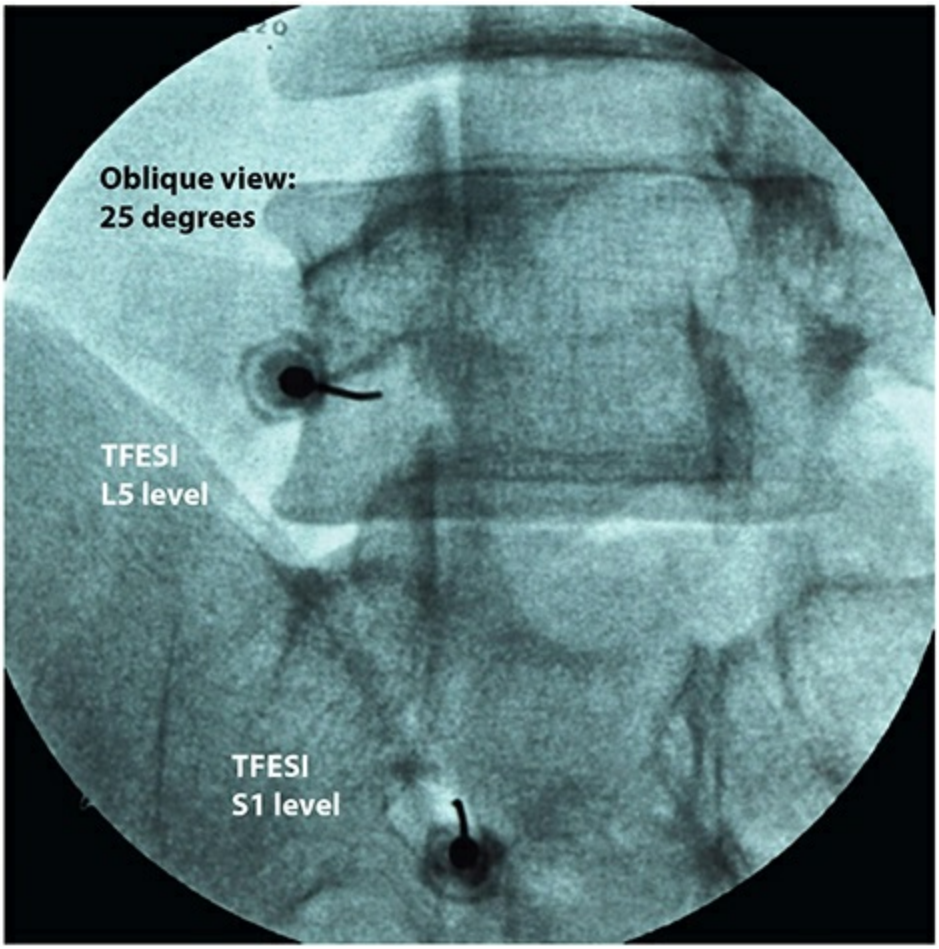

FIGURE 50.1. Transforaminal epidural steroid injection at L5 and S1 levels, oblique view at 25 degrees.

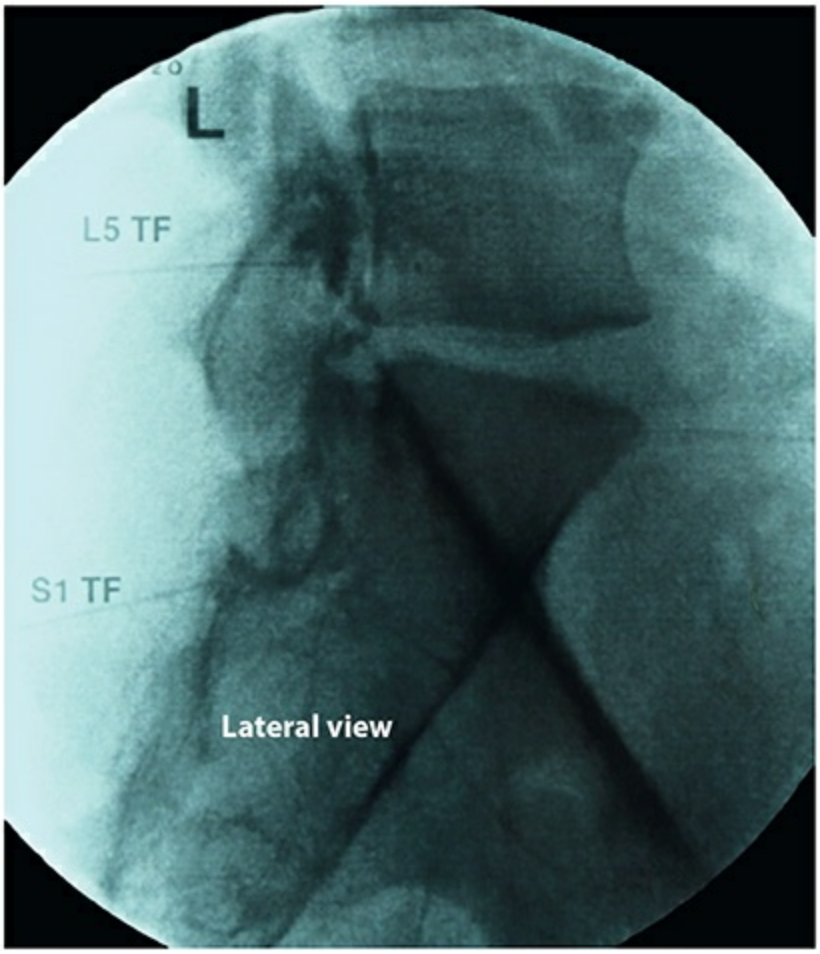

FIGURE 50.2. Transforaminal epidural steroid injection at L5 and S1 levels, lateral view.

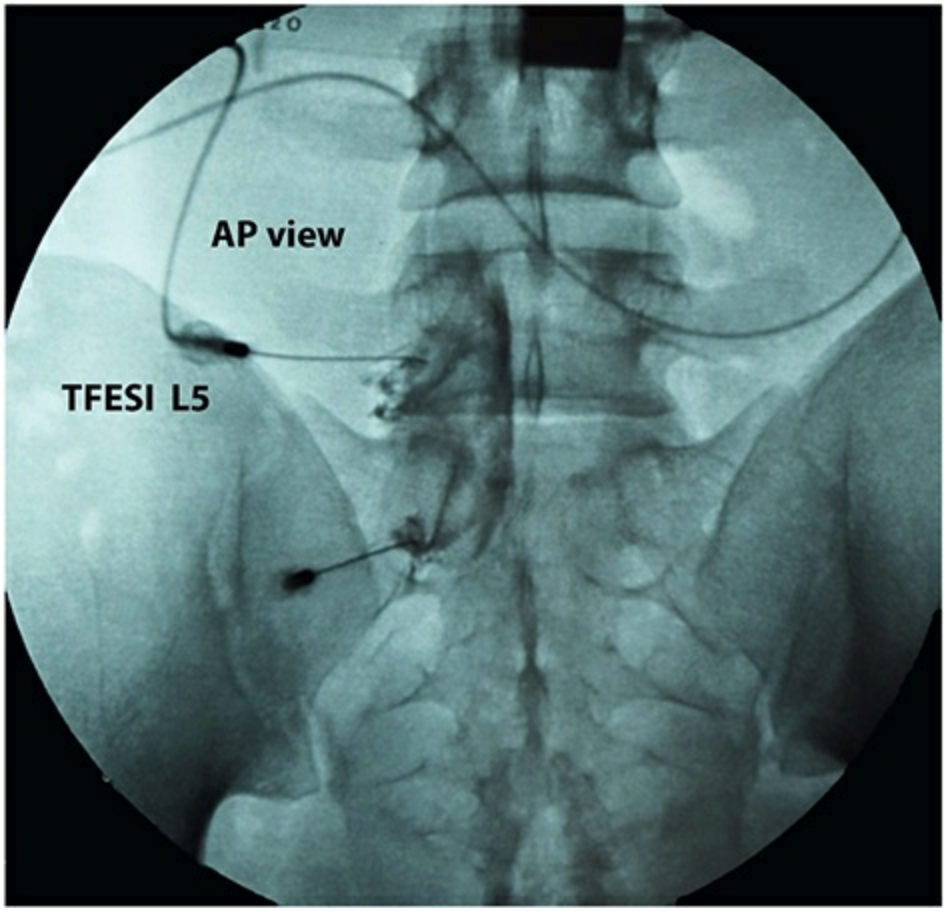

FIGURE 50.3. Transforaminal epidural steroid injection at L5 and S1 levels, anterior-posterior view (after digital subtraction image checking).

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Zhai J, Zhang L, Li M, et al. Epidural injection with or without steroid in managing chronic low back and lower extremity pain: a meta-analysis of ten randomized controlled trials. *Int J Clin Exp Med*. 2015;8(6):8304–8316.

B.4. What are some of other approaches in minimally invasive interventions?

There are different interventional techniques for the management of low back pain and sciatica that can be applied to

appropriately selected patients. These include the following:

- Epidural neuroplasty or epidural adhesiolysis
- Epiduroscopy (spinal canal endoscopy)
- Percutaneous radiofrequency denervation of medial branches for facet joint pain
- Automated percutaneous discectomy (APD) or percutaneous automated discectomy (PAD) or percutaneous automated nucleotomy (PAN)
- Percutaneous laser disc decompression (PLDD)
- Intradiscal electrothermal therapy (IDET)
- Percutaneous disc decompression using nucleoplasty
- Percutaneous lumbar discectomy using Dekompressor probe
- Minimally invasive lumbar decompression (MILD) procedure
- SCS/DRG stimulation
- Intrathecal drug delivery
- Percutaneous vertebroplasty (PV) and percutaneous kyphoplasty (PK)

Epidural neuroplasty or epidural adhesiolysis is done with hypertonic saline and hyaluronidase to lyse epidural adhesions. This technique involves placing a rigid catheter into the epidural space, with manipulation of the catheter to physically breakdown the adhesions and applying local anesthetic, steroid, hypertonic saline (10%), and hyaluronidase over several days.

Epiduroscopy (or spinal canal endoscopy) allows direct visualization of the epidural space using a flexible fiberoptic catheter. Adhesions are lysed with the catheter under direct vision; thereafter, better delivery of medications to the target area can be achieved.

Percutaneous radiofrequency denervation of the medial branches of the dorsal (or posterior) rami of segmental spinal nerves is achieved by applying heat to denature the nerves that innervate the painful facet joints. The success rate has been reported variably in the range of 17% to 90% for facet joint pain

of a few weeks' to several months' duration. With this technique, the pain may return several weeks to months after the axons regenerate; repeating the procedure is then indicated.

Percutaneous manual nucleotomy was first presented in 1975. It was proposed as a method of preventing perineural and epidural scar formation by avoidance of entry into the spinal canal. Thereafter, APD or PAD or PAN was designed as a procedure using a "nucleotome" (reciprocating suction-cutting probe) for intradiscal decompression in 1985. The cannula requires a sizable annular incision to reach the nucleus. Its success rate is approximately 70% to 80%.

PLDD is a technique, introduced in 1987, that uses neodymium:yttrium-aluminum-garnet (Nd:YAGq) laser to "vaporize" a small portion of the nucleus pulposus in an attempt to decompress the involved disc. It has been demonstrated that the inner pressure of the nucleus pulposus drops significantly after the disc ablation. Its success rate is approximately 78%. After 4 to 6 months from this treatment, it was demonstrated that one-third of repeat MRI scans showed a modest to moderate decrease in the size of disc herniation. There is concern, nevertheless, that the technique is potentially hazardous to bone and nerve tissue because of the significant rise in temperature resulting from thermal energy transfer.

IDET or annuloplasty, first reported by Saal and Saal in 2000, has been shown to be effective in managing discogenic pain. It is a minimally invasive procedure in which a catheter is inserted into the nucleus pulposus through which an electrode is passed so that a controlled level of heat at a temperature of 90°C (194°F) can be applied to a broad section of the affected disc's inner wall. This thermal therapy is postulated to alleviate discogenic pain by shrinking collagen at a target temperature of 65°C (149°F) to 75°C (167°F). Another proposed mechanism is denervation of exposed nociceptor endings in the outer disc

annulus starting at 45°C (113°F).

Percutaneous disc decompression with nucleoplasty is used for those patients whose symptoms are attributed to radiographically contained discs, that is, a disc with an intact outer annulus. Since 2000, by combining tissue removal with thermal treatment, disc decompression has been achieved. It applies a focused "coblation" technique, ablating while coagulating (by using bipolar radiofrequency) to reach the level of 40°C (104°F) to 70°C (158°F). At this temperature, molecular dissociation is achieved and thought to minimize the potential for surrounding tissue damage.

Percutaneous disc decompression using a Dekompressor probe is another option for those patients whose symptoms are attributed to radiographically contained discs. It provides objective evidence that disc was removed, the cellular character of that material, and provides a qualitative and quantitative measure.

MILD is a procedure that involves limited percutaneous laminotomy and thinning of the ligamentum flavum in order to increase the critical diameter of the stenosed spinal canal.

SCS is a technique in which electrodes are passed into the posterior epidural space. Electrical stimulation of the spinal cord has been shown to be effective in the management of certain neuropathic pain syndromes and postlaminectomy syndromes. The exact mechanism by which pain relief is achieved remains controversial. Frey et al. performed a systematic review of the literatures and found level II evidence for the use of SCS for FBSS on a long-term basis. Newer advances in spinal stimulation include high-frequency (10 kHz), burst, and DRG stimulation. High-frequency stimulation preferentially blocks larger diameter fibers and concomitantly recruits medium and small fibers. Burst stimulation involves delivering closely spaced, high-frequency stimuli to the spinal cord as opposed to

the usual low-frequency tonic stimulation, which is constant. Therefore, it may provide a benefit by breaking through the physiologic tolerance issue derived from tonic stimulation. The DRG contains the primary sensory neurons that transmit pain signals from the peripheral nerves to the brain. When stimulated, it can modulate or filter the transmission of peripheral painful signals to the brain. Recent study in 2018 by Kallewaard et al. demonstrated DRG stimulation induced pain relief in subjects with failed back pain syndrome. These reductions in pain were also associated with improvements in quality of life and disability.

Intrathecal drug delivery directly into the cerebrospinal fluid through an implanted catheter and pump can be used to treat intractable pain from a variety of causes, both nociceptive and neuropathic. A variety of medications and combinations thereof can be used depending on the type and location of symptoms. Among the experts, this is known as *intrathecal polyanalgesia*. This modality is indicated when increasing doses of opioid are required to achieve pain relief but at the expense of disabling side effects. The dose is effectively reduced to approximately 1/300, for example, when converting an oral dose of morphine to its equipotent equivalent delivered intrathecally.

PV and PK are both advanced techniques used in the treatment of painful compression fracture. In the United States, compression fractures occur in approximately 700,000 patients per year, and 80% of these fractures occur in women. The conventional management includes bed rest, analgesics, and bracing. PV was a technique developed in 1984 for the treatment of painful vertebral hemangiomas. It has since become popular for the treatment of osteoporotic vertebral body compression fracture. It involves the application of liquid cement (polymethylmethacrylate), tobramycin, and barium powder (as nonionic contrast) through a special metal needle inserted under

fluoroscopy. The cement provides vertebral solidification and buttresses the compressed bone within the vertebral body. The procedure usually takes 45 to 60 minutes, and the patient may be discharged several hours later. Some risks are involved with this procedure, such as leakage of cement into surrounding areas (i.e., disc, spinal cord, and nerve roots), infection, bleeding, worsened pain, embolism, and paralysis. Overall, more than 80% of treated patients had moderate to marked pain relief.

PK is a technique similar to PV, which involves the additional application of an inflatable balloon inside the collapsed vertebral body. The compressed fracture is thus expanded, the lost height of the vertebral body is restored, and an inner space or cavity is created for the cement. This procedure was approved by the FDA in 1998. A significant reconstitution of the curvature of the spine can be seen following kyphoplasty. According to Lieberman et al., in 70% of the collapsed vertebral bodies, the kyphoplasty restored 47% of lost height. This newer technique offers the additional advantage of realigning the spinal column and restoring height to the fractured vertebrae.

PV and PK are associated with pain relief in 67% to 100% of cases. Most patients experience significant pain relief within the first 1 to 2 days. There is also a report of 95% improvement in pain and significant improvement in function following treatment by either one of the two techniques.

Anderson SR, Racz GB, Heavner J. Evolution of epidural lysis of adhesions. *Pain Physician*. 2000;3:262–270.

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Falco FJ, Manchikanti L, Datta S, et al. An update of the effectiveness of

therapeutic lumbar facet joint interventions. *Pain Physician*. 2012;15:E909–E953.

Frey ME, Manchikanti L, Benyamin RM, et al. Spinal cord stimulation for patients with failed back surgery syndrome: a systematic review. *Pain Physician*. 2009;12(2):379–397.

Heavner JE, Racz GB, Raj P. Percutaneous epidural neuroplasty: prospective evaluation of 0.9% NaCl versus 10% NaCl with or without hyaluronidase. *Reg Anesth Pain Med*. 1999;24:202–207.

Kallewaard JW, Nijhuis H, Huygen F, et al. Prospective cohort analysis of DRG stimulation for failed back surgery syndrome pain following lumbar discectomy. *Pain Pract*. 2019;19(2):204–210.

Lieberman IH, Dudeney S, Reinhardt MK, et al. Initial outcome and efficacy of "kyphoplasty" in the treatment of painful osteoporotic vertebral compression fractures. *Spine (Phila Pa 1976)*. 2001;26:1631–1638.

Maroon JC. Current concepts in minimally invasive discectomy. *Neurosurgery*. 2002;51(5 suppl):S137–S145.

Peh WC, Gilula LA, Peck DD. Percutaneous vertebroplasty for severe osteoporotic vertebral body compression fractures. *Radiology*. 2002;223:121–126.

Saal JS, Saal JA. Management of chronic discogenic low back pain with a thermal intradiscal catheter. *Spine (Phila Pa 1976)*. 2000;25:382–388.

Schmidt GL. The use of spinal cord stimulation/neuromodulation in the management of chronic pain. *J Am Acad Orthop Surg*. 2019;27(9):e401–e407.

Sharps LS, Issac Z. Percutaneous disc decompression using nucleoplasty. *Pain Physician*. 2002;5:121–126.

van Kleef M, Barendse GA, Kessels A, et al. Randomized trial of radiofrequency lumbar facet denervation for chronic low back pain. *Spine (Phila Pa 1976)*. 1999;24:1937–1942.

Vannemreddy P, Slavin KV. Spinal cord stimulation: current applications for treatment of chronic pain. *Anesth Essays Res*. 2011;5:20–27.

Watts NB, Harris ST, Genant HK. Treatment of painful osteoporotic vertebral fractures with percutaneous vertebroplasty or kyphoplasty. *Osteoporos Int*. 2001;12:429–437.

B.5. What are the concerns about magnetic resonance imaging (MRI) safety in patients with a spinal cord stimulator (SCS)?

MRI safety recommendations vary between the models of SCS.

The most recent updates reveal that multiple models from different companies are more compatible with MRI full body scan (e.g., Prime Advanced SureScan, Restore Advanced SureScan, Restore Sensor SureScan and Intellis platform from Medtronic, Proclaim Elite SCS system from Abbott, Precision Montage from Boston Scientific, and Senza I from Nevro). Other models may only be compatible with a head only or "head and extremity" only MRI scan. In addition, each company's SCS has its certain parameters and limitations including MRI system type (1.5 T), radiofrequency Coil type, radiofrequency power specific absorption rate (SAR), gradient slew rate, spatial gradient, patient position, total active scan time limits (30 minutes on per 30 minutes off vs. 30 minutes on per 60 minutes off), and others.

Before an MRI is performed, it is imperative to ascertain that the system is intact, without any lead breaks or low impedances because these can result in heating of the SCS and injury to the patient. With an SCS, there is a risk of thermal injury to the patient at any point along the course of the device because of induction of current by the magnetic fields during the MRI.

During these scans, there is potential for heating or discomfort, and the patient must be advised to communicate with the technicians should this occur. The devices are also at risk for permanent malfunction after MRI, which would require surgical replacement. Magnetic pull could result in torque or rotation movement of the device with potential destruction of surrounding tissues. After the scan, the device must be interrogated for device damage/failure and turned back on. Ultimately, these devices have specific conditions under which MRI may be performed, and physicians must consult the manual for the specific implanted device before ordering MRI scans.

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perioperative management of spinal cord stimulators: literature review and initial recommendations. *Pain Physician*. 2017;20(4):319–329.

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B.6. When should surgery be considered?

Several surgeries are indicated for low back pain and sciatica. These include laminotomy, laminectomy, microdiscectomy, foraminotomy, intervertebral body insertion, spinal fusion, and others.

According to Weber's study, the long-term results appear to be no different in the surgical versus nonsurgical group in the case of low back pain. If the following situations occur, surgery should be considered:

- Failure to respond to conservative management for at least 3 months
- A profound or progressing neurologic defect such as a complete foot drop
- Recurring episodes of intractable sciatica involving the same segment—mainly to avoid the cumulative disability of repeated events

Muscle weakness is a dubious indication for surgery if the paresis is of unknown duration. If the pressure on the nerve root can be relieved immediately after the appearance of the paresis, surgery has been regarded as the therapy of choice. Unfortunately, most patients are unaware of the subtle loss of motor function. The greatest concern and complaints are largely centered on pain, paresthesia, and immobility.

Within the first 3 months of acute low back symptoms, surgery is considered only when serious spinal pathology or nerve root dysfunction resulting from an obviously herniated

lumbar disc is detected. Nerve root decompression can be considered for a patient if all of the following criteria exist:

- Sciatica is both severe and disabling.
- Symptoms of sciatica persist without improvement for longer than 4 weeks or with extreme progression.
- There is strong physiologic evidence of dysfunction of a specific nerve root with intervertebral disc herniation confirmed ipsilaterally at the corresponding level by imaging.

Patients with acute low back pain alone, without findings of serious conditions or significant nerve root compression, rarely benefit from a surgical consultation. With or without surgery, more than 80% of patients with obvious surgical indications eventually recover.

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Kim SS, Michelsen CB. Revision surgery for failed back surgery syndrome. *Spine (Phila Pa 1976)*. 1992;17:957–960.

McCulloch JA. Focus issue on lumbar disc herniation: macro- and microdiscectomy. *Spine (Phila Pa 1976)*. 1996;21:45S–56S.

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Zdeblick TA. A prospective, randomized study of lumbar fusion. Preliminary results. *Spine (Phila Pa 1976)*. 1993;18:983–991.

B.7. What surgical options are available for the treatment of disc disease?

- Artificial disc replacement (ADR) or total disc replacement (TDR)
- Interspinous process decompression system (X-STOP in 2005)
- Decompression (laminotomy, laminectomy, and/or discectomy) or decompression with fusion

In the mid-1980s, German orthopedic surgeons developed a metal and plastic prosthesis that has been in clinical use since then. The prosthesis is known as the *SB CHARITÉ*. The prosthesis design is currently in its third generation. Other prosthetic discs are available (e.g., ProDisc, Maverick, FlexiCore, and Kineflex). In October 2004, the CHARITÉ artificial disc became the first to be approved for disc replacement in the United States. It is composed of two metallic end plates and a polyethylene core that moves between them (**Figs. 50.4** to **50.7**). Traditional spinal fusion does change the mechanics of the segment that is fused. Adjacent segment degeneration can develop at approximately 3% per year (or 16.5% at 5 years, 36.1% at 10 years). One major theoretical advantage of ADR over spine fusion is that it results in no change in the biomechanics of the lower spine, thereby allowing the spine to maintain its normal range of motion and reducing or eliminating the risk for degeneration in the adjacent segments of the spine. The potential disadvantage of ADR is a limited durability. Because disc injury is a common cause of back pain in younger adults, an artificial disc in such patients needs to last for decades. The demands on that disc will be very great, and it may not outlast the lifetime of the patient, who may need revision surgery later. Revision ADR can be very dangerous because of scar tissue from the original surgery in nearby vascular structures. In addition, there is a 1% to 3% incidence of the complication of retrograde ejaculation in men.

FIGURE 50.4. **CHARITÉ disc.**

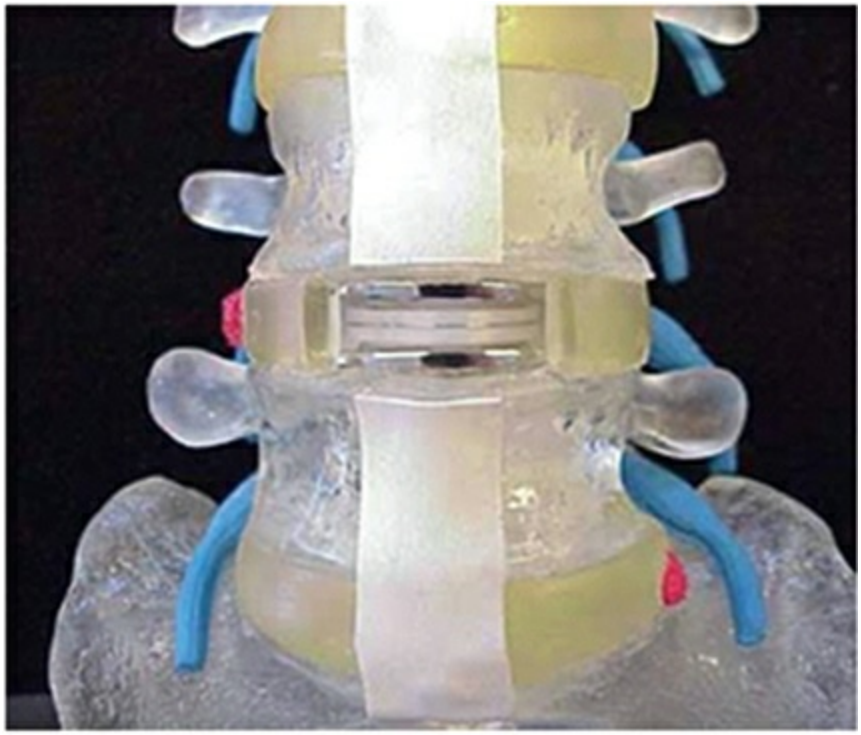


FIGURE 50.5. **CHARITÉ disc replacement at L4–L5.**

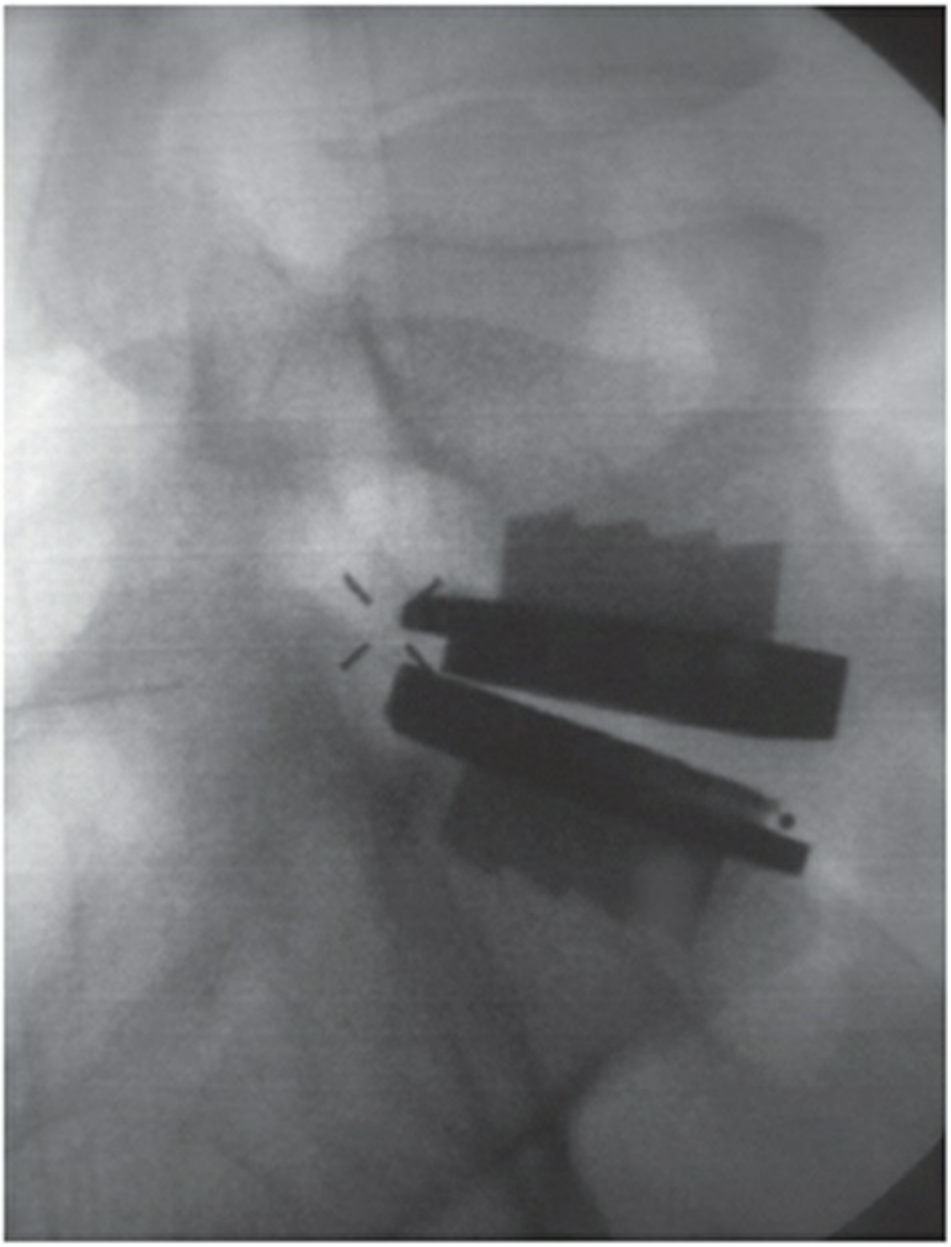


FIGURE 50.6. **L5–S1 ADR, lateral fluoroscopic view.**

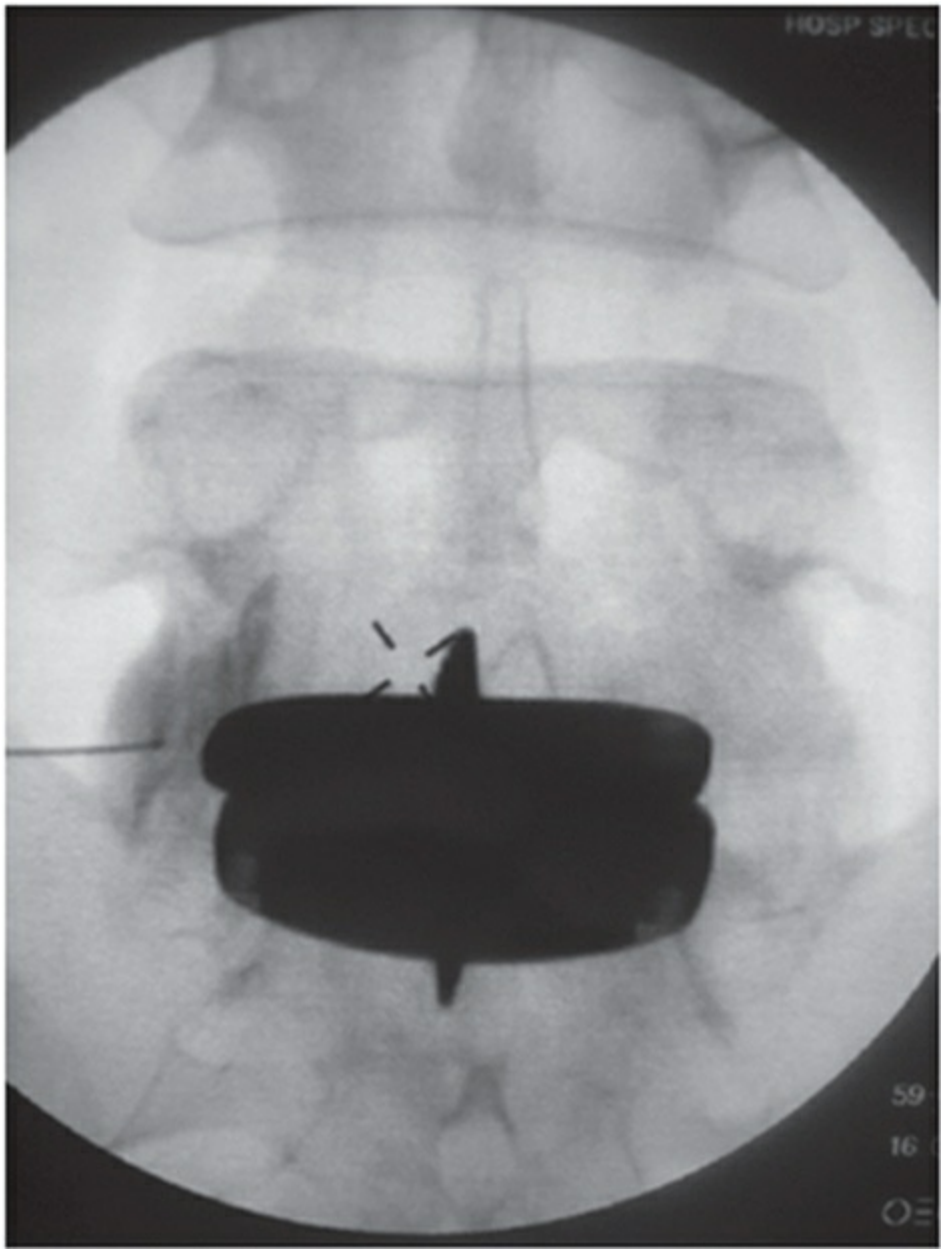


FIGURE 50.7. Anteroposterior fluoroscopic view of ARD.

Based on the systemic review of overlapping meta-analyses, the best available evidence indicated that TDR or ADR compared with fusion for lumbar degenerative disc disease (LDDD) had statistically, but not clinically, significant superiority regarding disability, pain relief, and quality of life in a selected group of patients in the short term. Therefore, considering that disadvantages may appear after years, spine

surgeons should be cautious about performing TDR on a large scale. Another similar meta-analysis result in 2019 suggests that TDR could be alternative treatment for LDDD because it yielded better clinical success and patient satisfaction, shorter hospital stays and operative time, less pain, and lower complication rates than did lumbar fusion.

In a recent retrospective study of ADR by Pettine et al., the overall clinical failure (one level operations performed at L4–L5 or L5–S1) occurred in 26% of patients at 2-year follow-up including Maverick (28%), Charité (39%) and Kinelfex (14%). It implied that overall clinical success may be improved most by patient selection and implant type.

The interspinous process decompression system (X-STOP) is a titanium metal implant made to fit between the lumbar spinous processes of the vertebrae (**Figs. 50.8** and **50.9**). It is designed to relieve narrowing of the spinal canal and neural foramen during extension, thereby reducing the symptoms of neurogenic intermittent claudication. The indications include spinal stenosis and degenerative lumbar spondylolisthesis. According to a Norwegian study in 2015, it revealed that the significantly higher cost of X-STOP is mainly due to implant cost and the significantly higher reoperation rate (33%) when compared to minimally invasive decompression surgery in patients with symptomatic lumbar spinal stenosis.

FIGURE 50.8. **Interspinous process decompression system (X STOP).**

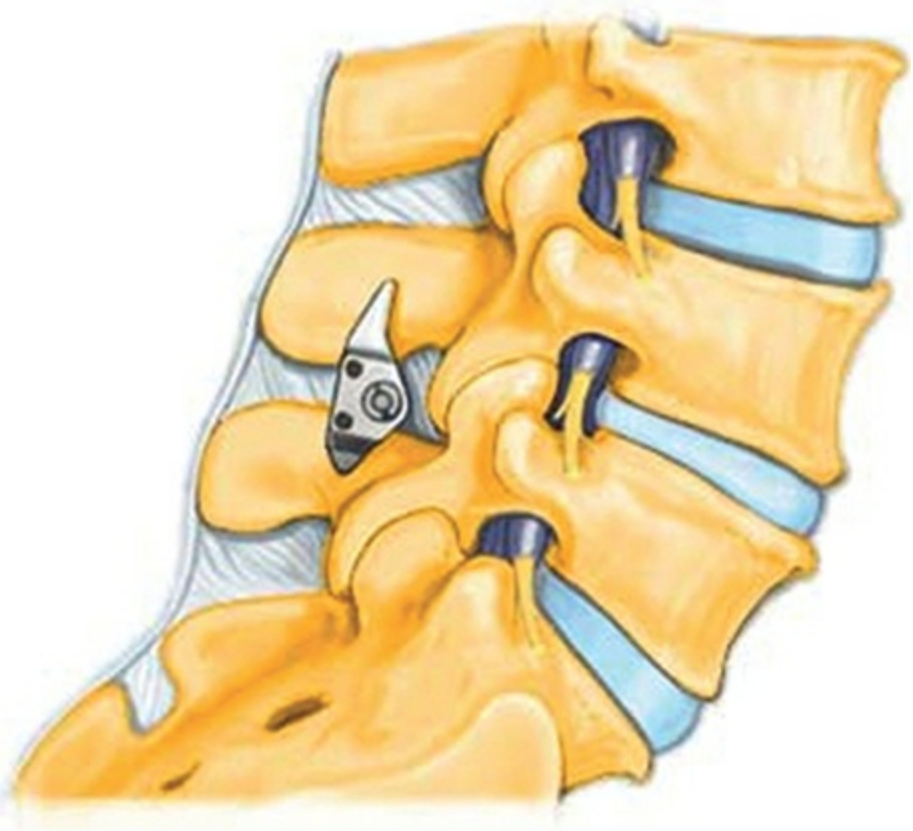


FIGURE 50.9. **Interspinous process decompression system (X STOP).**

Spinal surgery often involves direct decompression, where the pressure is reduced and/or removed from the nerve; it may include laminotomy, laminectomy, foraminotomy, and/or discectomy. These surgeries can be done by either a traditional

open approach or a minimally invasive technique/minimally invasive surgery (MIS). The latter can avoid separation of muscles and preserve stabilizing structures. It has many surgical advantages such as less muscle trauma, minimal postoperative back pain, shorter hospital stays, and faster recovery. The MIS decompression technique can be done by using a microscopic, tubular (using tubular retractors), or endoscopic decompression technique.

Degenerative spondylolisthesis in the lumbar spine occurs when the cephalad vertebral body slips relative to the caudal body. Symptoms may result from spinal stenosis and nerve root compression. Surgical management of this condition may entail decompression of the spinal canal followed by posterolateral fusion with or without an interbody fusion. The additional anterior stabilization of the vertebral column with an interbody fusion reduces the incidence of nonunion, degree of slippage, and recurrence of deformity in patients with degenerative spondylolisthesis. Additional anterior stabilization can be accomplished by using different approaches such as anterior lumbar interbody fusion (ALIF), posterior lumbar interbody fusion (PLIF), transforaminal lumbar interbody fusion (TLIF), or eXtreme lateral interbody fusion (XLIF).

Alimi M, Hofstetter CP, Pyo SY, et al. Minimally invasive laminectomy for lumbar spinal stenosis in patients with and without preoperative spondylolisthesis: clinical outcome and reoperation rates. *J Neurosurg Spine*. 2015;22(4):339–352.

Kim KT, Lee SH, Lee YH, et al. Clinical outcomes of 3 fusion methods through the posterior approach in the lumbar spine. *Spine (Phila Pa 1976)*. 2006;31:1351–1358.

Lee CW, Yoon KJ, Ha SS. Comparative analysis between three different lumbar decompression techniques (microscopic, tubular, and endoscopic) in lumbar canal and lateral recess stenosis: preliminary report. *Biomed Res Int*. 2019;2019:6078469.

Li YZ, Sun P, Chen D, et al. Artificial total disc replacement versus fusion for lumbar degenerative disc disease: an update systematic review and meta-

analysis [published online ahead of print November 17, 2018]. *Turk Neurosurg*. doi:10.5137/1019-5149.JTN.24799-18.2.

Lønne G, Johnsen LG, Aas E, et al. Comparing cost-effectiveness of X-Stop with minimally invasive decompression in lumbar spinal stenosis: a randomized controlled trial. *Spine (Phila Pa 1976)*. 2015;40:514–520.

Parikh K, Tomasino A, Knopman J, et al. Operative results and learning curve: microscope-assisted tubular microsurgery for 1- and 2-level discectomies and laminectomies. *Neurosurg Focus*. 2008;25(2):E14.

Pettine K, Ryu R, Techy F. Why lumbar artificial disk replacement (LADRs) fail. *Clin Spine Surg*. 2017;30(6):E743–E747.

Zippel H, Schellnack K, Büttner K. Exchanging intervertebral disks. The concept and clinical experience using a cement-free intervertebral disk endoprosthesis of the “Charité Modular SB” type. *Chir Narzadow Ruchu Ortop Pol*. 1986;51(4):245–248.

51 Perioperative Pain Management

Anuj Malhotra and Vinod Malhotra

A 60-year-old man with a smoking history of a pack of cigarettes a day for approximately 40 years and chronic obstructive pulmonary disease is scheduled for thoracotomy for removal of carcinoma in his right middle lobe.

A. Perioperative Pain Management for Thoracotomy

1. What would be your advice to the patient about the planned thoracotomy and postoperative pain relief?
2. How will you decide about the choice of anesthetic technique?
3. What is chronic postsurgical pain (CPSP)? Does video-assisted thoracic surgery reduce the risk of chronic pain after thoracotomy?
4. What would be your perioperative analgesic strategy?
5. Does the choice of analgesic technique influence postoperative outcome?
6. Does it matter if the epidural catheter is at the thoracic or lumbar level?
7. Does the choice of drugs influence the efficacy or safety of thoracic epidural analgesia (TEA)?

8. What are the usual doses and concentrations of the anesthetic combinations commonly employed in epidural analgesia?
9. If accidental dural puncture occurs during placement of the epidural needle, what steps should be taken?
10. What are the alternatives to TEA?
11. What is the usual clinical regimen for intravenous patient-controlled analgesia (IV-PCA) and is special patient monitoring required during its use?
12. What are the side effects and complications of epidural technique?
13. What recommendations for placement and removal of epidural catheter will you make if this patient is on antiplatelet or anticoagulant therapy or thromboprophylaxis is planned?

A 70-year-old woman with metastatic breast cancer has been treated for the last 6 months with transdermal fentanyl (Duragesic patch) for her cancer pain. She is currently on a 100-μg per hour patch every 72 hours. She is now scheduled for surgery for hip fracture after a fall. The patient was very dissatisfied with postoperative pain management after her breast surgery 3 months earlier.

B. Chronic Opioid Therapy and Perioperative Pain Management

1. How does chronic opioid therapy influence postoperative pain management?
2. What are the causes for increased postoperative pain and opioid consumption in patients chronically using opioids?
3. What are the main differences between a chronic opioid-consuming patient and a patient who abuses or is addicted to opioids?
4. What issues need to be considered in the opioid-tolerant

patient who is scheduled for surgery?
5. What would be your strategy regarding preoperative information and choice of anesthesia technique?
6. What are the choices for perioperative pain management in opioid-tolerant patients?
7. What issues need to be considered before discharging an opioid-tolerant patient?

A 38-year-old woman scheduled for ambulatory laparoscopic cholecystectomy requests to see the anesthesiologist preoperatively to discuss her postoperative analgesia strategy. She experienced severe pain at home for several days after a previous ambulatory laparoscopic gynecologic procedure.

C. Perioperative Pain Management for Ambulatory Surgery

1. What would be your preoperative considerations and advice to the patient?
2. What are the consequences of inadequate pain management after ambulatory surgery?
3. What is the role of premedication or preoperative analgesic?
4. Does the choice of anesthetic technique influence postoperative pain?
5. Are nonsteroidal anti-inflammatory drugs (NSAIDs) effective? If so, does the choice of drug matter?
6. What is the role of surgical technique in influencing postoperative pain after a laparoscopic cholecystectomy?
7. What would be your strategy for pain control after discharge home?

D. The Role of an Acute Pain Service (APS)

1. What is the extent of the problem, and which patients are at

greatest risk of undertreatment?
2. What are the consequences of inadequate postoperative pain relief?
3. What is the role of an APS in improving postoperative pain management?
4. Does an APS improve postoperative outcome?

A. Perioperative Pain Management for Thoracotomy

A.1. What would be your advice to the patient about the planned thoracotomy and postoperative pain relief?

It is essential that patients undergoing thoracotomy be informed about what to expect after surgery because an understanding of the procedure as well as realistic expectations of pain and rehabilitation can promote recovery and return to normal activity. Patients undergoing thoracotomy may suffer from severe acute postoperative pain as well as CPSP if analgesia is not managed appropriately. Pulmonary function is impaired as a result of thoracic surgery and lung reduction and may be worsened by the effects of pain such as splinting promoting atelectasis, or oversedation from analgesics promoting respiratory depression. Therefore, during the early postoperative period, optimization and balancing pain control and maintenance of pulmonary function are the major goals.

For preoperative improvement of pulmonary function, patients should be advised to stop smoking and be instructed in deep breathing exercises such as incentive spirometry. Different techniques may be used to manage different levels of pain intraoperatively, immediately following surgery, within the first few postoperative days, and for discharge home, and each of these should be discussed. Pain management for these cases

often involves a step-down approach from neuraxial analgesia to intravenous opioids to oral medication. The following issues should be addressed:

- Information must be given on how pain will be assessed, for example, the use of visual analog scores.
- Patients require a realistic expectation of the intensity and duration of postoperative pain.
- Pain management techniques that require patient involvement (IV-PCA, patient-controlled epidural analgesia [PCEA]) need to be properly explained.
- Resources for chronic pain management should be discussed in case the pain goes beyond the expected duration.

Crumley S, Schraag S. The role of local anaesthetic techniques in ERAS protocols for thoracic surgery. *J Thorac Dis*. 2018;10(3):1998–2004.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1709–1714, 2614–2638.

Zaccagnino MP, Bader AM, Sang CN, et al. The perioperative surgical home: a new role for the acute pain service. *Anesth Analg*. 2017;125(4):1394–1402.

A.2. How will you decide about the choice of anesthetic technique?

The decision about which anesthetic technique to use for an individual patient is based on a review of their overall medical condition and any medications that they are taking along with discussion with the surgeon. General anesthesia combined with epidural analgesia may be selected based on the patient's comorbidities and the planned procedure. Because lung volumes after thoracic surgery may be reduced by up to 50% through a combination of resection and splinting atelectasis, epidural analgesia can have benefit not only for pain relief but also for improving pulmonary function by improving respiratory mechanics and minimizing opioid-induced respiratory depression. Other factors such as surgeon preference,

anesthesiologist experience and practice, and institutional protocols for postoperative pain relief may also influence the choice of analgesic technique. If placement of an epidural catheter is included in the anesthetic plan, it may be used intraoperatively as an adjunct to general anesthesia or bolused at the end of the case prior to a postoperative infusion. Again, this decision is often based on patient and surgical considerations, such as potential blood loss, hypotension, need for fluid restriction, and invasiveness of surgery. Intraoperative epidural use prior to wake up has the benefit of ensuring epidural catheter function and can facilitate a more comfortable transition to the immediate postoperative period.

The use of TEA has become widespread for management of pain associated with thoracic and major abdominal surgery. Clinical studies have shown that TEA can have effects far beyond pain relief, including decreased opioid consumption, reduced risk of nausea and vomiting, increased lung volumes, reduced risk of pulmonary complications, improved bowel recovery, and a significant reduction in the incidence of myocardial infarction. There is also evidence that neuraxial block decreases the risk of recurrence after certain cancer resections, likely through an opioid-sparing effect.

Christopherson R, James KE, Tableman M, et al. Long-term survival after colon cancer surgery: a variation associated with choice of anesthesia. *Anesth Analg*. 2008;107:325–332.

Exadaktylos AK, Buggy DJ, Moriarty DC, et al. Can anesthetic technique for primary breast cancer surgery affect recurrence or metastasis? *Anesthesiology*. 2006;105:660–664.

Freise H, Van Aken HK. Risks and benefits of thoracic epidural anaesthesia. *Br J Anaesth*. 2011;107(6):859–868.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1709–1714, 2614–2638.

Pöpping DM, Zahn PK, Van Aken HK, et al. Effectiveness and safety of postoperative pain management: a survey of 18 925 consecutive patients

between 1998 and 2006 (2nd revision): a database analysis of prospectively raised data. *Br J Anaesth*. 2008;101:832–840.

A.3. What is chronic postsurgical pain (CPSP)? Does video-assisted thoracic surgery reduce the risk of chronic pain after thoracotomy?

CPSP is defined as pain that recurs or persists at least 2 months after surgery and is not related to ongoing tissue injury such as recurrence of tumor, wound dehiscence, or infection. Postthoracotomy pain syndrome (PTPS) is as subset of CPSP and is most commonly neuropathic in nature, with a reported incidence of 25% to 65%. Several studies suggest that severe perioperative pain is a predictor for development of CPSP, and thus aggressive management of early postoperative pain may be important to prevent this transition.

Although used with increasing frequency, thoracoscopic approaches have not had the favorable impact on pain that many had anticipated. Surprisingly, video-assisted thoracic surgery is associated with a prevalence of chronic pain comparable to that of open procedures, with rates of PTPS ranging from 22% to 63%, likely due to intercostal nerve and muscle damage from trocar insertion and chest tube placement.

Gerner P. Post thoracotomy pain management problems. *Anesthesiol Clin*. 2008;26(2):355–367.

Gottchalk A, Cohen SP, Yang S, et al. Preventing and treating pain after thoracic surgery. *Anesthesiology*. 2006;104:594–600.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1709–1714, 2614–2638.

A.4. What would be your perioperative analgesic strategy?

The analgesic plan should consider the entire perioperative period. A multimodal approach would be preferable to account for the multiple pathways by which nociceptive input is

conveyed to the central nervous system, the number of pharmacologically distinct mechanisms of modulating this input, the need for effective analgesia throughout the perioperative period and after discharge, and the importance of minimizing side effects, particularly respiratory depression.

TEA is the mainstay of recommended therapy for the reasons previously discussed. Contraindications to a thoracic epidural include patient refusal, coagulopathy, thrombocytopenia, therapeutic anticoagulation, previous thoracic spine surgery, and local infection over the entry site. When epidural catheters fail intraoperatively or have patchy coverage, intercostal nerve blocks (ICNBs) or paravertebral blocks may supplement epidural analgesia or serve as a bridge to the immediate postoperative period when an epidural catheter can be safely replaced.

NSAIDs are useful for treating shoulder pain secondary to referred diaphragmatic pain. This nociceptive input is carried by vagal and phrenic nerves and is often refractory to epidural analgesia. A concern with NSAIDs is platelet dysfunction; however, their efficacy and lack of respiratory side effects makes them an optimal choice for adjunct analgesia when possible. Cyclooxygenase-2 (COX-2) inhibitors have more limited effects on platelets aggregation and comparable efficacy to traditional NSAIDs and thus may be of use in this setting. Adverse cardiac side effects are unlikely with short-term perioperative dosing. Regular administration of paracetamol or acetaminophen (APAP) may also be useful for treating shoulder pain and can be used in addition to NSAIDs. Topical lidocaine patch or use of gabapentinoids may also have a role in select patients.

Gottchalk A, Cohen SP, Yang S, et al. Preventing and treating pain after thoracic surgery. *Anesthesiology*. 2006;104:594–600.

Mac TB, Girard F, Chouinard P, et al. Acetaminophen decreases early post-thoracotomy ipsilateral shoulder pain in patients with thoracic epidural analgesia: a double-blinded placebo-controlled study. *J Cardiothorac Vasc Anesth*. 2005;19(4):475–478.

Manion SC, Brennan TJ. Thoracic epidural analgesia and acute pain management. *Anesthesiology*. 2011;115:181–188.

Senard M, Deflandre EP, Ledoux D, et al. Effect of celecoxib combined with thoracic epidural analgesia on pain after thoracotomy. *Br J Anaesth*. 2010;105:196–200.

A.5. Does the choice of analgesic technique influence postoperative outcome?

Evidence from multiple studies strongly suggests that epidural analgesia is associated with lower rates of perioperative morbidity and, in particular, fewer pulmonary and cardiac complications. More recently, a meta-analysis of patients receiving TEA versus PCA after surgery requiring general anesthesia demonstrated decreased mortality in the thoracic epidural group. Compared with systemic opioids, epidural opioids decrease the incidence of postoperative atelectasis, hypoxemia, and pulmonary complications overall. Effective pain control with an epidural technique leads to improved pulmonary function, more effective coughing, earlier mobilization, and improved cooperation with respiratory physiotherapy.

Postoperative myocardial infarction rates are reduced when TEA is incorporated into anesthesia and extended at least 24 hours into the postoperative period. Supraventricular tachyarrhythmias, which are the most common form of cardiac morbidity after pulmonary resection and occur in up to 50% of cases, are reduced by TEA, even when compared with alternative analgesic regimens that confer equivalent pain control. The cardioprotective mechanism of TEA is believed to relate to its sympatholytic effects.

Epidural analgesia also provides superior postoperative analgesia compared with IV-PCA. As discussed earlier, better

postoperative pain relief may decrease the likelihood of developing CPSP, although it should be noted that this has not yet been demonstrated in longitudinal studies.

Dworkin RH, McDermott MP, Raja SN. Preventing chronic postsurgical pain: how much of a difference makes a difference? *Anesthesiology*. 2010;112(3):516–518.

Pöpping DM, Elia N, Van Aken HK, et al. Impact of epidural analgesia on mortality and morbidity after surgery: systematic review and meta-analysis of randomized controlled trials. *Ann Surg*. 2014;259(6):1056–1067.

Wu CL, Cohen SR, Richman JM, et al. Efficacy of postoperative patient-controlled and continuous infusion epidural analgesia versus intravenous patient-controlled analgesia with opioids: a meta-analysis. *Anesthesiology*. 2005;103(5):1079–1088.

A.6. Does it matter if the epidural catheter is at the thoracic or lumbar level?

TEA is currently the standard for analgesia for thoracic surgery, and in the absence of contraindications, all patients undergoing major open thoracic surgical procedures should have a thoracic epidural catheter placed preoperatively. The tip of the catheter should ideally reside at the dermatome along which the incision will be made.

Thoracic (vs. lumbar) placement of the epidural catheter is dose saving and decreases side effects such as hypotension and bladder dysfunction at equianalgesic doses. Thoracic placement also reduces motor block of the lower extremities, which allows for improved postoperative ambulation. However, if thoracic epidural placement is contraindicated or cannot be achieved, lumbar epidural anesthesia can be utilized. Lumbar placement can be efficacious, particularly when used with hydrophilic opioids such as morphine; however, local anesthetic volume dosing is significantly higher and may be limited by toxicity or side effects such as hypotension or motor block.

Crumley S, Schraag S. The role of local anaesthetic techniques in ERAS

protocols for thoracic surgery. *J Thorac Dis*. 2018;10(3):1998–2004.

Manion SC, Brennan TJ. Thoracic epidural analgesia and acute pain management. *Anesthesiology*. 2011;115:181–188.

A.7. Does the choice of drugs influence the efficacy or safety of thoracic epidural analgesia (TEA)?

Effective postoperative pain control may be achieved by delivering an opioid, local anesthetic, or a combination of both into the thoracic epidural space. Combinations are the standard because synergy between opioids and local anesthetic agents can enable an optimum balance between analgesia and minimizing blockade of motor function of the thorax and dynamic consequences of sympatholysis. Common components include opioids, such as morphine, fentanyl, or hydromorphone, and local anesthetic agents, such as bupivacaine, levobupivacaine, or ropivacaine. Systemic absorption effects (e.g., sedation) tend to be more common with the lipophilic opioids, such as fentanyl, presumably because of increased absorption into the epidural fat. Hydrophilic opioids, such as morphine, produce a wider dermatomal band of analgesia with less systemic absorption. Of the three commonly used local anesthetic agents, bupivacaine possesses the least favorable cardiac safety profile. In theory, ropivacaine offers the advantage of differential dose-dependent sensory and motor blockade; however, when used in dilute concentrations in combination with opioids, it is unlikely that any advantage of one agent over the other will be apparent. Addition of low-dose ketamine to epidural infusion or intravenously has not demonstrated beneficial effects in preventing postthoracotomy pain.

Freise H, Van Aken HK. Risks and benefits of thoracic epidural anaesthesia. *Br J Anaesth*. 2011;107(6):859–868.

Moyse DW, Kaye AD, Diaz JH, et al. Perioperative ketamine administration for thoracotomy pain. *Pain Physician*. 2017;20(3):173–184.

Ryu HG, Lee CJ, Kim YT, et al. Preemptive low-dose epidural ketamine for

preventing chronic postthoracotomy pain: a prospective, double-blinded, randomized, clinical trial. *Clin J Pain*. 2011;27:304–308.

A.8. What are the usual doses and concentrations of the anesthetic combinations commonly employed in epidural analgesia?

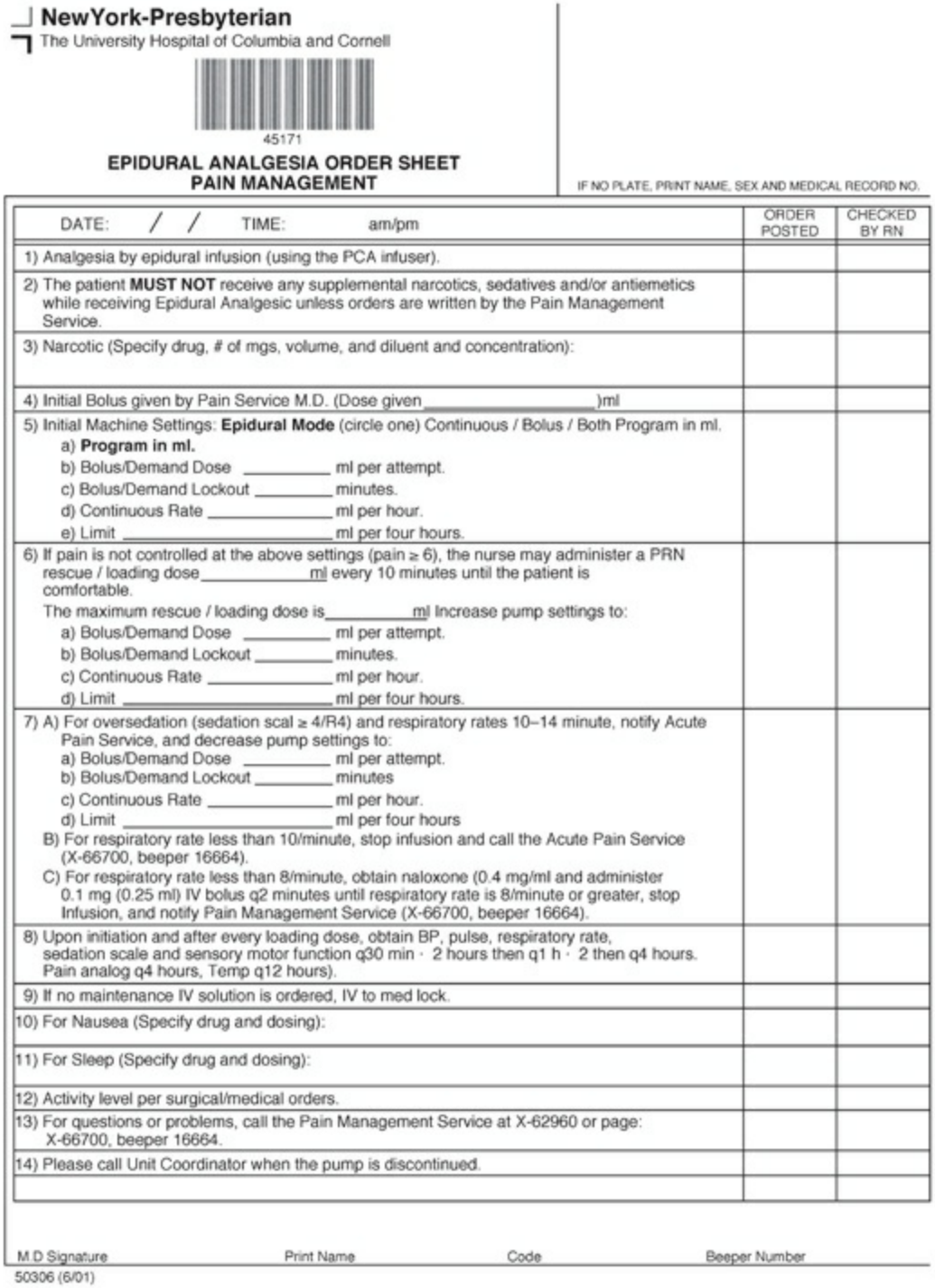
Before the initiation of PCEA, a test dose of 3 mL of 1.5% lidocaine with epinephrine 1:200,000 is usually employed with the patient awake to rule out intrathecal or intravascular placement of catheter. Once malposition is ruled out, the catheter is usually bolused (as allowed by hemodynamic status) prior to beginning continuous infusion.

Commonly employed combinations of epidural drugs vary. However, in the interest of patient safety, compliance, auditing, and quality assurance, standardization within the institution is recommended. Solutions and volumes can later be titrated to effect or to avoid side effects, for example, increasing or decreasing local anesthetic concentration to change block density, increasing or decreasing volume infused to increase spread, and adding or subtracting opioids to increase analgesia or decrease side effects such as itching, nausea, or sedation.

The following drugs and drug combinations are often used at a starting infusion rate of 4 to 6 mL per hour with each demand bolus of 2 to 3 mL as needed. This clinical dosing is consistent with fluoroscopic epidurography studies that have demonstrated vertebral spread of 7 to 8 levels with 2.5 to 5 mL bolus.

- Bupivacaine 0.0625% to 0.1% with fentanyl 5 μg per mL with a lockout period of 10 to 20 minutes between boluses
- Bupivacaine 0.0625% to 0.1% plain with a lockout of 20 minutes
- Fentanyl 5 to 10 μg per mL with a lockout period of 10 to 20 minutes
- Bupivacaine 0.0625% to 0.1% with Dilaudid 100 μg per mL

with a lockout period of 20 minutes (See sample order form, **Fig. 51.1**.)



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The University Hospital of Columbia and Cornell

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EPIDURAL ANALGESIA ORDER SHEET
PAIN MANAGEMENT

IF NO PLATE, PRINT NAME, SEX AND MEDICAL RECORD NO.

DATE: / / TIME: am/pm	ORDER POSTED	CHECKED BY RN
1) Analgesia by epidural infusion (using the PCA infuser).		
2) The patient **MUST NOT** receive any supplemental narcotics, sedatives and/or antiemetics while receiving Epidural Analgesic unless orders are written by the Pain Management Service.		
3) Narcotic (Specify drug, # of mgs, volume, and diluent and concentration):		
4) Initial Bolus given by Pain Service M.D. (Dose given _____)ml		
5) Initial Machine Settings: **Epidural Mode** (circle one) Continuous / Bolus / Both Program in ml. a) **Program in ml.** b) Bolus/Demand Dose _____ ml per attempt. c) Bolus/Demand Lockout _____ minutes. d) Continuous Rate _____ ml per hour. e) Limit _____ ml per four hours.		
6) If pain is not controlled at the above settings (pain ≥ 6), the nurse may administer a PRN rescue / loading dose_____ml every 10 minutes until the patient is comfortable. The maximum rescue / loading dose is_____ml Increase pump settings to: a) Bolus/Demand Dose _____ ml per attempt. b) Bolus/Demand Lockout _____ minutes. c) Continuous Rate _____ ml per hour. d) Limit _____ ml per four hours.		
7) A) For oversedation (sedation scal ≥ 4/R4) and respiratory rates 10–14 minute, notify Acute Pain Service, and decrease pump settings to: a) Bolus/Demand Dose _____ ml per attempt. b) Bolus/Demand Lockout _____ minutes c) Continuous Rate _____ ml per hour. d) Limit _____ ml per four hours B) For respiratory rate less than 10/minute, stop infusion and call the Acute Pain Service (X-66700, beeper 16664). C) For respiratory rate less than 8/minute, obtain naloxone (0.4 mg/ml and administer 0.1 mg (0.25 ml) IV bolus q2 minutes until respiratory rate is 8/minute or greater, stop Infusion, and notify Pain Management Service (X-66700, beeper 16664).		
8) Upon initiation and after every loading dose, obtain BP, pulse, respiratory rate, sedation scale and sensory motor function q30 min · 2 hours then q1 h · 2 then q4 hours. Pain analog q4 hours, Temp q12 hours).		
9) If no maintenance IV solution is ordered, IV to med lock.		
10) For Nausea (Specify drug and dosing):		
11) For Sleep (Specify drug and dosing):		
12) Activity level per surgical/medical orders.		
13) For questions or problems, call the Pain Management Service at X-62960 or page: X-66700, beeper 16664.		
14) Please call Unit Coordinator when the pump is discontinued.		

M.D Signature Print Name Code Beeper Number

50306 (6/01)

FIGURE 51.1. Epidural analgesia order sheet. BP, blood pressure; IV, intravenous; PCA, patient-controlled analgesia; PRN, as needed; RN, registered nurse. (*Source: NewYork-Presbyterian Hospital, NYC.*)

Hong J, Jung SW. Fluoroscopically guided thoracic interlaminar epidural injection: a comparative epidurography study using 2.5 mL and 5 mL of contrast dye. *Pain Physician*. 2016;19(7):E1013–E1018.

A.9. If accidental dural puncture occurs during placement of the epidural needle, what steps should be taken?

If accidental dural puncture occurs during placement of epidural needle, the general practice is to remove the needle and place the epidural catheter at adjacent intervertebral spaces. The likelihood of intrathecal spread should be carefully assessed with the test dose. Epidural infusion may be started at the usual rate. Frequent monitoring for sensory and sympathetic block should continue in a controlled setting until the efficacy and safety of the epidural analgesia is established. In addition, the patient should be assessed for any symptoms of neuropathy relevant to the level attempted. The patient should be informed of the dural puncture and the potential for postdural puncture headache, although this is less frequent than with lumbar dural puncture.

Freise H, Van Aken HK. Risks and benefits of thoracic epidural anaesthesia. *Br J Anaesth*. 2011;107(6):859–868.

Manion SC, Brennan TJ. Thoracic epidural analgesia and acute pain management. *Anesthesiology*. 2011;115:181–188.

A.10. What are the alternatives to TEA?

There are times when for technical, medical, or other reasons thoracic epidural catheter placement is unsuccessful, undesirable, or not possible. Alternatives to mid-TEA include lower thoracic and lumbar epidural catheter placement, ICNBs, paravertebral blocks, serratus anterior blocks, erector spinae blocks, intrathecal opioids, intrapleural catheters, local anesthetic infiltration, and systemic analgesia with one or more agents.

Lumbar epidural placement can be efficacious, particularly

when used with hydrophilic opioids such as morphine to increase dermatomal spread. Lumbar epidurals are most limited by the need for increased local anesthetic dosing and the higher incidence of side effects such as hypotension, motor block, and urinary retention versus thoracic epidurals.

If epidural placement is ruled out altogether for the reasons previously discussed, ICNBs can be performed percutaneously using anatomic or ultrasound-guided techniques or under direct vision intraoperatively, using single injections or placement of an intercostal catheter. Although often initially effective, unpredictable spread of local anesthetic and rapid local anesthetic absorption by surrounding vessels make this technique less effective than epidural analgesia. Furthermore, indwelling intercostal catheters cannot adequately control pain after posterolateral thoracotomy because posterior primary rami and sympathetic fibers are not blocked. Additionally, percutaneous positioning and securing of intercostal catheters may be technically problematic.

Paravertebral block results in ipsilateral somatic and sympathetic nerve blockade in multiple contiguous thoracic dermatomes above and below the site injection. Paravertebral analgesia has been found to produce good pain relief and preservation of pulmonary function after thoracotomy and is probably the best available alternative to epidural analgesia. Because the concomitant sympathetic blockade is unilateral, the incidence of adverse effects, such as hypotension and urinary retention, is lower. Paravertebral blocks can be performed as single injections or through a paravertebral catheter. Paravertebral catheters can be placed percutaneously via anatomic or ultrasound-guided approaches or intraoperatively under direct vision. In some studies, paravertebral blocks have been shown to be as effective as TEA with respect to acute pain control and preservation of pulmonary function after

thoracotomy.

A preoperative single bolus of spinal morphine as part of multianalgesic regimen can be considered in order to decrease the need for systemic opioids. Alternatively, pleural catheters may be placed intraoperatively to decrease pleural and visceral pain; however, they do not affect incisional pain and require high volumes of local anesthetic to be effective. Similarly, direct local anesthetic wound infiltration can be used but must be combined with longer acting strategies to provide adequate pain control throughout the perioperative period. Although systemic opioids have been well documented to reduce postthoracotomy pain, their adverse effects on the respiratory system after general anesthesia, even using patient-controlled delivery systems, and their inability to provide optimal dynamic pain relief favor regional anesthetic techniques, when possible, in thoracotomy patients. Systemic analgesics are best suited as adjuncts to these techniques and should become the mainstay of analgesic therapy only when invasive approaches are discontinued.

Crumley S, Schraag S. The role of local anaesthetic techniques in ERAS protocols for thoracic surgery. *J Thorac Dis*. 2018;10(3):1998–2004.

Forero M, Adhikary SD, Lopez H, et al. The erector spinae plane block: a novel analgesic technique in thoracic neuropathic pain. *Reg Anesth Pain Med*. 2016;41(5):621–627.

Madabushi R, Tewari S, Gautam SK, et al. Serratus anterior plane block: a new analgesic technique for post-thoracotomy pain. *Pain Physician*. 2015;18(3):E421–E424.

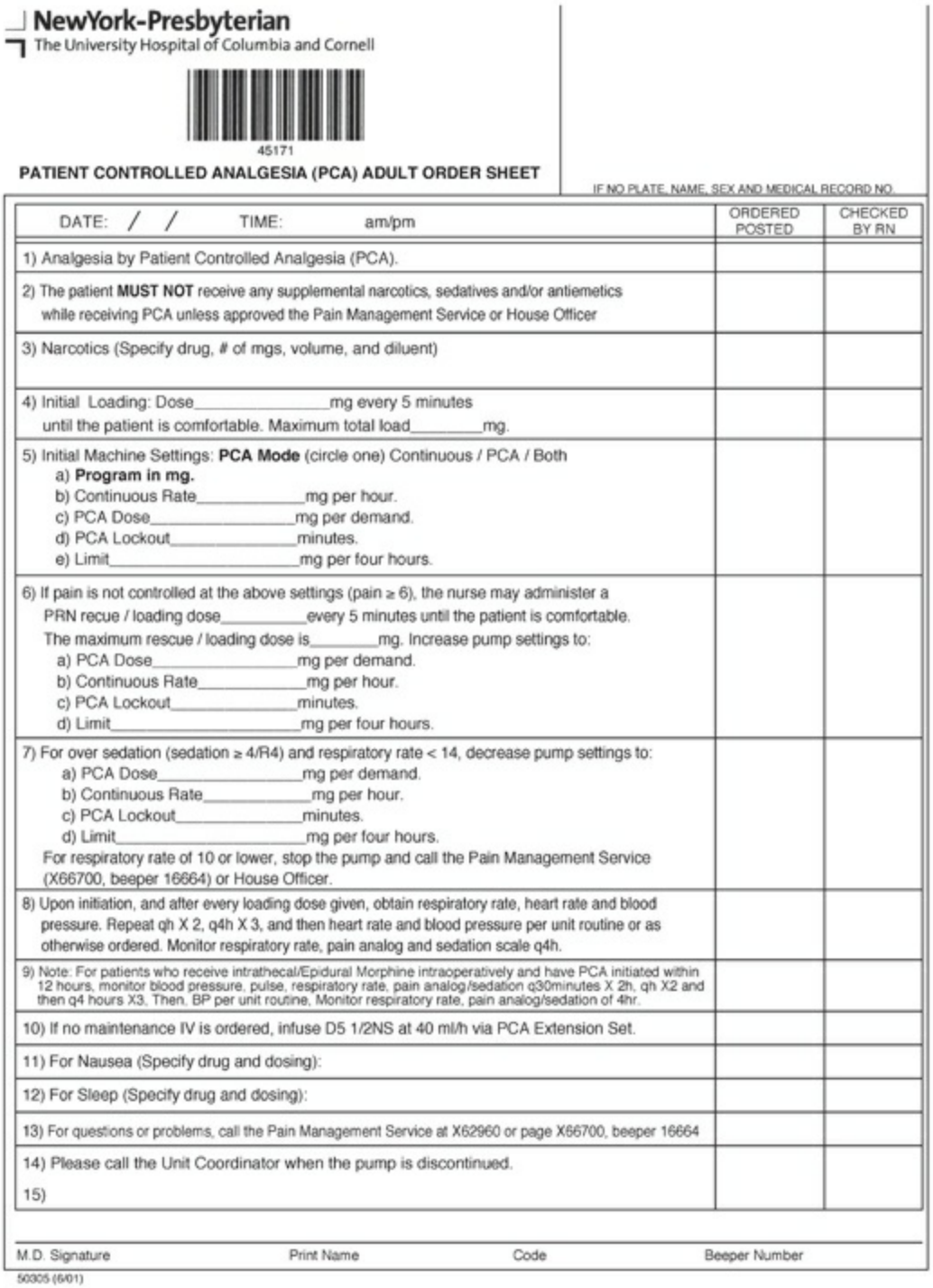
Pöpping DM, Zahn PK, Van Aken HK, et al. Effectiveness and safety of postoperative pain management: a survey of 18 925 consecutive patients between 1998 and 2006 (2nd revision): a database analysis of prospectively raised data. *Br J Anaesth*. 2008;101:832–840.

Yeung JH, Gates S, Naidu BV, et al. Paravertebral block versus thoracic epidural for patients undergoing thoracotomy. *Cochrane Database Syst Rev*. 2016;(2):CD009121.

A.11. What is the usual clinical regimen for intravenous

patient-controlled analgesia (IV-PCA) and is special patient monitoring required during its use?

Clinical regimens for IV-PCA vary among institutions, but the most commonly used opioids are fentanyl, morphine, and hydromorphone. Continuous delivery, or basal rate, of the drug is commonly avoided to decrease the likelihood of respiratory depression. For opioid-naive patients, boluses of fentanyl 10 to 15 μg, morphine sulfate 1 to 2 mg, or Dilaudid 0.2 to 0.3 mg are given per demand with a lockout period of 8 to 10 minutes. Incremental boluses may be given by the nurse if pain is not controlled. The dose may be decreased or the opioid may be discontinued if respiratory depression occurs. Close monitoring and rescue strategies must be in place to ensure patient safety, particularly for at-risk individuals, including central monitoring of oxygenation and ventilation (see sample order form, **Fig. 51.2**).



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PATIENT CONTROLLED ANALGESIA (PCA) ADULT ORDER SHEET

IF NO PLATE, NAME, SEX AND MEDICAL RECORD NO.

DATE: / / TIME: am/pm	ORDERED POSTED	CHECKED BY RN
1) Analgesia by Patient Controlled Analgesia (PCA).		
2) The patient **MUST NOT** receive any supplemental narcotics, sedatives and/or antiemetics while receiving PCA unless approved the Pain Management Service or House Officer		
3) Narcotics (Specify drug, # of mgs, volume, and diluent)		
4) Initial Loading: Dose_____mg every 5 minutes until the patient is comfortable. Maximum total load_____mg.		
5) Initial Machine Settings: **PCA Mode** (circle one) Continuous / PCA / Both a) **Program in mg.** b) Continuous Rate_____mg per hour. c) PCA Dose_____mg per demand. d) PCA Lockout_____minutes. e) Limit_____mg per four hours.		
6) If pain is not controlled at the above settings (pain ≥ 6), the nurse may administer a PRN recue / loading dose_____every 5 minutes until the patient is comfortable. The maximum rescue / loading dose is_____mg. Increase pump settings to: a) PCA Dose_____mg per demand. b) Continuous Rate_____mg per hour. c) PCA Lockout_____minutes. d) Limit_____mg per four hours.		
7) For over sedation (sedation ≥ 4/R4) and respiratory rate < 14, decrease pump settings to: a) PCA Dose_____mg per demand. b) Continuous Rate_____mg per hour. c) PCA Lockout_____minutes. d) Limit_____mg per four hours. For respiratory rate of 10 or lower, stop the pump and call the Pain Management Service (X66700, beeper 16664) or House Officer.		
8) Upon initiation, and after every loading dose given, obtain respiratory rate, heart rate and blood pressure. Repeat qh X 2, q4h X 3, and then heart rate and blood pressure per unit routine or as otherwise ordered. Monitor respiratory rate, pain analog and sedation scale q4h.		
9) Note: For patients who receive intrathecal/Epidural Morphine intraoperatively and have PCA initiated within 12 hours, monitor blood pressure, pulse, respiratory rate, pain analog/sedation q30minutes X 2h, qh X2 and then q4 hours X3. Then, BP per unit routine, Monitor respiratory rate, pain analog/sedation of 4hr.		
10) If no maintenance IV is ordered, infuse D5 1/2NS at 40 ml/h via PCA Extension Set.		
11) For Nausea (Specify drug and dosing):		
12) For Sleep (Specify drug and dosing):		
13) For questions or problems, call the Pain Management Service at X62960 or page X66700, beeper 16664		
14) Please call the Unit Coordinator when the pump is discontinued.		
15)		

M.D. Signature Print Name Code Beeper Number

50305 (6/01)

FIGURE 51.2. PCA adult order sheet. BP, blood pressure; IV, intravenous. (*Source: NewYork-Presbyterian Hospital, NYC.*)

A workshop of the Anesthesia Patient Safety Foundation (APSF) looked at the issue of dangers of postoperative opioids. The observed incidence of respiratory depression in these cases

is 0.1% to 1.0% and increases to 3.2% in those older than 80 years. Patients with obstructive sleep apnea and the elderly are understandably at a higher risk for opioid-induced respiratory depression, but there is also a low and unpredictable incidence of life-threatening respiratory depression in young, healthy patients. The workshop highlighted the argument that in the United States, The Joint Commission's emphasis on pain as the "fifth vital sign" has had the unintended consequence of creating an expectation among patients that they will have little to no pain after surgery. As a result, more patients may be receiving inappropriate amounts of analgesics to meet this expectation. The conclusions of the APSF committee were that continuous monitoring of oxygenation and ventilation can prevent patient harm; any monitoring system should be centrally linked so that a health care professional can be summoned in a timely manner; programs should be instituted to educate providers and patients about the risks of opioid-associated life-threatening respiratory depression; governmental agencies and nongovernmental entities should provide increased support for scientific research in this area; and while treatment of postoperative, opioid-induced depression is an important consideration, prevention may be the more effective strategy.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1709–1714, 2614–2638.

Weinger MB. Dangers of postoperative opioids. APSF workshop and white paper address prevention of postoperative respiratory complications. *APSF Newsl Winter*. 2006–2007;21(4):61–67.

A.12. What are the side effects and complications of epidural technique?

TEA interferes with sympathetic outflow and can produce hypotension through cardiodepressant action (blockade of cardiac accelerator fibers) and a reduction in systemic vascular

resistance (blockade of sympathetic chain). The use of dilute local anesthetic solutions has led to clinically insignificant motor blockade while maintaining adequate sensory block, although some small-muscle weakness may be observed. Opioid-related side effects include sedation, nausea and vomiting, pruritus, delayed gastrointestinal motility, urinary retention, and respiratory depression. The incidence of delayed respiratory depression after administration of epidural opioids is very low, and epidural opioid analgesia can be used safely on most hospital units. All patients who receive epidural analgesia should have standard orders for the treatment of breakthrough pain and side effects.

The overall catheter-related complication rate is low and includes such complications as dural puncture, paresthesia, pneumothorax, and neurologic injury. The most common documented complication is unsuccessful placement, reported at about 6%. Paraplegia associated with epidural analgesia may result from epidural hematoma, or less commonly epidural abscess. The potentially catastrophic complications of epidural or intrathecal hematoma are best prevented by realization that motor blockade should not occur with dilute local anesthetic solutions, and postoperative motor weakness should trigger immediate imaging evaluation (magnetic resonance imaging [MRI]) and neurosurgical consultation. Clearly, significant concerns about coagulopathy or local overlying infection should limit epidural catheter placement.

Block BM, Liu SS, Rowlingson AJ, et al. Efficacy of postoperative epidural analgesia: a meta-analysis. *JAMA*. 2003;290:2455–2463.

Pöpping DM, Elia N, Van Aken HK, et al. Impact of epidural analgesia on mortality and morbidity after surgery: systematic review and meta-analysis of randomized controlled trials. *Ann Surg*. 2014;259(6):1056–1067.

A.13. What recommendations for placement and removal

of epidural catheter will you make if this patient is on antiplatelet or anticoagulant therapy or thromboprophylaxis is planned?

On the basis of current practice and the fourth consensus statement for Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic Therapy developed by the American Society of Regional Anesthesia and Pain Medicine (ASRA), the following guidelines may be helpful.

Prophylactic Unfractionated Heparin

In the setting of twice or thrice daily subcutaneous prophylaxis with low-dose 5,000 U heparin, there is no contraindication to the use of neuraxial techniques. The clinician should keep in mind that subcutaneous heparin reaches peak effect 1 to 2 hours after administration and persists 4 to 6 hours after administration; therefore, the recommendation is that heparin be held 4 to 6 hours prior to neuraxial catheter placement or removal. Administration can resume at any time following.

Therapeutic Intravenous Unfractionated Heparin

- Neuraxial techniques combined with intraoperative IV anticoagulation (excluding the full anticoagulation of cardiac surgery) are acceptable with certain precautions. Neuraxial techniques should be avoided in patients with baseline coagulopathies (idiopathic or iatrogenic) in addition to heparinization. Placement or removal of catheters can occur 4 to 6 hours after last dosing and once normal coagulation status is verified. Dosing of heparin may resume 1 hour afterward. There is insufficient data to warrant canceling a case due to bloody or difficult block placement; however, discussion of risks and benefits with the surgeon regarding proceeding is warranted. Postoperative care should monitor for signs of hematoma such as motor blockade. Use of weak

local anesthetic solutions may facilitate detection.

Preoperative Low Molecular Weight Heparin (Enoxaparin)

Neuraxial blockade should not be performed if the patient is on other antiplatelet or oral anticoagulant medications in combination with low molecular weight heparin (LMWH). LMWH has its peak effect 2 to 4 hours after administration.

- *Prophylactic LMWH*. An example of a prophylactic dose is enoxaparin 40 mg every day or 30 mg every 12 hours. Block placement should occur no sooner than 12 hours after the last dose of LMWH, and a catheter should be maintained only if single-daily dosing is planned. If LMWH is administered within 2 hours of surgery (prophylactic dose), neuraxial blockade should be avoided.
- *Treatment dose LMWH*. An example of a treatment dose is enoxaparin 1.5 mg per kg every day or 1 mg per kg every 12 hours. Block placement should occur no sooner than 24 hours after the last dose of LMWH and only if treatment dosing is being discontinued.

Postoperative Low Molecular Weight Heparin

- *Prophylactic LMWH, twice-daily dosing*. This dosing regimen is associated with an increased risk of hematoma. The first dose of LMWH should be administered no sooner than 12 hours after needle or catheter placement. Epidural catheters should not be maintained in this situation and should be removed at least 4 hours before the first LMWH dose and no earlier than 12 hours after needle placement.
- *Prophylactic LMWH, single-daily dosing*. Epidural catheters may be maintained in this situation but only after a thorough risk/benefit analysis. The first dose of LMWH should be given greater than 12 hours postoperatively. The second dose should be given no sooner than 24 hours after the first dose.

The epidural catheter should be removed 12 hours after the last dose of LMWH, and the subsequent dose should be given no sooner than 4 hours after catheter removal.

- *Treatment dose LMWH*. Epidural catheters should not be maintained in this situation. The first dose of LMWH should be given 24 hours after needle placement or 4 hours after catheter removal, whichever is greater.

Oral Anticoagulants

- *Aspirin*. There is no contraindication to neuraxial anesthesia in patients taking aspirin alone (81 mg or 325 mg).
- *NSAIDs*. There is no contraindication to neuraxial anesthesia in patients taking NSAIDs alone.
- *Dipyridamole*. Discontinue 24 hours prior to neuraxial block and resume 6 hours after needle placement or catheter removal. Indwelling catheters are not recommended with continued use.
- *Preoperative Coumadin*

  Coumadin should be stopped 5 days before a neuraxial block, and the patient should not be on any additional antiplatelet or anticoagulant medications.

  The prothrombin time/international normalized ratio (PT/INR) should be measured before the block and should be normalized, which many clinicians define as less than 1.3. Of note, if warfarin is stopped for less than 4 days, INR (determined mainly by factors II and X) may not be reflective of coagulation status (determined mainly by factor VII).

  This differs from INR threshold for patients not taking warfarin chronically, as in this case, the INR is more reflective of overall coagulation factor status and an INR less than 1.5 is adequate.

  For patients receiving an initial preoperative Coumadin dose,

the PT/INR should be checked before neuraxial block if the first dose was given more than 24 hours earlier or if a second dose has been given.

- *Postoperative Coumadin*

  Epidural catheters may be maintained in patients on Coumadin up until the INR is less than 1.5. The PT/INR should be monitored daily and assessed before catheter removal.

  Epidural catheters should be removed while the INR is less than 1.5 and at 12 to 24 hours after initial warfarin dosing.

- *Preoperative clopidogrel (Plavix) and ticlopidine (Ticlid)*

  Clopidogrel must be held 5 to 7 days before neuraxial block placement and Ticlid must be held 10 days before neuraxial block placement. A loading dose may be administered 6 hours after needle placement or catheter removal. If no loading dose is given, therapy can resume immediately and catheters can be maintained 1 to 2 days.

- *Preoperative abciximab, eptifibatide, and tirofiban*

  GPIIb/IIIa inhibitors are profound inhibitors of platelet aggregation. Confirmation of normal platelet function is recommended prior to neuraxial block, particularly as patients are often on dual therapy with another agent. If resumption of therapy is planned, neither single shot nor catheter techniques are recommended.

  Abciximab must be held for a minimum of 24 to 48 hours prior to neuraxial blockade.

  Eptifibatide and tirofiban must be held 4 to 8 hours prior to block placement.

Newer Agents

Because many of these medications have not been available long, little postmarket surveillance data is available to determine complication rates. Accordingly, many of the following

recommendations are based on pharmacokinetics and the goal of allowing five half-lives to elapse to allow drug clearance prior to neuraxial blockade. All medications are recommended to be restarted greater than 6 hours after manipulation/catheter removal, and indwelling catheters with continued use is not recommended.

Apixaban should be held 3 days prior to neuraxial blockade.

Rivaroxaban should be held 3 days prior to neuraxial blockade.

Dabigatran should be held 5 days prior to block placement. May consider 3 to 5 days based on creatinine clearance (CrCl) if no additional risk factors.

Ticagrelor should be held 5 to 7 days prior to neuraxial block placement. May be resumed immediately after catheter removal if 24 hours after needle placement and if no loading dose, otherwise after 6 hours.

Prasugrel should be held 7 to 10 days prior to block placement. Similar recommendations for resuming as for aforementioned ticagrelor.

Gupta R. New anticoagulants present new challenges. *APSF Newsletter*. 2012;27(1):9–17.

Horlocker TT, Vandermeuelen E, Kopp SL, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Fourth Edition). *Reg Anesth Pain Med*. 2018;43(3):263–309.

B. Chronic Opioid Therapy and Perioperative Pain Management

B.1. How does chronic opioid therapy influence postoperative pain management?

In recent years, a greater emphasis has been placed on pain as an important health problem, with The Joint Commission even labeling pain as the "fifth vital sign." Consequently, opioids now

play a greater role in the treatment of chronic pain of various causes. This has resulted in a rapid increase in the consumption of opioid analgesics. For example, between 1999 and 2003, the annual sales of outpatient opioid analgesics in the United States increased by approximately 130%. Because more patients are treated chronically with opioids, every anesthesiologist is likely to be confronted with acute pain management issues in these patients. Chronic opioid-consuming patients can experience significant postoperative pain given that health care professionals are not accustomed to their markedly increased opioid requirements.

Patients on long-term opioid therapy are more likely to require higher doses of opioids postoperatively. Although the prevalence of chronic opioid-consuming patients who present for surgery is not described, the growing use of opioids is likely to increase the number of such patients. Patients with chronic pain are more likely to have high levels of postoperative pain, and increased postoperative pain has been associated with an increased risk of CPSP. Therefore, the aggressive treatment of postoperative pain is important for patients with chronic pain because they may represent a population that is particularly vulnerable to develop CPSP.

Although available data are limited, the management of postoperative pain seems to be more difficult in chronic opioid-consuming patients even when they consume only a modest daily opioid dose. Tolerance to any one opioid preparation usually results in a clinically measurable increased tolerance to most others.

Carroll IR, Angst MS, Clark JD. Management of perioperative pain in patients chronically consuming opioids. *Reg Anesth Pain Med*. 2004;29:576–591.

Mehta V, Langford RM. Acute pain management for opioid dependent patients. *Anaesthesia*. 2006;61:269–276.

Swenson JD, Davis JJ, Johnson KB. Postoperative care of the chronic opioid-

consuming patient. *Anesthesiol Clin North America*. 2005;23:37–48.

B.2. What are the causes for increased postoperative pain and opioid consumption in patients chronically using opioids?

Chronic exposure to opioids may result in a need to increase the dose over time to maintain the desired analgesic effect. The need for escalating the dose is often attributed to the development of tolerance. However, dose escalation can be the result of other factors, such as progression of the underlying disease.

Recent evidence points to opioid-induced hyperalgesia as an alternative neuropharmacologic phenomenon to explain the need to escalate the opioid dose over time. Paradoxically, administration of opioids may induce an increased sensitivity to pain (hyperalgesia). Further complicating matters, the phenomena of tolerance and hyperalgesia can coexist.

Clinical surveys of long-term opioid use in patients with both cancer and non–malignancy-associated pain have not shown escalating drug dosage to be inevitable; however, some degree of dose increase over time is often observed, particularly in younger patients and with use of short-acting opioids.

Carroll IR, Angst MS, Clark JD. Management of perioperative pain in patients chronically consuming opioids. *Reg Anesth Pain Med*. 2004;29:576–591.

Malhotra V, Bal R, Diwan S. Perioperative pain management. In: *AUA Update Series*. Linthicum, MD: American Urological Association, Education and Research; 2007;26:338–343.

Mitra S, Sinatra RS. Perioperative management of acute pain in the opioid-dependent patient. *Anesthesiology*. 2004;101:212–227.

B.3. What are the main differences between a chronic opioid-consuming patient and a patient who abuses or is addicted to opioids?

Patients undergoing surgery may not admit that they are actively abusing or addicted to pain medications; however, several

differences may clue the practitioner to possible aberrant use. First, the daily dose of opioid consumed by opioid-abusing patients before surgery is typically larger and may differ from that prescribed, which can be confirmed by checking a State Prescription Monitoring Program. Second, opioid-abusing or opioid-addicted patients often have identifiable risk factors and may suffer from coexisting psychiatric diseases. For example, heroin addicts have an elevated prevalence of depression, anxiety, psychosis, and personality disorders. Depression and anxiety are also independent predictors of severe pain after surgery and may complicate the management of postoperative pain. Although it is useful to identify abuse or addiction, many of the perioperative management issues with respect to chronic pain opioid-consuming patients also apply to patients who abuse or are addicted to opioids. The attitude of health care providers toward the use of opioids for controlling pain may be influenced by the abuse history, which makes these patients particularly vulnerable to inadequate postoperative pain control.

Farrell C, McConaghy P. Perioperative management of patients taking treatment for chronic pain. *BMJ*. 2012;345:e4148.

Hudson S, Wimsatt LA. How to monitor opioid use for your patients with chronic pain. *Fam Pract Manag*. 2014;21(6):6–11.

Lewis NL, Williams JE. Acute pain management in patients receiving opioids for chronic and cancer pain. *Contin Educ Anaesth Crit Care Pain*. 2005;5(4):127–129.

B.4. What issues need to be considered in the opioid-tolerant patient who is scheduled for surgery?

Tolerance develops at different rates to desired (analgesia) and undesired effects (sedation, nausea, euphoria, respiratory depression, constipation). Long-term use of opioids results in tolerance to some opioid effects such as analgesia, nausea, sedation, and respiratory depression but not to miosis or constipation. Cross-tolerance with other opioids also occurs.

Opioid-tolerant patients report higher pain scores at rest and on movement and also remain longer under the care of APSs than do other patients. The incidence of opioid-induced nausea and vomiting, however, may be lower in opioid-tolerant patients.

Farrell C, McConaghy P. Perioperative management of patients taking treatment for chronic pain. *BMJ*. 2012;345:e4148.

Lewis NL, Williams JE. Acute pain management in patients receiving opioids for chronic and cancer pain. *Contin Educ Anaesth Crit Care Pain*. 2005;5(4):127–129.

B.5. What would be your strategy regarding preoperative information and choice of anesthesia technique?

Acute pain management in opioid-dependent patients is a complex issue. There is a tendency among providers to use opioids sparingly, resulting in both poor pain management and withdrawal phenomena. As a result, patients may react with a degree of suspicion, mistrust, or even hostility. Patients need to be reassured that their drug history and dependence will not be an obstacle to the relief of pain. During assessment, care should be exercised to maintain privacy and confidentiality.

Despite the increasing prevalence of opioid dependency, there are few controlled studies available to guide the anesthesiologist in optimizing anesthetic and analgesic care. Because the minimum daily opioid dose that significantly increases postoperative opioid requirements and pain is not known, all patients on chronic opioids should be informed about the potential for difficult to control pain and increased opioid requirements during the postoperative period. Patients should be informed about alternative analgesic techniques that complement opioids.

The selection of anesthesia technique has to be done on an individual basis because there are no data favoring general, regional, or combined anesthesia for this specific patient

population. Although there is no evidence indicating superiority of regional anesthesia for chronic pain patients, individual consideration is likely to favor regional anesthesia. Expert opinion suggests that opioid-tolerant patients should be offered regional or neuraxial anesthesia or analgesia when possible.

Crumley S, Schraag S. The role of local anaesthetic techniques in ERAS protocols for thoracic surgery. *J Thorac Dis*. 2018;10(3):1998–2004.

Farrell C, McConaghy P. Perioperative management of patients taking treatment for chronic pain. *BMJ*. 2012;345:e4148.

Kopf A, Banzhaf A, Stein C. Perioperative management of the chronic pain patient. *Best Pract Res Clin Anaesthesiol*. 2005;19:59–76.

Lewis NL, Williams JE. Acute pain management in patients receiving opioids for chronic and cancer pain. *Contin Educ Anaesth Crit Care Pain*. 2005;5(4):127–129.

B.6. What are the choices for perioperative pain management in opioid-tolerant patients?

Management of these patients should focus on two main goals: (1) effective analgesia and (2) prevention of withdrawal. Preexisting opioid medications must be continued throughout the perioperative period to provide baseline analgesia and to avoid withdrawal. This applies for general anesthesia as well as regional anesthesia. During surgery, the required opioid dose consists of the daily opioid dose taken before surgery and the opioid dose necessary for the surgical intervention. The use of a continuous infusion of opioid or long-acting intravenous opioid may be the best way to provide a steady serum concentration if the oral route is unavailable, as is the case intraoperatively.

Catching up on the opioid dose in the postoperative period can be difficult because of inevitable delays in obtaining and administering opioids at the bedside, the high levels of pain that patients may experience, and a possible reluctance of recovery room staff to administer a sufficiently large opioid dose. Requirements for individual patients are difficult to predict;

however, patients who use even modest opioid doses (<50 mg per day oral morphine equivalent) before surgery may require their baseline opioid dose plus two or more times the amount of opioids typically used for adequate pain control in opioid-naive patients.

Regional anesthesia techniques have many benefits and may be particularly useful in chronic opioid-consuming patients because they provide excellent analgesia, avoid the need for high-dose opioids, and may be extended in duration with use of catheter-based techniques. Neuraxial opioids have also been used effectively in opioid-tolerant patients, and although higher doses are often required, these generally do not result in an increase in adverse effects.

Nevertheless, chronic opioid-consuming patients treated with regional and neuraxial techniques for postoperative pain control should also have access to systemic opioids by the intravenous or oral route for prevention of opioid withdrawal. IV-PCA is a useful modality for pain relief in opioid-tolerant patients. Larger bolus doses will often be needed. Opioid rotation (i.e., using an opioid that is different from their preadmission opioid) may also be of use. If preoperative opioid use is substantial, a long-acting intravenous agent such as methadone or a basal rate PCA may be required, although in general the amount of opioid to avoid withdrawal is much lower than the patient's usual dose. Withdrawal from opioids should be prevented by maintenance of normal preadmission opioid regimens where possible, or appropriate substitutions with another opioid or the same opioid through another route.

Ketamine can reduce opioid requirements in opioid-tolerant patients, both intraoperatively and postoperatively. It is an *N*-methyl-D-aspartic acid receptor antagonist and results in analgesia by inhibiting the processing of nociceptive information. Evidence shows that the addition of *N*-methyl-D-

aspartic acid receptor antagonists with other analgesics or as a sole agent for chronic (e.g., complex regional pain syndrome), ischemic, or neuropathic pain states can reduce the requirement for other analgesic agents. When ketamine is used as a continuous infusion in the postoperative setting, it can have an opioid-sparing effect, although there is no reduction in opioid-related side effects. It can also serve as a bridge until the patient is able to tolerate their home oral regimen. Perioperatively, ketamine is best used as an adjunct to opioid medications.

Multimodal analgesic regimens including combinations of NSAIDs, APAP, gabapentinoids, and topical local anesthetics are likely to provide benefit as well. Opioid antagonists (naloxone, naltrexone) or mixed agonist–antagonists (e.g., buprenorphine, pentazocine) should be avoided because their use precipitates acute withdrawal reactions in the setting of high full-agonist opioids.

Farrell C, McConaghy P. Perioperative management of patients taking treatment for chronic pain. *BMJ*. 2012;345:e4148.

Lewis NL, Williams JE. Acute pain management in patients receiving opioids for chronic and cancer pain. *Contin Educ Anaesth Crit Care Pain*. 2005;5(4):127–129.

Subramaniam K, Subramaniam B, Steinbrook RA. Ketamine as adjuvant analgesic to opioids: a quantitative and qualitative systematic review. *Anesth Analg*. 2004;99:482–495.

B.7. What issues need to be considered before discharging an opioid-tolerant patient?

Discharge planning must take into account the potential for prescribed opioids to be abused or misused by the patient as well as the home situation and anyone at risk for harm from misuse (children). Appropriate use of nonopioid analgesics where possible, communication with the primary physician, and patient education and support must all be considered.

Chronic opioid-consuming patients typically require

significantly higher postoperative opioid doses for adequate pain control than they received before surgery for their chronic pain symptoms. Attempting to discharge chronic opioid-consuming patients on the same opioid regimen they adhered to before surgery often results in inadequate pain control. Whatever the final oral dose chronic opioid-consuming patients are stabilized on at discharge, a tapering from this dose toward the preoperative opioid dose over 2 to 4 weeks is often a reasonable goal. In the case under consideration, the transdermal fentanyl patch should be left in place to provide the patient's preexisting opioid requirement, and additional short-acting analgesics should be prescribed for postoperative pain. It is also advisable to counsel the patient to discuss opioid prescribing with the existing outpatient provider preoperatively because many physicians require an opioid contract with single-provider prescribing for controlled substances.

Farrell C, McConaghy P. Perioperative management of patients taking treatment for chronic pain. *BMJ*. 2012;345:e4148.

Lewis NL, Williams JE. Acute pain management in patients receiving opioids for chronic and cancer pain. *Contin Educ Anaesth Crit Care Pain*. 2005;5(4):127–129.

C. Perioperative Pain Management for Ambulatory Surgery

C.1. What would be your preoperative considerations and advice to the patient?

Adequate postoperative pain management is often the limiting factor when determining whether a patient can have surgery performed as an ambulatory surgical procedure. Ensuring that the patient has appropriate expectations of the outcome of laparoscopic cholecystectomy is critical for a successful

conclusion to the procedure, especially with regard to postoperative pain. Unrealistic expectations for no pain at all can be met with anger, disappointment, and the fear and anxiety that something has gone wrong.

Planning for postoperative pain management should begin in the preoperative period. Patient education regarding the degree of pain that might be expected and discussion of the pain assessment tools and modalities of pain treatment that might be utilized should reduce the patient's anxiety and the fear of unrelieved pain. Reduced patient anxiety has been shown to reduce the incidence and severity of postoperative pain. In addition, patients have to be made aware of the importance of communicating their analgesic needs. Patients should receive instruction on the importance of coughing, deep breathing, ambulation, and postoperative rehabilitation. Patient information on acute postoperative pain management is available from reliable public sources such as the American Society of Anesthesiologists website, and patients can be directed to these sources for self-study.

Details of the complications of laparoscopic cholecystectomy given to patients vary between countries and cultures. The most relevant for postoperative pain is to mention the risk of conversion to open laparotomy in a small percentage of cases, which will be associated with a significantly larger incision, more pain, and longer period of hospitalization. Patients need to be informed that there are three types of pain often associated with laparoscopic cholecystectomy: (1) incisional, (2) visceral, and (3) shoulder pain. It is helpful to describe, in particular, the high incidence of referred pain in the shoulder and to reassure the patient that this is related to the laparoscopy and not necessarily his or her heart or chest. The patient should be informed that there is a relatively high risk of postoperative nausea and vomiting after laparoscopic cholecystectomy

(approximately 30% to 50%) and that appropriate prophylaxis will be administered (antiemetic strategies can be tailored based on clinical risk assessments such as the Apfel risk score for nausea and vomiting).

Predischarge patient information should also include the following: (1) that patients will receive analgesic and/or antiemetic medications for management of pain and postoperative nausea and vomiting at home, (2) that the care team will make a follow-up call and schedule a follow-up appointment, and (3) that he or she will get contact numbers in case there are problems or questions.

Apfel CC, Heidrich FM, Jukar-Rao S, et al. Evidence-based analysis of risk factors for postoperative nausea and vomiting. *Br J Anaesth*. 2012;109(5):742–753.

Crews JC. Multimodal pain management strategies for office-based and ambulatory procedures. *JAMA*. 2002;288:629–632.

Farrell C, McConaghy P. Perioperative management of patients taking treatment for chronic pain. *BMJ*. 2012;345:e4148.

C.2. What are the consequences of inadequate pain management after ambulatory surgery?

In the ambulatory setting, the type of surgery is a significant predictor of severity of postoperative pain. Even when postoperative pain is effectively treated in the postanesthesia care unit, it often recurs once the patient has returned home. A common example is a peripheral nerve block for orthopedic surgery, which provides excellent analgesia until the block has worn off several hours later.

Uncontrolled pain is associated with an increased incidence of postoperative nausea, agitation, prolonged postanesthesia care unit stay, delayed discharge from an ambulatory facility, and unanticipated hospital admission. Inadequate postoperative pain control is also the most frequent reason for patients to contact their provider after discharge from the hospital. More important,

the presence of postoperative symptoms including pain contributes to patient dissatisfaction with their surgical experience (**Table 51.1**).

TABLE 51.1 Consequences of Inadequate Pain Management after Ambulatory Surgery

Increased postanesthesia care unit stay
Increased phase II unit stay
Delayed discharge at home
Unanticipated hospital admission
Increased contact with family practitioner
Delayed return to daily living function
Decreased patient satisfaction

Dickerson DM. Acute pain management. *Anesthesiol Clin*. 2014;32(2):495–504.

C.3. What is the role of premedication or preoperative analgesic?

Preoperative administration of nonopioid analgesics reduces postoperative morphine requirements and pain scores. Commonly used agents include NSAIDs, acetaminophen, and gabapentinoids. These may be continued throughout the perioperative period or given as a one-time preoperative dose. Most commonly, these agents are given the morning of surgery with a small sip of water as part of a protocol for specific surgeries (orthopedic hip and knee arthroplasty having the most data).

Preemptive analgesia refers to the concept that an analgesic medication or intervention administered before surgical tissue injury may produce a greater effect than the same medication or intervention administered following surgical tissue injury. This preemptive analgesic effect has been demonstrated for several different medications in animal models, but clinical studies do not support a significant role for preemptive analgesia in human

patients. For multiple surgical procedures including thoracic and abdominal procedures, laparoscopic, and open, there is no strong evidence that preincisional timing of analgesic administration (preemptive analgesia) decreases the intensity or duration of postoperative pain, when compared with intraoperative or postoperative administration.

Elvir-Lazo OL, White PF. The role of multimodal analgesia in pain management after ambulatory surgery. *Current Opin Anesthesiol*. 2010;23:697–703.

Møiniche S, Kehlet H, Dahl JB. A qualitative and quantitative systematic review of preemptive analgesia for postoperative pain relief: the role of timing of analgesia. *Anesthesiology*. 2002;96:725–741.

C.4. Does the choice of anesthetic technique influence postoperative pain?

The choice of anesthetic technique has been shown to have a significant influence on postoperative analgesia in patients undergoing ambulatory surgery. Regional or neuraxial anesthesia techniques offer a number of advantages in outpatient surgery, including prolonged postoperative analgesia and decreased opioid side effects, but at the expense of prolonged recovery and time to discharge. For the case in question, a neuraxial or regional technique is not recommended for routine anesthetic management as most patients undergoing laparoscopic cholecystectomy do not convert to open procedures, and thus, the incisions are small and minimally painful postoperatively.

Total intravenous anesthesia (TIVA) offers an alternative to inhalational anesthesia, and although rapid recovery from anesthesia and reduction in nausea and vomiting are recognized benefits, the analgesic components of commonly used agents in TIVA have either no analgesic effect (propofol) or a very short duration (remifentanil) and do not contribute significantly to postoperative analgesia.

Opioids remain the primary drugs used to provide intraoperative and postoperative analgesia in the United States. However, the role of opioids in ambulatory surgery remains controversial. The use of opioids may be associated with a dose-dependent increase in adverse effects, including nausea, vomiting, sedation, bladder dysfunction, and respiratory depression, all of which may contribute to a delayed recovery.

Consensus recommendations for anesthetic management of laparoscopic cholecystectomy include use of paracetamol or acetaminophen and NSAID preoperatively, dexamethasone intraoperatively, and opioids primarily for rescue analgesia. Gabapentinoids, intraperitoneal local anesthetic, neuraxial techniques, and transversus abdominis plane blocks are not usually indicated.

Barazanchi AWH, MacFater WS, Rahiri JL, et al. Evidence-based management of pain after laparoscopic cholecystectomy: a PROSPECT review update. *Br J Anaesth*. 2018;121(4):787–803.

Kehlet H, Gray AW, Bonnet F, et al. A procedure-specific systematic review and consensus recommendations for postoperative analgesia following laparoscopic cholecystectomy. *Surg Endosc*. 2005;19:1396–1415.

C.5. Are nonsteroidal anti-inflammatory drugs (NSAIDs) effective? If so, does the choice of drug matter?

The opioid-sparing effects of NSAIDs lower the risk of postoperative nausea and vomiting, pruritus, constipation, and respiratory depression, thereby improving patient comfort and allowing for an earlier discharge.

The introduction of parenteral preparations of NSAIDs and the widespread acceptance of the concept of multimodal "balanced" analgesia has increased their use in the management of perioperative pain. NSAIDs commonly available for intravenous use include ketorolac, diclofenac, and ibuprofen. NSAIDs have weaker analgesic properties than opioids and also exhibit a "ceiling effect" but may be more effective to decrease

the risk of breakthrough pain because of their more prolonged duration of action and are valuable adjuvants when used in combination with other agents.

There is no documented evidence of superiority of any particular NSAID for perioperative use. Therefore, the choice of NSAID is dependent on the route of administration, the duration of analgesia, propensity for side effects, availability, and cost. The oral bioavailability of most NSAIDs is high, and this is the preferred route when tolerated.

COX-2 inhibitors have been demonstrated in multiple clinical trials to produce analgesic efficacy equal to that of the traditional nonselective NSAIDs with fewer cyclooxygenase-1 (COX-1)–mediated adverse effects (gastrointestinal discomfort, decreased renal blood flow, platelet inhibition). NSAIDs used over a short period for postoperative analgesia have not been demonstrated to cause any major adverse events in healthy patients, although use can precipitate congestive heart failure (CHF) exacerbation in at-risk patients and has been associated with anastomotic leak in colorectal surgery.

Argoff CE. Recent management advances in acute postoperative pain. *Pain Pract*. 2014;14(5):477–487.

Gupta A, Bah M. NSAIDs in the treatment of postoperative pain. *Curr Pain Headache Rep*. 2016;20(11):62.

Malhotra V, Bal R, Diwan S. Perioperative pain management. In: *AUA Update Series*. Linthicum, MD: American Urological Association, Education and Research; 2007;26:338–343.

C.6. What is the role of surgical technique in influencing postoperative pain after a laparoscopic cholecystectomy?

There are three types of pain after laparoscopic cholecystectomy: incisional, subphrenic, and shoulder pain. Factors responsible for the pain may be related to surgical

incisions, carbon dioxide (CO_2) insufflation during surgery, and residual gas postprocedure. Higher insufflation pressures should be avoided because they can significantly increase the severity of postoperative pain. Subphrenic and shoulder pain after laparoscopic procedures can arise from diaphragmatic and phrenic nerve irritation due to insufflated CO_2. Residual insufflating gas can also increase the intensity of postlaparoscopic pain. This pain tends to be aggravated positionally and may persist for several days after surgery. Evidence from prospective studies to prevent postoperative pain after laparoscopy includes the following findings:

- Low-pressure CO_2 pneumoperitoneum is superior to conventional CO_2 pneumoperitoneum.
- Peritoneal saline lavage after CO_2 pneumoperitoneum is effective in reducing postoperative pain.
- Aspiration of residual pneumoperitoneum prior to closure is recommended.
- Single-port incision techniques have not been found to decrease postoperative pain.

Barazanchi AWH, MacFater WS, Rahiri JL, et al. Evidence-based management of pain after laparoscopic cholecystectomy: a PROSPECT review update. *Br J Anaesth*. 2018;121(4):787–803.

Phelps P, Cakmakkaya OS, Apfel CC, et al. A simple clinical maneuver to reduce laparoscopy-induced shoulder pain: a randomized controlled trial. *Obstet Gynecol*. 2008;111(5):1155–1160.

C.7. What would be your strategy for pain control after discharge home?

After discharge, APAP, NSAIDs, or opioids, either alone or in combination, are frequently used to provide postoperative pain relief.

APAP and paracetamol are thought to work through central inhibition of prostaglandin synthesis, possibly through a

cyclooxygenase-3 (COX-3) inhibitory mechanism. They are commonly used due to easy tolerability and good safety profile. Care should be taken when using opioid/APAP combination products as the APAP component of the combination should be considered the limiting factor for use, generally no more than 3 to 4 g daily.

NSAIDs inhibit cyclooxygenase either nonspecifically or targeted to COX-2, thereby decreasing inflammation and pain related to local tissue injury. They inhibit platelet function to variable degrees and for this reason are sometimes contraindicated in the immediate postoperative period. Nonetheless, because the majority of postoperative pain is nociceptive and inflammatory, NSAIDs can often be of great benefit.

Opioids are indicated in the acute postoperative period, exerting their effects centrally in the spinal cord and brain. Generally, because postsurgical pain is acute rather than chronic in nature, short-acting opioids such as oxycodone, hydromorphone, or hydrocodone for breakthrough pain every 3 to 4 hours as needed are sufficient. If necessary, a dose range may be provided to cover mild, moderate, and severe pain. In patients with frequent need for breakthrough dosing and history of chronic opioid use and tolerance, however, a long-acting formulation (methadone, fentanyl patch, or extended-release formulation of a short-acting opioid) on a scheduled basis may also be required.

If pain does not improve or if escalating rather than tapering doses of opioids are observed, antineuropathic agents are often initiated. These include topical agents such as lidocaine 5% cream or patch, gabapentinoids, tricyclic antidepressants, and selective norepinephrine reuptake inhibitors. If a patient requires these additional interventions, they will often benefit from an APS consult and possible outpatient pain management follow-

up.

Jacob B, Chen D, Towfigh S, eds. *The SAGES Manual of Groin Pain*. Switzerland: Springer International; 2016: 267–276.

D. The Role of an Acute Pain Service (APS)

D.1. What is the extent of the problem, and which patients are at greatest risk of undertreatment?

Pain relief after surgery continues to be a major medical challenge. Despite a significant improvement over the last decade in our understanding of acute and chronic pain mechanisms and the establishment of APSs, recent studies continue to report that postoperative pain management is not satisfactory for many patients. In addition, publications of guidelines for acute pain management, the introduction of pain as "the fifth vital sign," and the incorporation of the standards advocated by The Joint Commission have not yet translated into improved postoperative analgesia.

More than 30% of patients report moderate-to-severe pain after surgery. More recent surveys of postdischarge pain put that number even higher. Clinical risk scores to identify patients most at risk for postoperative pain are scarce and not commonly used in practice. Certain patient subpopulations are at greater risk of undertreatment, including infants and children, the elderly, ethnic minorities, and patients with psychiatric illness or those unable to communicate.

Apfelbaum JL, Chen C, Mehta SS, et al. Postoperative pain experience: results from a national survey suggest postoperative pain continues to be undermanaged. *Anesth Analg*. 2003;97:534–540.

Ashburn MA, Caplan RA, Carr DB, et al. Practice guidelines for acute pain management in the perioperative setting. *Anesthesiology*. 2004;100:1573–1581.

D.2. What are the consequences of inadequate postoperative pain relief?

Evidence suggests that inadequate relief of postoperative pain results in harmful physiologic and psychological consequences that lead to significant morbidity, delaying recovery and the return to activities of daily living. Acutely, postoperative splinting can lead to atelectasis, whereas autonomic lability associated with pain can result in increased myocardial oxygen demand and increased incidence of perioperative myocardial infarction in at-risk adults. In children, postoperative pain has been found to be an important cause for long-lasting temper tantrums and behavioral changes. In addition, the presence of postoperative pain significantly contributes to patients' dissatisfaction with their anesthesia and surgical experience.

CPSP has long been recognized as a major factor in delaying recovery and return to normal daily living. Long-lasting pain is often reported after several common surgical procedures including thoracotomy, mastectomy, hernia repair, and limb amputation. Predisposing risk factors include the severity of preoperative and postoperative pain, intraoperative nerve injury, and psychological vulnerability. Specific early analgesic interventions may reduce the incidence.

Dworkin RH, McDermott MP, Raja SN. Preventing chronic postsurgical pain: how much of a difference makes a difference? *Anesthesiology*. 2010;112(3):516–518.

Joshi GP, Ogunnaike BO. Consequences of inadequate postoperative pain relief and chronic persistent postoperative pain. *Anesthesiol Clin North America*. 2005;23:21–36.

Mittnacht A, Shariat A, Weiner M, et al. Regional techniques for cardiac and cardiac-related procedures. *J Cardiothorac Vasc Anesth*. 2019;33:532–546.

D.3. What is the role of an APS in improving postoperative pain management?

The immediate solution to the problem of inadequate pain relief

lies not so much in the development of new analgesic drugs or technologies but in the development of an appropriate organization to utilize existing expertise effectively.

Moreover, effective acute pain management results from education and organizational structure for the delivery of pain relief rather than the specific analgesic techniques themselves. Even simple methods of pain relief can be more effective if proper attention is given to their appropriate, evidence-based use. In many institutions, APSs assume responsibility for managing more advanced methods of pain relief such as patient-controlled analgesia, epidural analgesia, and peripheral nerve catheters to ensure patients receive optimum care from providers well-versed with these analgesic modalities. Additionally, APSs often follow chronic pain patients who are difficult for primary teams to manage and whose complex pain issues are best treated using a multimodal approach. With a growing focus on the perioperative surgical home and the anesthesiologist's place in providing continued care before and after surgery, the role of APSs is likely to expand even further.

American Society of Anesthesiologists. Practice guidelines for acute pain management in the perioperative setting: an updated report by American Society of Anesthesiologists, Task Force on Acute Pain Management. *Anesthesiology*. 2012;116:248–273.

Zaccagnino MP, Bader AM, Sang CN, et al. The perioperative surgical home: a new role for the acute pain service. *Anesth Analg*. 2017;125(4):1394–1402.

D.4. Does an APS improve postoperative outcome?

The introduction of APSs has led to an increase in the appropriate use of specialized analgesic techniques such as IV-PCA, neuraxial blockade, and peripheral nerve catheters. The implementation of these techniques is an advance in improving analgesia and patient well-being and in reducing postoperative morbidity. In addition, an APS may reduce "analgesic gaps" that can occur during the transition from IV-PCA or epidural

analgesia to oral analgesic therapy. Although evaluating the safety of analgesic techniques is an important objective of an APS, its role in preventing and reducing adverse events has not been well-documented; however, consolidation of decisions regarding pain regimens under one service is likely to have several benefits. First, standardization of protocols decreases prescription or drug administration error. Second, having one service responsible for pain orders decreases the incidence of redundancy and multiple opioid orders. Finally, the availability of a service primarily dedicated to pain is likely to increase the speed and efficacy of interventions and decrease patient pain scores.

In a literature review, evaluating the effects of an APS on postoperative outcome in 44 retrospective and 4 prospective clinical trials including 84,097 postoperative patients, the authors found that the implementation of an APS was associated with a significant decrease in pain scores. In addition, the introduction of an APS was associated with less postoperative nausea and vomiting and urinary retention. However, the authors could not draw clear conclusions about patient satisfaction or postoperative morbidity due to a large variability in the studies regarding composition of the APSs and services provided.

Pöpping DM, Zahn PK, Van Aken HK, et al. Effectiveness and safety of postoperative pain management: a survey of 18 925 consecutive patients between 1998 and 2006 (2nd revision): a database analysis of prospectively raised data. *Br J Anaesth*. 2008;101:832–840.

Werner MU, Søholm L, Rotbøll-Nielsen P, et al. Does an acute pain service improve postoperative outcome? *Anesth Analg*. 2002;95:1361–1372.

52 Acupuncture

Yuan-Chi Lin

A 58-year-old woman with a history of osteoarthritis was scheduled for arthroscopic surgery of her right knee. She experienced severe postoperative nausea and vomiting in the postanesthesia care unit. Despite the use of conventional therapies, her nausea and vomiting persisted. Her past medical history was significant with knee osteoarthritis for 10 years, a mastectomy 5 years ago related to breast cancer, an anxiety disorder, chronic headaches, chronic neck and back pain, peptic ulcer disease, and an allergy to Novocain. What role can acupuncture therapy play in her care?

A. Acupuncture as a Complementary Medical Therapy

1. What is acupuncture?
2. How is acupuncture practiced? (**Video 52.1**)
3. What are the mechanisms of acupuncture analgesia?
4. What were the conclusions of the National Institutes of Health Consensus Conference about acupuncture?
5. Can acupuncture be a novel nonopioid alternative pain therapy?

B. Acupuncture for the Treatment of Chronic Conditions

1. What are the rationales in integrating acupuncture for the treatment of postoperative nausea and vomiting?

2. Can acupuncture be used for the treatment of chemotherapy-induced nausea and vomiting?
3. How effective is acupuncture for the management of chronic headache?
4. Can acupuncture be used for the treatment of chronic neck and back pain?
5. Can acupuncture be used for the treatment of osteoarthritis?
6. What role can acupuncture play in the care of patients with cancer?
7. Can acupuncture/acupressure be used to decrease anxiety?
8. What is ear acupuncture/acupressure? Can it be useful for alleviating anxiety and pain? (**Video 52.2**)

C. Complications

1. What are the possible complications of acupuncture treatment?

A. Acupuncture as a Complementary Medical Therapy

A.1. What is acupuncture?

Acupuncture is one of the treatment modalities of comprehensive traditional Chinese medicine (TCM). The word *acupuncture* is derived from the Latin words *acus*, "needle," and *punctura*, "a pricking." The original Chinese term for acupuncture is *Jin Jiao*, which describes the practice of "acupuncture and moxibustion." Moxibustion is the burning of moxa (*Artemisia vulgaris*) over the acupuncture points.

The history of TCM can be traced back 3,000 years. *The Yellow Emperor's Classic of Internal Medicine* from the fourth century BC described the practice of puncturing the body for pain relief. TCM is a system of thoughts and practices that are based on the investigations of nature, causes, and effects. It takes the principles of realism and ethics and then employs them for the

prevention of diseases and healing of illnesses.

The concept *yin and yang* underlies the theoretical framework of acupuncture. Yin and yang are two opposite dynamics that cannot exist in isolation. Rather, they are in a constant state of dynamic balance. If yin and yang are not balanced, illnesses can occur.

The human body is controlled by a vital force called *Qi* (pronunciation "chee"). *Qi* circulates throughout the body and defends its various parts. There are 365 identified acupuncture points in the body, which fall along 12 principal and 8 extrameridian systems. *Qi* is postulated to flow through these meridians in the body.

A.2. How is acupuncture practiced? (Video 52.1)

Acupuncture utilizes a technique of inserting very fine thread-thin needles into strategic points in the body called *acupuncture points*. Acupuncture needles vary from 36 to 42 gauge and 0.5 to 5 inches in length. There are a wide variety of needles currently available. In *The Yellow Emperor's Internal Classic*, book of Ling Shu, it described nine shapes of acupuncture needles. Sterile, disposable stainless-steel acupuncture needles are the current standard for acupuncture treatment.

After cleaning the site of the needle entrance on the skin, the acupuncture needle is inserted a few millimeters into the epidermis. Following placement of the acupuncture needle, stimulation of the acupuncture point may be achieved manually or by the application of low-voltage electrodes onto the needle in a method called *electroacupuncture*.

Each acupuncture point has a prescribed depth of insertion. Manual techniques may involve the lifting and thrusting of the needle, or twisting and twirling. *De-Qi* is a typical sensation that is associated with proper acupuncture needle position. Patients describe the sensation as a feeling of soreness, numbness,

warmth, heaviness, or pressure around the area where the needle is inserted. Many practitioners consider this sensation to be crucial in achieving the effects of acupuncture. Electroacupuncture achieves a similar effect through the use of high- or low-frequency electricity.

Minimal pain is associated with acupuncture. For various conditions, multiple acupuncture treatment sessions over an extended period may be required to achieve its greatest effectiveness.

Auricular, hand, and scalp acupuncture can be used as microsystems of acupuncture. For example, auricular acupuncture (**Fig. 52.1**) manipulates the upper region of the external ear to alleviate conditions in the leg and feet. The middle region of the external ear corresponds to chest and back pain. The lower regions are used to relieve headache and neurologic conditions. Auricular acupuncture can also be used for preoperative anxiety control.

FIGURE 52.1. Auricular acupuncture. Δ, heart point; •, shen men; ♦, autonomic point. (*Reprinted from www.permacharts.com with permission.*)

The frequency, as well as the number of acupuncture treatments, varies among acupuncture providers. Most practitioners would agree that more than one treatment is necessary to experience the full effect of acupuncture.

Chernyak GV, Sessler DI. Perioperative acupuncture and related techniques. *Anesthesiology*. 2005;102:1031–1049.

A.3. What are the mechanisms of acupuncture analgesia?

Acupuncture inhibits the transmission of pain according to the gate control theory. It may act by stimulating sensory A-β fibers, thereby directly inhibiting the spinal transmission of pain by a smaller A-δ and C fibers.

Acupuncture stimulates the production of endogenous opioid peptides, such as endorphins and enkephalins, and stimulates the endogenous descending inhibitory pathways. In human studies, analysis of cerebrospinal fluid showed elevated levels of serotonin, endorphins, and enkephalins following acupuncture treatments. Acupuncture analgesia is mainly achieved by the activation of the endogenous antinociceptive system to modulate pain transmission and pain response. Low-frequency (2 Hz) and high-frequency (100 Hz) electrical acupuncture selectively induces the release of enkephalins and dynorphins in both experimental animals and humans. Acupuncture analgesia can be reversed by naloxone.

Functional magnetic resonance imaging has been used to investigate the effect of acupuncture in normal volunteers. With functional magnetic resonance imaging, acupuncture needle manipulation on the LI4 (He Gu, 合谷) point (**Fig. 52.2**) is seen to modulate the activity of the limbic system and subcortical structure. Individual variation occurs in the cortical activation patterns elicited by electrical acupuncture stimulation. Real

acupuncture elicited significantly higher activation than sham acupuncture over the hypothalamus and primary somatosensory and motor cortex and deactivation over the rostral segment of anterior cingulated cortex.

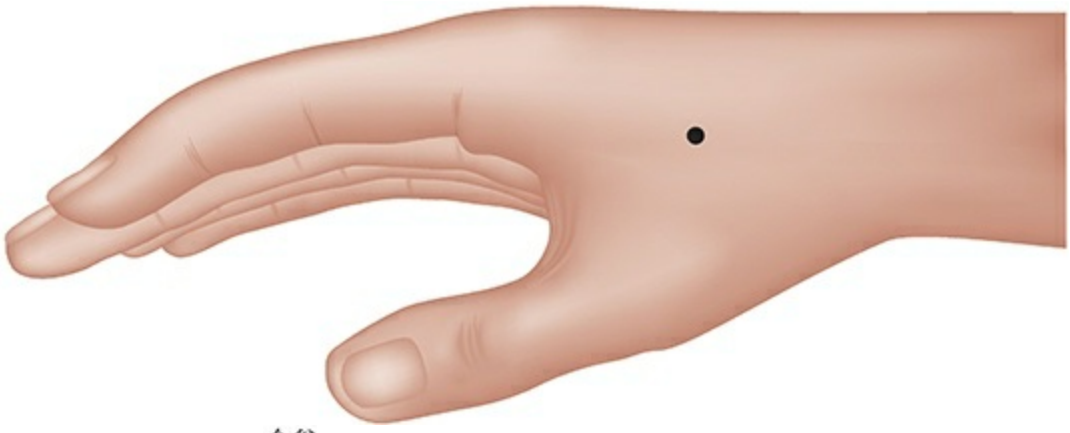

FIGURE 52.2. LI4 (He Gu, 合谷) acupuncture point is on the dorsum of the hand, between the first and second metacarpal bones, radial to the midpoint of the second metacarpal bone. (*Reprinted from www.permacharts.com with permission.*)

Han JS. Acupuncture and endorphins. *Neurosci Lett*. 2004;361(1–3):258–261.

Hui KK, Liu J, Makris N, et al. Acupuncture modulates the limbic system and subcortical gray structures of the human brain: evidence from fMRI studies in normal subjects. *Hum Brain Mapp*. 2000;9:13–25.

Wu MT, Sheen JM, Chuang KH, et al. Neuronal specificity of acupuncture response: a fMRI study with electroacupuncture. *Neuroimage*. 2002;16:1028–1037.

Zhang R, Lao L, Ren K, et al. Mechanisms of acupuncture-electroacupuncture on persistent pain. *Anesthesiology*. 2014;120(2):482–503.

A.4. What were the conclusions of the National Institutes of Health Consensus Conference about acupuncture?

A National Institutes of Health Consensus Conference concluded that acupuncture is an effective therapeutic intervention that is widely practiced in the United States. Promising results have emerged supporting the efficacy of acupuncture in adult postoperative and chemotherapy-related nausea and vomiting and in postoperative dental pain. In other conditions, such as addiction, stroke rehabilitation, headache,

menstrual cramps, tennis elbow, fibromyalgia, myofascial pain, osteoarthritis, low back pain, carpal tunnel syndrome, and asthma, acupuncture may also be useful as an adjunct treatment or as an acceptable alternative when included in a comprehensive management program. Further research is expected to uncover additional areas in which acupuncture interventions are useful.

National Institutes of Health Consensus Conference. Acupuncture. *JAMA*. 1998;280:1518–1524.

A.5. Can acupuncture be a novel nonopioid alternative pain therapy?

Prescribing opioid analgesics has been used in the management of acute and chronic pain. However, there are adverse effects associated with opioid use and the potential for addiction with chronic usage. More concerned about whether the overprescribing of opioids for chronic pain is contributing to the current opioid crisis. Novel nonopioid alternative pain therapies are being investigated given the current opioid crisis; however, focus on exploration in complementary and alternative therapies is also of importance. Acupuncture as an integrative medicine for pain can play a major role in reducing the frequency and amount of opioid usage. Supported by evidence review, acupuncture is categorized as having strong positive evidence in pain management. It may be integrated more routinely into pain management.

Lin YC, Wan L, Jamison RL. Using integrative medicine in pain management: an evaluation of current evidence. *Anesth Analg*. 2017;125:2081–2093.

Volkow ND, Collins FS. The role of science in addressing the opioid crisis. *N Engl J Med*. 2017;377:391–394.

B. Acupuncture for the Treatment of Chronic

Conditions

B.1. What are the rationales in integrating acupuncture for the treatment of postoperative nausea and vomiting?

Postoperative nausea and vomiting occur frequently following surgery and are best avoided whenever possible. Acupuncture is a commonly used therapy for the treatment of these symptoms. Stimulation of the acupuncture PC6 (*Nei Guan* 內關 *acupuncture point*; in Chinese, this means *gate of the internal organ*) points by acupuncture needles, electrical apparatus, pressure, or magnets is used to achieve relief of nausea and vomiting. The PC6 acupuncture point is located 2 cun (tsun), approximately 2.6 in., above the transverse crease of the wrist, and between the tendons of the muscle palmaris longus and muscle flexor carpi radialis (**Fig. 52.3**).

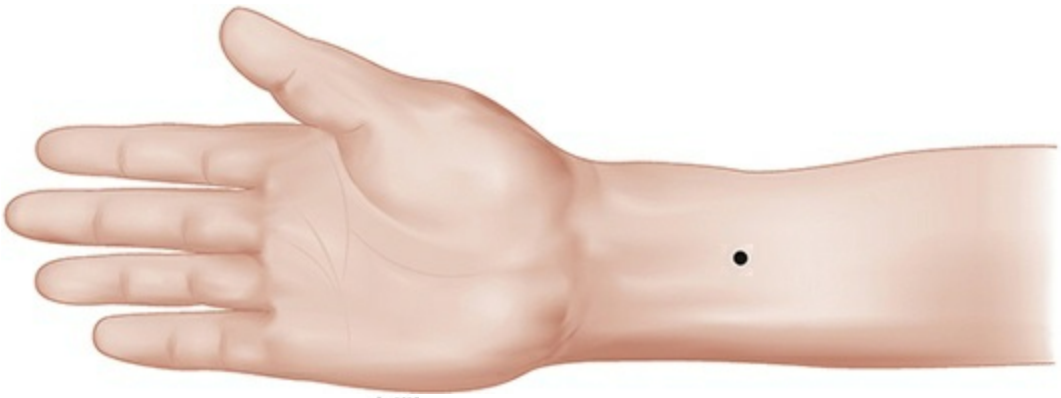

FIGURE 52.3. The PC6 (Nei Guan, 內關) acupuncture point is located 2 cun (tsun), approximately 2.6 in., above the transverse crease of the wrist, between the tendons of the muscle palmaris longus and muscle flexor capri radialis.

Studies support the use of acupuncture for the treatment of postoperative nausea and vomiting. A systemic review was conducted of 33 randomized controlled trials of acupuncture and acupressure. The results were positive in 27 of these trials. A randomized controlled trial of pediatric patients undergoing

tonsillectomy using electroacupuncture in conscious patients showed significant reduction in the occurrence of nausea compared with those in the sham and control groups. The efficacy of acupuncture for postoperative nausea and vomiting prevention is similar to that of commonly used pharmacotherapies. A double-blind, randomized, placebo-controlled study revealed that hand acupressure is an effective method for reducing postoperative vomiting in children after strabismus repair.

PC6 acupressure is a noninvasive method that may have a place as prophylactic antiemetic therapy during gynecologic surgery. Alkaissi et al. did a prospective randomized controlled trial of acupressure for the prevention of postoperative nausea and vomiting for women undergoing general anesthesia for elective gynecologic surgery with positive results.

Alkaissi A, Evertsson K, Johnsson VA, et al. P6 acupressure may relieve nausea and vomiting after gynecological surgery: an effectiveness study in 410 women. *Can J Anaesth*. 2002;49:1034–1039.

Frey UH, Scharmann P, Löhlein C, et al. P6 acustimulation effectively decreases postoperative nausea and vomiting in high-risk patients. *Br J Anaesth*. 2009;102:620–625.

Gan TJ, Diemunsch P, Habib AS, et al. Consensus guideline for the management of postoperative nausea and vomiting. *Anesth Analg*. 2014;118:85–113.

B.2. Can acupuncture be used for the treatment of chemotherapy-induced nausea and vomiting?

Acupuncture/acupressure at the PC6 acupuncture point has been shown to have a protective effect on people experiencing chemotherapy-induced nausea and vomiting. A review of 11 randomized controlled trials studying the effectiveness of acupuncture point stimulation on chemotherapy-induced nausea and vomiting revealed that electroacupuncture reduced chemotherapy-induced acute vomiting.

Ezzo JM, Richardson MA, Vickers A, et al. Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting. *Cochrane Database Syst Rev*. 2006;(2):CD002285.

B.3. How effective is acupuncture for the management of chronic headache?

Acupuncture therapy for migraine headaches has been reported to be effective in several adult studies. In a randomized controlled trial of 160 women with migraines, acupuncture was proven to be adequate for migraine prophylaxis. Relative to flunarizine, acupuncture treatment exhibited greater efficacy in the first months of therapy and better patient tolerance. A systemic review of 22 trials including a total of 1,042 patients suggests that acupuncture has a role in the treatment of recurrent headaches. In a randomized controlled trial of 401 patients with chronic migraine headaches, it was also shown that through 12 months of follow-up, acupuncture was relatively cost-effective. Compared with the patients in the control groups, patients receiving acupuncture used 15% less medication, made 25% fewer visits to general practitioners, and took 15% fewer sick days from work.

Cochrane database of systematic review of 11 trials with 2,317 patients with episodic or chronic tension-type headache revealed that acupuncture could be a valuable nonpharmacologic tool in patients with frequent episodic or chronic tension-type headaches. In regard to acupuncture for migraine prophylaxis, meta-analysis of 22 trials with 4,419 participants shows acupuncture to be at least as effective as, and possibly more effective than, prophylactic drug treatment with fewer adverse effects. Acupuncture should be considered a treatment option for patients willing to undergo this treatment.

Linde K, Allais G, Brinkhaus B, et al. Acupuncture for tension-type headache. *Cochrane Database Syst Rev*. 2016;(4):CD007587.

Linde K, Allais G, Brinkhaus B, et al. Acupuncture for the prevention of

episodic migraine. *Cochrane Database Syst Rev*. 2016;(6):CD001218.

Melchart D, Linde K, Fischer P, et al. Acupuncture for recurrent headaches: a systematic review of randomized controlled trials. *Cephalalgia*. 1999;19:779–786.

Vickers AJ, Rees RW, Zollman CE, et al. Acupuncture for chronic headache in primary care: large, pragmatic, randomized trial. *BMJ*. 2004;328:744.

B.4. Can acupuncture be used for the treatment of chronic neck and back pain?

In a randomized controlled trial of 177 patients with chronic neck pain, the effectiveness of acupuncture, massage, and "sham" laser acupuncture were compared. A study followed 14,161 patients with chronic neck pain for a period of more than 6 months. The patients in the acupuncture group received up to 15 acupuncture sessions over 3 months. The reported neck pain levels and disability scores of the members of the acupuncture group were improved over those of the control group. Treatment success was followed and maintained for 6 months.

A large German clinical study involved 1,162 patients with chronic low back pain indicated that both "real" and "sham" acupuncture treatment were significantly better than conventional therapy for at least 6 months. Another large German study of 1,549 patients with chronic low back pain showed acupuncture plus routine care was associated with marked clinical improvements in patients with chronic low back pain and was relatively cost-effective. A systemic review that involved 23 trials of 6,359 patients with low back pain revealed that acupuncture can be a useful supplement to other forms of conventional therapy for nonspecific low back pain.

Haake M, Müller HH, Schade-Brittinger C, et al. German Acupuncture Trials (GERAC) for chronic low back pain: randomized, multicenter, blinded, parallel-group trial with 3 groups. *Arch Intern Med*. 2007;167:1892–1898.

Irnich D, Behrens N, Molzen H, et al. Randomised trial of acupuncture compared with conventional massage and "sham" laser acupuncture for treatment of chronic neck pain. *BMJ*. 2001;322:1574–1578.

Witt CM, Jena S, Brinkhaus B, et al. Acupuncture for patients with chronic neck pain. *Pain*. 2006;125:98–106.

Yuan J, Purepong N, Kerr DP, et al. Effectiveness of acupuncture for low back pain: a systematic review. *Spine*. 2008;33:887–900.

B.5. Can acupuncture be used for the treatment of osteoarthritis?

Evidence exists for the efficacy of acupuncture for reducing the pain and dysfunction of osteoarthritis. In a study of 300 patients with chronic osteoarthritis of the knee, participants were randomly assigned to acupuncture, minimal acupuncture, or wait-list control group. After 8 weeks of treatment, pain and joint function were improved more with acupuncture than with minimal or no acupuncture.

In another randomized controlled trial of 570 patients with osteoarthritis of the knee, the acupuncture group received 23 true acupuncture sessions over 26 weeks. Acupuncture was shown to provide improvement in function and pain relief as an adjunctive therapy for osteoarthritis of the knee when compared with credible sham acupuncture and education control groups.

In a trial of 30 patients with symptomatic osteoarthritis of the knee, participants were randomized into one of three treatment groups. One group of patients received acupuncture alone, another group of patients received acupuncture but continued on their symptomatic medication, and the third group of patients used their symptomatic medication for the first 5 weeks and then had a course of acupuncture added. The patients receiving acupuncture were treated twice weekly over 5 weeks. The results of this study concluded that manual and electroacupuncture causes a significant improvement in the symptoms of osteoarthritis of the knee, either alone or as an adjunct therapy, with no loss of benefit after 1 month.

Current evidence supports the usage of acupuncture for osteoarthritis. A systemic review of acupuncture in osteoarthritis

pain management indicates reduction in pain intensity, improvement in functional mobility and quality of life.

Berman BM, Lao L, Langenberg P, et al. Effectiveness of acupuncture as adjunctive therapy in osteoarthritis of the knee: a randomized, controlled trial. *Ann Intern Med*. 2004;141:901–910.

Manyanga T, Froese M, Zarychanski R, et al. Pain management with acupuncture in osteoarthritis: a systemic review and meta-analysis. *BMC Complement Altern Med*. 2014;14:312–320.

Tukmachi E, Jubb R, Dempsey E, et al. The effect of acupuncture on the symptoms of knee osteoarthritis—an open randomized controlled study. *Acupunct Med*. 2004;22:14–22.

Witt C, Brinkhaus B, Jena S, et al. Acupuncture in patients with osteoarthritis of the knee: a randomised trial. *Lancet*. 2005;366:136–143.

B.6. What role can acupuncture play in the care of patients with cancer?

A report of a randomized controlled trial of 90 patients with cancer pain revealed clear benefit from auricular acupuncture for cancer patients experiencing pain, despite stable analgesic treatment. It is reasonable to use acupuncture for the management of chronic cancer-related pain management. Acupuncture can also be used to control chemotherapy-related nausea and vomiting.

Alimi D, Rubino C, Pichard-Léandri E, et al. Analgesic effect of auricular acupuncture for cancer pain: a randomized, blinded, controlled trial. *J Clin Oncol*. 2003;21:4120–4126.

Ezzo JM, Richardson MA, Vickers A, et al. Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting. *Cochrane Database Syst Rev*. 2006;(2):CD002285.

B.7. Can acupuncture/acupressure be used to decrease anxiety?

Acupuncture or acupressure on Yin-Tang acupuncture point is effective in producing sedation. The Yin-Tang acupuncture point is on the forehead, at the midpoint between the two

eyebrows.

Acar et al. did a prospective, randomized, single-blind, controlled study of 52 patients receiving acupuncture on Yin-Tang or sham acupuncture. The bispectral index (BIS) values in the acupuncture group were significantly lower than in the sham group. Paraskeva et al. did a study of 50 patients randomly assigned to acupuncture of the Yin-Tang point or control point. Acupuncture application significantly decreased the BIS value compared to the control group.

Acar HV, Cuvaş O, Ceyhan A, et al. Acupuncture on Yintang point decreases preoperative anxiety. *J Altern Complement Med*. 2013;19(5):420–424.

Paraskeva A, Melemeni A, Petropoulos G, et al. Needling of the extra 1 point decreases BIS values and preoperative anxiety. *Am J Chin Med*. 2004;32(5):789–794.

B.8. What is ear acupuncture/acupressure? Can it be useful for alleviating anxiety and pain? (Video 52.2)

Auricular acupressure is an effective treatment for anxiety during ambulance transport. Kober et al. studied 36 patients who required ambulance transport to medical facilities; patients were randomized to receive auricular acupressure at the relaxation point or at a sham point. Patients in the auricular acupressure group reported significantly less anxiety than patients in the sham group on arrival to the hospital. Barker et al. reported a randomized controlled trial of 38 patients with acute hip fractures receiving either bilateral auricular acupressure or the sham control during ambulance transport; the patients in the acupressure group had less pain, less anxiety, and lower heart rates on arrival to the hospital.

Auricular acupuncture points may be stimulated for a longer period of time by using ear seeds or ear tacks. Ear seeds can be small seeds from the dry Vaccaria plant or can be made from stainless steel seed. These seeds are held in place on the ear with

a small piece of adhesive tape (**Video 52.3**).

Barker R, Kober A, Hoerauf K, et al. Out-of-hospital auricular acupressure in elder patients with hip fracture: a randomized double-blinded trial. *Acad Emerg Med*. 2006;13(1):19–23.

Kober A, Scheck T, Schubert B, et al. Auricular acupressure as a treatment for anxiety in prehospital transport settings. *Anesthesiology*. 2003;98(6):1328–1332.

C. Complications

C.1. What are the possible complications of acupuncture treatment?

Acupuncture is extremely safe. Rarely, a patient may have some bruising at an acupuncture site that is swiftly resolved. The major risk is infection from the use of improperly sterilized needles. This can be avoided by using disposable sterile acupuncture needles and the proper insertion of the needles. Vasovagal scope may occur in very rare incidents. Case reports have documented a pneumothorax caused by improperly inserted acupuncture needles.

A study of the adverse effects of 34,000 acupuncture consultations in the United Kingdom revealed that the most common adverse events were bleeding, needling pain, and aggravation of symptoms. None of these events were serious. Similarly, a review of nine surveys showed that the most common adverse events were needle pain, tiredness, and bleeding. Feelings of faintness and syncope were uncommon. Feelings of relaxation were reported by as many as 86% of patients. The report of pneumothorax was extremely rare, occurring only twice in nearly a quarter of a million treatments.

A study was conducted involving a prospective postal audit of treatments performed by 1,848 professional acupuncturists in the United Kingdom over a 4-week period. They reported 43 minor

adverse events, a rate of 1.3 per 1,000 treatments. The events report included severe nausea, fainting, prolonged aggravation of the symptoms, pain, and bruising. The overall frequency of acupuncture-related adverse events is exceptionally low, and prospective studies have indicated that even minor adverse events are uncommon.

Acupuncture is considered to be a very safe intervention when applied appropriately by a competent practitioner; adverse effects from acupuncture are particularly uncommon.

Ernst E, White A. Prospective studies of the safety of acupuncture: a systemic review. *Am J Med*. 2001;110:481–485.

MacPherson H, Thomas K, Walters S, et al. The York acupuncture safety study: prospective survey of 34,000 treatments by traditional acupuncturists. *BMJ*. 2001;323:486–487.

von Riedenauer WB, Baker MK, Brewer RJ. Video-assisted thoracoscopic removal of migratory acupuncture needle causing pneumothorax. *Chest*. 2007;131:899–901.

SECTION 12 Miscellaneous

53 Myasthenia Gravis

James B. Eisenkraft and
Bryan S. Carter

A 28-year-old woman with a history of myasthenia gravis (MG) presents for bilateral video-assisted thoracoscopic surgery (VATS) and complete thymectomy. She was diagnosed with MG 3 years ago after developing progressive bilateral ptosis, proximal limb weakness, dysphagia, and intermittent dyspnea (MG class IIIb). Her current medications are pyridostigmine (Mestinon) 60 mg TID and prednisone 10 mg QD. Vital signs are: pulse rate, 75 beats per minute; blood pressure, 120/74 mmHg; respiratory rate, 18 breaths per minute; and Spo_2, 100% breathing room air. She is 163 cm tall and weighs 56 kg, and her body mass index (BMI) is 21 kg per m^2.

A. Medical Disease and Differential Diagnosis

1. What is MG?
2. What is the etiology and pathophysiology of MG?
3. Describe the clinical classification of MG.
4. How is the diagnosis of MG made?

5. What should be considered in the differential diagnosis?
6. How does myasthenic syndrome (Lambert-Eaton syndrome) differ from MG?
7. What treatments are available for a patient with MG?

B. Preoperative Evaluation and Preparation

1. Describe the preoperative evaluation of this patient.
2. What preoperative laboratory data are required?
3. How should the patient's medications be managed preoperatively?

C. Intraoperative Management

1. What are your considerations in the choice of anesthetic technique?
2. How should this patient be monitored intraoperatively?
3. What anesthetic regimen would you choose for this patient?
4. Can neuromuscular blocking drugs be used safely in a patient with MG?
5. Should the MG patient who is in remission (i.e., symptom free without treatment) be managed differently?

D. Postoperative Management

1. What factors will help you predict this patient's need for continued intubation or other postoperative ventilatory support?
2. How will you determine if this patient's trachea can be safely extubated?
3. How will you manage postoperative analgesia?
4. How will you define and manage postextubation ventilatory failure in this patient?

A. Medical Disease and Differential Diagnosis

A.1. What is MG?

MG is an autoimmune disorder affecting the neuromuscular junction and therefore of great significance to the anesthesiologist. It is a chronic disorder characterized by fluctuating painless weakness and fatigability of voluntary muscles made worse on exertion with improvement following rest. The onset is usually slow and insidious; any skeletal muscle or muscle group may be affected. The most common onset is ocular, presenting with ptosis and diplopia. If the symptoms remain localized to the eyes for 2 years, the likelihood of progression to generalized disease is about 10%. In many cases, however, MG is generalized and may involve the bulbar musculature (muscles innervated by cranial nerves IX, X, XI, and XII), causing problems with breathing, speaking, mastication, and swallowing. Proximal muscles are more commonly involved than distal. Peripheral muscle weakness may manifest as clumsiness, difficulty holding up the head, or in ambulating. Respiratory muscle weakness may cause dyspnea as well as a decrease in the ability to cough and clear secretions.

The annual incidence of MG is estimated at 7 to 23 new cases per 1,000,000 people per year; the prevalence is approximately 70 to 320 per 100,000. It occurs more commonly in women than men. The disease affects all ages, but the age of onset has a bimodal distribution displaying an early peak in the second and third decades (female predominance) and a late peak in the sixth to eighth decades (male predominance).

Carr AS, Cardwell CR, McCarron PO, et al. A systematic review of population based epidemiological studies in myasthenia gravis. *BMC Neurol*. 2010;10:46.

Gilhus NE. Myasthenia gravis. *N Engl J Med*. 2017;376(13):e25.

McGrogan A, Sneddon S, de Vries CS. The incidence of myasthenia gravis: a systematic literature review. *Neuroepidemiology*. 2010;34(3):171–183.

A.2. What is the etiology and pathophysiology of MG?

In normal neuromuscular transmission, the acetylcholine released from the motor nerve terminal stimulates postsynaptic nicotinic receptors at the motor end plate to generate an action potential leading to depolarization of the membrane and contraction of the motor unit. The normal neuromuscular junction has a very large number of postsynaptic acetylcholine receptors (AChRs) such that muscle weakness only becomes apparent when 75% or more of the receptors have been blocked. This excess of receptors has been termed the "margin of safety of neuromuscular transmission." MG patients have a significant decrease in the number of postsynaptic AChRs at the end plates of affected muscles resulting in a decreased margin of safety of neuromuscular transmission.

MG is an autoimmune disorder, and about 80% of affected patients have detectable circulating antibodies to the nicotinic AChR. These anti-AChR antibodies may cause complement-mediated lysis of the postsynaptic membrane, directly block the receptors, or may modulate the receptor turnover such that the rate of degradation exceeds the rate of resynthesis. Studies of the motor end plate area show loss of synaptic folds and a widening of the synaptic cleft. Approximately 10% of MG patients who do not have anti-AChR antibodies have antibodies to muscle-specific tyrosine kinase (MuSK). The MuSK antibody–positive MG patients often develop prominent oculobulbar muscle weakness, but the MG is not limited to the eyes. In MuSK antibody–positive individuals, cholinesterase inhibitors have little or no effect and may even exacerbate symptoms.

The cause of MG is unknown but appears to be related in some way to the thymus gland. It has been suggested that thymic T cells are stimulated to produce antibodies following sensitization by a protein similar to the AChR. MG patients also have a higher incidence of other autoimmune diseases including autoimmune thyroid disease, rheumatoid arthritis, and systemic

lupus erythematosus.

Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. *Acta Anaesthesiol Scand*. 2012;56(1):17–22.

Gilhus NE. Myasthenia gravis. *N Engl J Med*. 2017;376(13):e25.

Gilhus NE, Nacu A, Andersen JB, et al. Myasthenia gravis and risks for comorbidity. *Eur J Neurol*. 2015;22(1):17–23.

Paton WD, Waud DR. The margin of safety of neuromuscular transmission. *J Physiol*. 1967;191(1):59–90.

A.3. Describe the clinical classification of MG.

Since the original clinical classification by Osserman and Genkins (1971), who described four classes and two subclasses, several other classifications have been published. The one now most commonly used is that of the Medical Scientific Advisory Board of the Myasthenia Gravis Foundation of America Clinical Classification, which describes five main classes and several subclasses as follows:

- Class I: any ocular muscle weakness; may have weakness of eye closure; all other muscle strength is normal.
- Class II: mild weakness affecting other than ocular muscles; may also have ocular muscle weakness of any severity
  - Class IIa: predominantly affecting limb, axial muscles, or both; may also have lesser involvement of oropharyngeal muscles
  - Class IIb: predominantly affecting oropharyngeal, respiratory muscles, or both; may also have lesser or equal involvement of limb, axial muscles, or both
- Class III: moderate weakness affecting other than ocular muscles; may also have ocular muscle weakness of any severity
  - Class IIIa: predominantly affecting limb, axial muscles, or both; may also have lesser involvement of oropharyngeal muscles

  - Class IIIb: predominantly affecting oropharyngeal, respiratory muscles, or both; may also have lesser or equal involvement of limb, axial muscles, or both
- Class IV: severe weakness affecting other than ocular muscles; may also have ocular muscle weakness of any severity
  - Class IVa: predominantly affecting limb, axial muscles, or both; may also have lesser involvement of oropharyngeal muscles
  - Class IVb: predominantly affecting oropharyngeal, respiratory muscles, or both; may also have lesser or equal involvement of limb, axial muscles, or both; use of a feeding tube without intubation
- Class V: defined by the need for intubation, with or without mechanical ventilation, except when used during routine postoperative management

Jaretzki A III, Barohn RJ, Ernstoff RM, et al. Myasthenia gravis: recommendations for clinical research standards. Task Force of the Medical Scientific Advisory Board of the Myasthenia Gravis Foundation of America. *Neurology*. 2000;55(1):16–23.

Osserman KE, Genkins G. Studies in myasthenia gravis: review of a twenty-year experience in over 1200 patients. *Mt Sinai J Med*. 1971;38(6):497–537.

A.4. How is the diagnosis of MG made?

The diagnosis of MG is suspected from the patient's history and confirmed by clinical, electrophysiologic, pharmacologic, or immunologic testing. Typically, the patient cannot sustain or repeat muscular contraction. Clinical tests of fatigability include maintaining an upward gaze, holding out an affected limb, and respiratory function testing (vital capacity, maximum breathing capacity).

The electrical counterpart of fatigability is demonstrated by the repetitive nerve stimulation (RNS) test. The RNS involves the application of supramaximal stimulation to a peripheral

nerve at 2 to 5 Hz. If a decrement of ≥10% is observed in the compound muscle action potential amplitude between the first and the fourth or fifth waveforms, this is considered diagnostic of MG. This is the most specific neurophysiologic test for MG, but it can be performed only on certain muscles, which may not be the ones affected in an individual patient. A more sensitive electrophysiologic test is single-fiber electromyography (EMG), which examines the variability in time interval or "jitter" between two single-muscle fibers from the same motor unit.

Historically, pharmacologic testing for MG was performed by administering the anticholinesterase edrophonium (Tensilon) and observing a rapid improvement in function; mechanical and electrical (e.g., EMG) decrements improve with 2 to 10 mg of intravenous edrophonium (Tensilon test). However, this medication is no longer available in the United States but an equivalent dose of neostigmine or pyridostigmine should produce a similar improvement.

Antibodies to the AChR are detectable in 80% of patients with MG. In equivocal cases, a positive result of a test for anti-AChR or MuSK antibodies is considered diagnostic.

Abraham A, Alabdali M, Alsulaiman A, et al. Repetitive nerve stimulation cutoff values for the diagnosis of myasthenia gravis. *Muscle Nerve*. 2017;55(2):166–170.

Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. *Acta Anaesthesiol Scand*. 2012;56(1):17–22.

A.5. What should be considered in the differential diagnosis?

A number of disorders can mimic MG and should be included in the initial differential diagnosis.

Thyroiditis and resulting thyrotoxicosis can present with generalized weakness and abnormal thyroid function. Patients with neurasthenia characteristically have weakness, which

disappears when individual muscle groups are tested. Progressive external ophthalmoplegia; restrictive cardiomyopathies; muscular dystrophies; brain tumors; amyotrophic lateral sclerosis; myasthenic polymyopathy with hypersensitivity to neostigmine; and drugs such as D-penicillamine, aminoglycosides, quinine, procainamide, and calcium channel blockers can also cause myasthenia-like symptoms.

Gilhus NE. Myasthenia gravis. *N Engl J Med*. 2017;376(13):e25.

Gilhus NE, Nacu A, Andersen JB, et al. Myasthenia gravis and risks for comorbidity. *Eur J Neurol*. 2015;22(1):17–23.

A.6. How does myasthenic syndrome (Lambert-Eaton syndrome) differ from MG?

Myasthenic syndrome is a very rare immune-mediated disorder of neuromuscular transmission, associated with antibodies to the presynaptic voltage-gated calcium channel. The prevalence is estimated to be about 3 to 4 per million. It is associated with small cell carcinoma of the lung in 50% to 60% of cases. Complaints of weakness may be mistaken for MG, but in Lambert-Eaton syndrome, symptoms do not respond to administration of anticholinesterases or steroids and activity improves strength. The defect in this condition is prejunctional, is associated with diminished release of acetylcholine from motor nerve terminals, and is improved by “facilitating” agents such as 4-aminopyridine or 2,3-diaminopyridine that potentiate the release of acetylcholine. Affected patients are particularly sensitive to the effects of nondepolarizing muscle relaxants, which should be used with great caution or avoided entirely. The possibility of Lambert-Eaton syndrome should be considered in all patients with known malignant disease and those patients undergoing diagnostic procedures for suspected carcinoma of the lung. Anesthesia considerations in these patients are

essentially the same as in those with MG.

Brown JC, Charlton JE. A study of sensitivity to curare in myasthenic disorders using a regional technique. *J Neurol Neurosurg Psychiatry*. 1975;38(1):27–33.

Schoser B, Eymard B, Datt J, et al. Lambert-Eaton myasthenic syndrome (LEMS): a rare autoimmune presynaptic disorder often associated with cancer. *J Neurol*. 2017;264(9):1854–1863.

Weingarten TN, Araka CN, Mogensen ME, et al. Lambert-Eaton myasthenic syndrome during anesthesia: a report of 37 patients. *J Clin Anesth*. 2014;26(8):648–653.

A.7. What treatments are available for a patient with MG?

Medical Therapy

Mary Walker was the first physician to report the similarity between the symptoms and signs of MG and curare poisoning and to use an anticholinesterase to treat MG. Anticholinesterases are used to prolong the action of acetylcholine at the postsynaptic membrane and may also exert their own agonist effect at the postsynaptic AChRs. They are the most commonly used therapy in MG. Interestingly, no randomized controlled trial has been conducted on the use of acetylcholinesterase inhibitors in patients with MG because the response in observational studies was such that a placebo group could not be justified. MG patients learn to regulate their anticholinesterase medication and titrate dose to optimum effect (**Table 53.1**). If several muscle groups/functions are affected, the patient titrates therapy according to the most important group. Anticholinesterase overdose results in the muscarinic effects of acetylcholine and may cause a cholinergic crisis. Excessive amounts of acetylcholine at the neuromuscular junction cause persistent depolarization of the muscle membrane. Insufficient dosing causes weakness or a myasthenic crisis. In a patient with weakness, distinction between the two types of crisis may be

made by titrating small doses of neostigmine, or by examining pupil size, which will be large (mydriatic) in a myasthenic crisis but small (miotic) in a cholinergic crisis. Muscarinic side effects (bradycardia, bronchospasm, oral and respiratory tract secretions, and gastrointestinal cramps) are treatable with atropine; however, many MG patients treated with anticholinesterases seem to develop a resistance to the muscarinic effects.

TABLE 53.1 Anticholinesterase Drugs Used to Treat Myasthenia Gravis (Dose in mg)

Drug	Oral	IV	IM	Efficacy
Pyridostigmine (Mestinon)	60	2	2–4	1
Neostigmine (Prostigmin)	1.5	0.5	0.7–1.0	1

IM, intramuscular; IV, intravenous.

Pyridostigmine (Mestinon) is the anticholinesterase drug most commonly used to treat MG and has fewer muscarinic side effects than neostigmine (Prostigmin). Its onset of action following oral administration is 15 to 30 minutes, effect peaks at 1 to 2 hours, and duration of action is 3 to 4 hours. Daily dosage is typically 30 to 120 mg orally given in divided doses. For patients who are weak on awakening in the morning, a long-acting formulation of 180 mg is available and can be taken at bedtime. MG patients who are MuSK antibody–positive generally have little or no response to anticholinesterase medications.

The immunologic basis of MG has led to the use of short- and long-term immunosuppressive drugs. Patients who do not meet treatment goals typically require immunosuppressive therapy. First-line therapy is generally a steroid combined with an immunomodulatory agent. Prolonged use of steroids may produce unwanted effects, such as peptic ulcer disease and osteoporosis. Alternate day dosing of either prednisone or

prednisolone is generally prescribed to reduce side effects. Steroids often produce initial deterioration before an improvement. For long-term effect, immunomodulatory agents such as azathioprine, cyclophosphamide, cyclosporine, methotrexate, mycophenolate mofetil, rituximab, and tacrolimus have been used. Rapid short-term immunomodulation has been achieved in acute exacerbations or to improve muscle strength prior to surgery. Plasmapheresis (PLEX) may produce dramatic but transient improvements in muscle strength with decreases in anti-AChR and anti-MuSK titers as well as other inflammatory mediators. Intravenous immunoglobulin (IVIG) and PLEX are usually reserved for severe MG—both have been found to be equally effective therapies. PLEX has been shown to improve respiratory function in both postoperative and nonoperated patients with MG. PLEX also causes a decrease in plasma cholinesterase levels, which may prolong the effect of drugs such as succinylcholine that are normally broken down by this enzyme system.

Surgical Therapy

Thymectomy is always indicated in those patients with thymoma and is now considered the treatment of choice in most patients with MG, excluding those with only ocular myasthenia. A recent randomized control trial has demonstrated a benefit of thymectomy in adults with AChR-antibody-positive, nonthymomatous MG with the addition of glucocorticoids versus glucocorticoid therapy alone. Overall, these patients required less glucocorticoid over the 3-year study period, had an improvement in symptoms, and had fewer hospitalizations for management of MG symptoms. Patients who have either MuSK-antibody-positive disease do not benefit from a thymectomy. Approximately 70% of MG patients demonstrate thymic hyperplasia; 10% have a thymoma.

Barth D, Nabavi Nouri M, Ng E, et al. Comparison of IVIg and PLEX in patients with myasthenia gravis. *Neurology*. 2011;76(23):2017–2023.

Gilhus NE. Myasthenia gravis. *N Engl J Med*. 2017;376(13):e25.

Mehndiratta MM, Pandey S, Kuntzer T. Acetylcholinesterase inhibitor treatment for myasthenia gravis. *Cochrane Database Syst Rev*. 2011; (2):CD006986.

Wolfe GI, Kaminski HJ, Aban IB, et al. Randomized trial of thymectomy in myasthenia gravis. *N Engl J Med*. 2016;375(6):511–522.

B. Preoperative Evaluation and Preparation

B.1. Describe the preoperative evaluation of this patient.

Several problems must be considered: history of MG, VATS procedure with the patient in both left and right lateral decubitus positions, and anxiety state.

The preoperative interview should be used to identify factors that suggest the need for postoperative ventilation. This information can guide the anesthesiologist in formulating the anesthetic plan, selection of preoperative medications, and arranging for postoperative care. When possible, patients with MG should be scheduled for elective surgery while in remission, and the surgery should be scheduled for early in the day when the patient is at her or his strongest. The patient's physical and emotional states should be optimized. Current drug therapy should be reviewed and possible drug interactions considered. The patient should be informed of the possible need for postoperative intubation and ventilation.

Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. *Acta Anaesthesiol Scand*. 2012;56(1):17–22.

Gilhus NE. Myasthenia gravis. *N Engl J Med*. 2017;376(13):e25.

B.2. What preoperative laboratory data are required?

Laboratory studies should be individualized to the patient. In addition to routine preoperative laboratory data, electrolyte

abnormalities, particularly hypokalemia, which can exacerbate weakness, should be ruled out. If the patient is or has recently been receiving corticosteroids, blood glucose levels should be determined. Because this particular patient will require a general anesthetic for the planned procedure, a preoperative arterial blood gas analysis and pulmonary function tests would serve as the baseline for determining readiness for extubation. A respiratory therapist should educate the patient about breathing exercises and the use of an incentive spirometer.

Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. *Acta Anaesthesiol Scand*. 2012;56(1):17–22.

B.3. How should the patient's medications be managed preoperatively?

Ideally, patients with MG should be scheduled to be the first case of the day in the operating room.

The management of anticholinesterase medication preoperatively should be individualized to the patient. Anticholinesterase therapy should be continued if the patient would be physically weak or if he or she is psychologically dependent on it. Traditional practice is to withhold pyridostigmine therapy on the morning of surgery so that the patient is weak on arrival to the operating room. This avoids interactions with other drugs used in the operating room. For example, anticholinesterase inhibits both plasma cholinesterase and acetylcholinesterase; therefore, the metabolism of succinylcholine will be slowed. Others recommend continuing pyridostigmine, including an oral dose just before induction (**Table 53.1**). Preoperative PLEX has been discussed previously but should not be necessary for this patient. Anxiolysis is satisfactorily achieved with a benzodiazepine. Opioids are usually avoided because of the potential for causing respiratory depression.

Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. *Acta Anaesthesiol Scand*. 2012;56(1):17–22.

C. Intraoperative Management

C.1. What are your considerations in the choice of anesthetic technique?

The necessity of one-lung ventilation, ability to control ventilation, and positioning require general endotracheal anesthesia for this patient. Some other surgical procedures may be possible with purely regional or local anesthesia, and in those cases, utilization of those methods should be prioritized. Additionally, for cases involving general endotracheal anesthesia, short-acting, easily titratable medications are preferred, along with avoidance of neuromuscular blocking drugs whenever possible. In anticipation of providing opioid-sparing postoperative analgesia, preoperative placement of a thoracic epidural catheter should be considered and discussed with the patient.

Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. *Acta Anaesthesiol Scand*. 2012;56(1):17–22.

C.2. How should this patient be monitored intraoperatively?

Standard American Society of Anesthesiologists (ASA) monitors must be used. In addition, an arterial line is useful to draw arterial blood samples for gas analysis intra- and postoperatively. A peripheral nerve stimulator, and ideally a means to quantify responses to stimulation (e.g., EMG, accelerometer, kinemyography), should be used from the beginning even if neuromuscular blocking drugs will be avoided. This is because the potent inhaled anesthetics also depress neuromuscular transmission, and a monitor of recovery

from this effect is similarly needed. Once the patient is asleep, baseline recordings should be made before any potent inhaled or neuromuscular blocking drug is administered. Subsequent responses may then be quantitatively compared to baseline. In MG patients, fade in response to train-of-four and tetanic stimulation occurs in the affected muscles at baseline (see section A4). If a total intravenous anesthesia (TIVA)–based anesthetic is used, a bispectral index monitor is helpful to evaluate depth of anesthesia.

Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. *Acta Anaesthesiol Scand*. 2012;56(1):17–22.

C.3. What anesthetic regimen would you choose for this patient?

For this procedure, the safest approach is general endotracheal anesthesia. Maintenance of anesthesia in the intubated, ventilated MG patient can be achieved with an inhalational anesthetic, a balanced technique, or TIVA.

Prior to induction of anesthesia, the patient should be well oxygenated breathing 100% oxygen until the end-tidal oxygen concentration is greater than 90%. Ideally, it should be 95%, the other 5% of the exhaled gas mixture being carbon dioxide. Induction of anesthesia is readily achieved with propofol or etomidate. In most cases, intubation of the trachea, maintenance, and relaxation may be achieved using a potent inhaled anesthetic agent. Anesthetic depth is increased using the potent inhaled agent and the trachea intubated under its effect. MG patients are more sensitive than normal patients to the neuromuscular depressant effects of the potent inhaled agents. In patients with MG, isoflurane at 1.9 minimum alveolar concentration (MAC) end-tidal concentration decreased train-of-four ratio by 41%, whereas halothane at 1.8 MAC decreased train-of-four ratio by 28%. The less soluble inhaled agents, sevoflurane and

desflurane, are even more rapidly taken up and withdrawn; they are now the most commonly used anesthetic drugs for patients with MG. Whichever agent is used, at the end of the procedure, the inhaled agent is discontinued and recovery of neuromuscular function begins. Another strategy for induction of anesthesia to achieve adequate intubating conditions without the use of neuromuscular blockade includes the use of propofol (1 to 2 mg per kg) and remifentanil (5 μg per kg).

Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. *Acta Anaesthesiol Scand*. 2012;56(1):17–22.

Imani F, Alebouyeh MR, Taghipour Anvari Z, et al. Use of remifentanil and alfentanil in endotracheal intubation: a comparative study. *Anesth Pain Med*. 2011;1(2):61–65.

Nilsson E, Muller K. Neuromuscular effects of isoflurane in patients with myasthenia gravis. *Acta Anaesthesiol Scand*. 1990;34(2):126–131.

Nitahara K, Sugi Y, Higa K, et al. Neuromuscular effects of sevoflurane in myasthenia gravis patients. *Br J Anaesth*. 2007;98(3):337–341.

C.4. Can neuromuscular blocking drugs be used safely in a patient with MG?

If the patient cannot tolerate the depth of anesthesia needed to produce relaxation with the potent inhaled agent, or TIVA, neuromuscular blocking drugs may be used, titrating dose against monitored effect. Patients with MG are sensitive (i.e., show a decrease in ED_{50} and ED_{95} when compared with non-MG patients) to the nondepolarizing neuromuscular blocking drugs because of the decreased number of postsynaptic receptors at the motor end plate. All nondepolarizing relaxants have been successfully and uneventfully used with careful monitoring in patients with MG. Because the sensitivity of any individual MG patient is unknown, these drugs should be titrated in 1/10 of the usual dose. Sensitivity to nondepolarizing neuromuscular blocking drugs is increased during the coadministration of a potent inhaled anesthetic. Upon completion of the surgical

procedure, the residual relaxation may be reversed using incremental doses of an anticholinesterase drug while neuromuscular transmission is carefully monitored to obtain maximum antagonism yet avoid a cholinergic crisis.

Sugammadex is a novel γ-cyclodextrin drug that was designed to bind rocuronium with a great affinity; it also binds vecuronium. Before the introduction of sugammadex, anticholinesterase drugs were the only options for antagonism of residual nondepolarizing neuromuscular blockade, and in MG patients, anticholinesterases must be administered with caution so as to avoid myasthenic or cholinergic crises. Sugammadex has been reported to safely reverse rocuronium-induced neuromuscular blockade within 117 seconds in patients with MG at various levels of neuromuscular blockade. It offers significant advantages in the management of the MG patient because anticholinesterase drugs would not be required for reversal. For reversal of neuromuscular blockade, the recommended doses of sugammadex are 2 mg per kg in patients who have two twitches present on train-of-four stimulation, 4 mg per kg in patients who have 1 to 2 posttetanic twitches, and 16 mg per kg for immediate reversal in patients who have just received an intubating dose of 1.2 mg per kg of rocuronium. If sugammadex is not available, cisatracurium may be the preferred neuromuscular blocking drug because of its short elimination half-life, small volume of distribution, lack of cumulative effect, and high clearance.

MG patients are resistant to the neuromuscular blocking effects of succinylcholine due to the decrease in number of postsynaptic receptors at the motor end plate. The ED_{95} is 2.6 times normal (0.8 mg per kg vs. 0.3 mg per kg) in these patients. Clinically, however, the use of succinylcholine has been without incident, with the usual clinical doses producing adequate relaxation for endotracheal intubation and a normal recovery

time, despite the occasionally reported early onset of phase II block. Doses of 0.2 to 1.0 mg per kg have been used in a number of patients with MG, and most did not show fasciculation before becoming paralyzed. Fade in response to train-of-four stimulation was observed in some patients during recovery, but recovery was not delayed. Prior administration of an anticholinesterase may complicate the response to succinylcholine by delaying its metabolism.

Baraka AS, Taha SK, Kawkabani NI. Neuromuscular interaction of sevoflurane—cisatracurium in a myasthenic patient. *Can J Anaesth*. 2000;47(6):562–565.

Eisenkraft JB, Book WJ, Mann SM, et al. Resistance to succinylcholine in myasthenia gravis: a dose-response study. *Anesthesiology*. 1988;69(5):760–763.

Eisenkraft JB, Book WJ, Papatestas AE. Sensitivity to vecuronium in myasthenia gravis: a dose-response study. *Can J Anaesth*. 1990;37(3):301–306.

Keating GM. Sugammadex: a review of neuromuscular blockade reversal. *Drugs*. 2016;76(10):1041–1052.

Vymazal T, Krecmerova M, Bicek V, et al. Feasibility of full and rapid neuromuscular blockade recovery with sugammadex in myasthenia gravis patients undergoing surgery—a series of 117 cases. *Ther Clin Risk Manag*. 2015;11:1593–1596.

C.5. Should the MG patient who is in remission (i.e., symptom free without treatment) be managed differently?

Although it is well established that MG patients are sensitive to nondepolarizing and resistant to depolarizing neuromuscular blocking drugs, there is no consensus on the response to these drugs during a remission. It is therefore prudent to manage the patient as if he or she had active disease and titrate neuromuscular blocking drugs to effect while monitoring the responses.

Abel M, Eisenkraft JB, Patel N. Response to suxamethonium in a myasthenic patient during remission. *Anaesthesia*. 1991;46(1):30–32.

Basaranoglu G, Erden V, Delatioglu H. Anesthesia of a patient with cured myasthenia gravis. *Anesthesia Analg*. 2003;96(6):1842–1843.

Wainwright AP, Brodrick PM. Suxamethonium in myasthenia gravis. *Anaesthesia*. 1987;42(9):950–957.

D. Postoperative Management

D.1. What factors will help you predict this patient's need for continued intubation or other postoperative ventilatory support?

MG places the patient at an increased risk for respiratory failure after general anesthesia. Several studies have attempted to identify specific characteristics of MG patients undergoing surgery that could help predict increased likelihood of postoperative respiratory failure relative to other MG patients. Predictors of continued postoperative ventilation have shown to be increasing Osserman grade of disease, presence of thymoma, preoperative vital capacity less than 2.9 L, and presence of anti-AChR antibodies. Duration of disease was demonstrated in earlier studies to be associated with the need for continued postoperative ventilation. Maximum static expiratory pressure has also been suggested as a marker because expiratory effort necessarily determines the ability to clear respiratory secretions. A more recent (2014) scoring system to predict postoperative myasthenic crisis and need for ventilatory support has been proposed, which cites as its chief risk factors advanced staging of the patient's MG (bulbar involvement and rapid progression conferring greater risk), BMI >28 kg per m^2, history of prior myasthenic crisis, duration of symptoms >2 years, and association with a pulmonary resection. More invasive surgery increases risk of respiratory failure (transsternal vs. transcervical

thymectomy; open abdominal procedure vs. peripheral surgery), as does evidence of recent MG exacerbation (e.g., patient is currently receiving steroid therapy). Although a definitive risk stratification system has not yet been validated, it is important to assess each patient on a case-by-case basis and engage in frank preoperative discussions regarding risk of postoperative myasthenic crisis and possible need for prolonged ventilatory support.

Chigurupati K, Gadhinglajkar S, Sreedhar R, et al. Criteria for postoperative mechanical ventilation after thymectomy in patients with myasthenia gravis: a retrospective analysis. *J Cardiothorac Vasc Anesth*. 2018;32(1):325–330.

Eisenkraft JB, Papatestas AE, Kahn CH, et al. Predicting the need for postoperative mechanical ventilation in myasthenia gravis. *Anesthesiology*. 1986;65(1):79–82.

Leuzzi G, Meacci E, Cusumano G, et al. Thymectomy in myasthenia gravis: proposal for a predictive score of postoperative myasthenic crisis. *Eur J Cardiothorac Surg*. 2014;45(4):e76–e88.

Mori T, Yoshioka M, Watanabe K, et al. Changes in respiratory condition after thymectomy for patients with myasthenia gravis. *Ann Thorac Cardiovasc Surg*. 2003;9(2):93–97.

D.2. How will you determine if this patient's trachea can be safely extubated?

Postoperative weakness is the greatest contributing factor to perioperative respiratory failure in MG patients. As such, it is important to establish that the patient is fully awake and alert prior to attempting extubation and that any residual neuromuscular blockade has been completely reversed. If a quantitative neuromuscular monitoring device is used, a train-of-four ratio greater than 0.9 should be achieved prior to extubation. Adequate respiratory effort should be confirmed by ability to generate a negative inspiratory pressure of at least −20 cm H_2O. Although MG patients often experience improvement in respiratory function and other MG symptoms after thymectomy, it is more difficult to predict response to surgeries

unrelated to MG. After extubation, it is essential to monitor the patient closely for signs of fatigue, weakness, or evidence of deteriorating respiratory status (hypercarbia, hypoxemia, tachypnea). If the patient was taking pyridostigmine preoperatively, oral dosing should be reestablished as soon as possible after extubation; if necessary, alternative anticholinesterase medications may be used as a bridging measure. The dosage equivalents are shown in **Table 53.1**.

Care should be taken to ensure that somnolence related to opioid administration does not place the patient at increased risk for hypoventilation. In addition, vigilance is required to ensure that impending myasthenic crisis is not masked by intraoperative reversal agents that may wear off in the postanesthesia care unit.

Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. *Acta Anaesthesiol Scand*. 2012;56(1):17–22.

D.3. How will you manage postoperative analgesia?

MG patients are especially sensitive to the central respiratory depressive effects of parenteral opioid administration. On the other hand, inadequately treated pain related to abdominal or thoracic surgery can inhibit ventilatory effort and thus can also worsen respiratory status. Nonopioid pain regimens should be used whenever possible. Following the VATS thymectomy, this patient would benefit from thoracic epidural analgesia via the catheter that was placed preoperatively. Neuraxial analgesia and regional anesthesia where appropriate greatly reduce the total dose of opioid required compared to parenteral administration to achieve an equivalent analgesic effect. Paravertebral blocks have been demonstrated to decrease pulmonary complications such as atelectasis and pneumonia following thoracotomy, whereas thoracic epidural analgesia has not. More recently, continuous erector spinae plane blocks have been used to effectively control postoperative pain after thoracotomy. Intravenous nonsteroidal

anti-inflammatory drug (NSAID) regimens have also been effective in controlling pain in MG patients without causing respiratory depression. If oral or parenteral opioids are used, the dose should be decreased for MG patients receiving anticholinesterase therapy because these medications have been reported to increase the efficacy of opioids.

Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. *Acta Anaesthesiol Scand*. 2012;56(1):17–22.

Joshi GP, Bonnet F, Shah R, et al. A systematic review of randomized trials evaluating regional techniques for postthoracotomy analgesia. *Anesth Analg*. 2008;107(3):1026–1040.

Raft J, Chin KJ, Belanger ME, et al. Continuous erector spinae plane block for thoracotomy analgesia after epidural failure. *J Clin Anesth*. 2018;54:132–133.

Su C, Su Y, Chou CW, et al. Intravenous flurbiprofen for post-thymectomy pain relief in patients with myasthenia gravis. *J Cardiothorac Surg*. 2012;7:98.

D.4. How will you define and manage postextubation ventilatory failure in this patient?

The postsurgical state is uniquely perilous to the MG patient for respiratory decompensation after extubation; indeed, cases have been reported in which previously undetected MG was diagnosed as a result of unexpected respiratory failure in the postoperative period. Suggested criteria for reintubation have included tachypnea (respiratory rate greater than 40 breaths per minute), respiratory acidosis not due to narcotics, or vital capacity ≤8 mL per kg; however, for a patient in myasthenic crisis, inspiratory and expiratory forces are a better indicator of muscle strength, although the presence of a radiologic finding of atelectasis is the strongest predictor of extubation failure or need for reintubation.

Although a myasthenic crisis and a cholinergic crisis may both present with muscle weakness, salivation, and sweating, cholinergic crisis is a rare complication. If available, the preferred therapies for myasthenic crisis are IVIG and PLEX.

Anticholinesterase therapy can also be administered and titrated to effect; however, if IVIG or PLEX is available anticholinesterase medications should be decreased or discontinued to reduce pulmonary secretions. The treatment for cholinergic crisis may incorporate antimuscarinic drugs to treat salivation and sweating but is mostly supportive and may require mechanical ventilation until the crisis is resolved.

Cheng SP, Liu SC, Chou CL, et al. An uncommon cause of postthyroidectomy respiratory failure. *Thyroid*. 2009;19(10):1129–1130.

Gorback MS, Moon RE, Massey JM. Extubation after transsternal thymectomy for myasthenia gravis: a prospective analysis. *South Med J*. 1991;84(6):701–706.

Seneviratne J, Mandrekar J, Wijdicks EF, et al. Predictors of extubation failure in myasthenic crisis. *Arch Neurol*. 2008;65(7):929–933.

Wendell LC, Levine JM. Myasthenic crisis. *Neurohospitalist*. 2011;1(1):16–22.

54 Malignant Hyperthermia

Henry Rosenberg, Harvey K. Rosenbaum, and Vinod Malhotra

A 7-year-old boy with kyphoscoliosis was scheduled for ambulatory surgery for repair of strabismus under general anesthesia. Previous anesthetic history included an uneventful sevoflurane and nitrous oxide anesthesia for bilateral myringotomy. However, the mother was very nervous because a first cousin of the boy had died under anesthesia in Wisconsin the previous year.

A. Medical Disease and Differential Diagnosis

1. What was the problem of concern in this case?
2. What is malignant hyperthermia (MH)?
3. What are the clinical features of a susceptible patient?
4. Does the history of previous uneventful sevoflurane anesthesia reasonably exclude the patient's susceptibility to MH?
5. What are the clinical features of the syndrome?
6. What are the laboratory findings during an acute crisis of MH?
7. What is the incidence of this syndrome?
8. What is the mode of inheritance of the disease? Does MH "skip" generations?

9. What genetic disorder results in MH susceptibility?
10. What is the pathophysiology of the syndrome?
11. What laboratory tests can further substantiate the susceptibility of the patient to MH?
12. What is neuroleptic malignant syndrome (NMS)?

B. Preoperative Evaluation and Preparation

1. How would you prepare this patient for anesthesia and surgery?
2. Is dantrolene prophylaxis indicated?
3. What laboratory tests would you obtain before surgery?
4. Is outpatient surgery appropriate for this patient?
5. In anticipation of general anesthesia, what preparations would you make?

C. Intraoperative Management

1. What anesthetic techniques and agents would you employ?
2. Should body (core) temperature be monitored during general anesthesia lasting more than a short time?
3. What anesthetic agents are contraindicated?
4. If the surgeon wants to use local anesthesia for a procedure, what agents will you recommend?
5. What is the significance of masseter muscle spasm occurring after succinylcholine administration?
6. Twenty minutes into the procedure with sevoflurane anesthesia, the patient developed increasing tachycardia with ventricular premature beats and mottled skin. What emergency measures would you take?
7. What modalities would you monitor closely during management of the crisis?
8. What steps should be taken to avoid major morbidity from MH?
9. How does the new formulation of dantrolene (Ryanodex) compare with the existing formulation of dantrolene (Dantrium

or Revonto)?

D. Postoperative Management

1. What complications may follow this syndrome?
2. What would be your follow-up in this case?
3. What would you advise the patient and the family?
4. What precautions should an MH-susceptible patient take outside of the operating room (OR)?

A. Medical Disease and Differential Diagnosis

A.1. What was the problem of concern in this case?

The patient was a 7-year-old boy with kyphoscoliosis and strabismus and a history of an anesthetic-related death in the family in Wisconsin. Therefore, in addition to the respiratory problems associated with kyphoscoliosis, he presented a likelihood of susceptibility to MH syndrome. The supporting factors for strong suspicion were the family history, kyphoscoliosis, and the geographic location. There is a high density of MH-susceptible families in Wisconsin.

Jungbluth H, Voermans NC. Congenital myopathies: not only a paediatric topic. *Curr Opin Neurol*. 2016;29:642–650.

Li G, Brady JE, Rosenberg H, et al. Excess comorbidities associated with malignant hyperthermia diagnosis in pediatric hospital discharge records. *Paediatr Anaesth*. 2011;21(9):958–963.

Rosenberg H, Sambuughin N, Riazi S, et al. *Malignant Hyperthermia Susceptibility*. Seattle, WA: University of Washington: GeneReviews; 2003. Revised 2006, 2009, and 2013.

A.2. What is malignant hyperthermia (MH)?

MH, first described by Denborough and Lovell in 1960, is an inherited clinical syndrome characterized by elevated core temperature, tachycardia, tachypnea, hypercarbia, rigidity, acidosis, and hyperkalemia. The underlying abnormality relates

to an uncontrolled elevation of intracellular calcium in skeletal muscle cells leading to activation of muscle contractile elements and hypermetabolism. These changes are reversed with the administration of dantrolene, but in the absence of timely treatment, death is likely. In almost every instance, the clinical syndrome occurs in a susceptible patient when a "triggering" anesthetic agent is employed. However, not all signs appear in all cases. In rare situations, an MH crisis has appeared in humans in the absence of anesthetic drugs.

Denborough MA, Lovell RRH. Anesthetic deaths in a family. *Lancet*. 1960;2:45.

Litman RS, Griggs SM, Dowling JJ, et al. Malignant hyperthermia susceptibility and related diseases. *Anesthesiology*. 2018;128(1):159–167.

Zvaritch E, Gillies R, Kraeva N, et al. Fatal awake malignant hyperthermia episodes in a family with malignant hyperthermia susceptibility: a case series. *Can J Anaesth*. 2019;66(5):540–545.

A.3. What are the clinical features of a susceptible patient?

A family history, if present, particularly in a first-degree relative, is a strong indicator of MH susceptibility. Epidemiologic studies have demonstrated that certain comorbidities such a scoliosis and muscle disorders are more frequent in MH-susceptible patients. There are a few myopathic disorders that are known to be associated with MH susceptibility. They include central core disease, King-Denborough syndrome, multiminicore disease, congenital myopathy with cores and rods, nemaline rod myopathy, idiopathic hyperCKemia, and Native American myopathy; hypokalemic periodic paralysis has been rarely associated with MH susceptibility (**Table 54.1**). However, most patients susceptible to MH do not have obvious musculoskeletal disorders or a positive family history.

Patients who have Duchenne or Becker muscular dystrophy

should not be anesthetized with MH trigger agents because hyperkalemia and rhabdomyolysis may result.

TABLE 54.1	Associated Musculoskeletal Disorders/Signs in Patients Susceptible to Malignant Hyperthermia
Scoliosis	
Hypotonia	
Exercise-induced rhabdomyolysis	
Strabismus	
Central core disease	
Multiminicore disease	
King-Denborough syndrome	
Congenital myopathy with cores and rods	
Nemaline rod myopathy	
Idiopathic hyperCKemia	
Native American myopathy	
Hypokalemic periodic paralysis (rarely associated with malignant hyperthermia susceptibility)	

Larach MG, Gronert GA, Allen GC, et al. Clinical presentation, treatment, and complications of malignant hyperthermia in North America from 1987 to 2006. *Anesth Analg*. 2010;110(2):498–507.

Litman RS, Griggs SM, Dowling JJ, et al. Malignant hyperthermia susceptibility and related diseases. *Anesthesiology*. 2018;128(1):159–167.

Rosenberg H, Pollock N, Schiemann A, et al. Malignant hyperthermia: a review. *Orphanet J Rare Dis*. 2015;10:93.

A.4. Does the history of previous uneventful sevoflurane anesthesia reasonably exclude the patient's susceptibility to MH?

No, it does not. Cases may occur during a second or subsequent anesthetic course.

Heytens L, Forget P, Scholtès JC, et al. The changing face of malignant hyperthermia: less fulminant, more insidious. *Anaesth Intensive Care*. 2015;43(4):506–511.

Larach MG, Gronert GA, Allen GC, et al. Clinical presentation, treatment, and complications of malignant hyperthermia in North America from 1987 to 2006. *Anesth Analg*. 2010;110(2):498–507.

Litman RS. Malignant hyperthermia: diagnosis and management of acute crisis. Published July 25, 2019. https://www.uptodate.com/contents/malignant-hyperthermia-diagnosis-and-management-of-acute-crisis?search=malignant%20hyperthermia%20treatment&source=search_result&selec Accessed May 31, 2019.

A.5. What are the clinical features of the syndrome?

The clinical features of MH are the result of an uncontrolled, exaggerated, hypermetabolic state triggered by the use of potent inhalation anesthetic agents and/or succinylcholine. In humans, a few cases of MH have been thought to occur as a result of environmental factors other than anesthetic agents. Common manifestations include the following:

Specific for MH

- Increase in end-tidal carbon dioxide (CO_2) during constant ventilation (the most sensitive and specific sign)
- Generalized rigidity (extremely high specificity); when due to MH, it does NOT improve with administration of paralytics or increasing anesthetic depth
- Masseter muscle rigidity (MMR)

Nonspecific

- Tachycardia (the earliest and most consistent clinical sign, however; not specific)
- Tachypnea
- Increased temperature, which may exceed 40°C
- Arrhythmias
- Skin mottling
- Profuse sweating
- Altered blood pressure—may observe hypotension or hypertension

Increased temperature is unexpected during anesthesia for an elective procedure or during trauma surgery. Although an important sign of MH, it is nonspecific. Failure to measure

temperature or reliance on inaccurate temperature monitors is associated with increased mortality from an MH episode.

Hyperkalemic Cardiac Arrest

Sudden hyperkalemic cardiac arrest has been reported after the administration of MH trigger agents in children with undiagnosed myopathy, especially the dystrophinopathies, Duchenne or Becker muscular dystrophy. This response is due to acute muscle membrane destruction leading to hyperkalemia. The pathway leading to the abnormal response to potent inhalational anesthetics is not clear. Fulminant MH may also result in hyperkalemic cardiac arrest associated with severe acidosis, rhabdomyolysis, and hyperthermia.

The treatment for hyperkalemia includes glucose and insulin, calcium chloride or gluconate, and hyperventilation.

Gurnaney H, Brown A, Litman RS. Malignant hyperthermia and muscular dystrophies. *Anesth Analg*. 2009;109(4):1043–1048.

Larach MG, Brandom BW, Allen GC, et al. Malignant hyperthermia deaths related to inadequate temperature monitoring, 2007-2012: a report from the North American malignant hyperthermia registry of the Malignant Hyperthermia Association of the United States. *Anesth Analg*. 2014;119(6):1359–1366.

Larach MG, Gronert GA, Allen GC, et al. Clinical presentation, treatment, and complications of malignant hyperthermia in North America from 1987 to 2006. *Anesth Analg*. 2010;110(2):498–507.

Larach MG, Rosenberg H, Gronert GA, et al. Hyperkalemic cardiac arrest during anesthesia in infants and children with occult myopathies. *Clin Pediatr (Phila)*. 1997;36(1):9–16.

Nathan A, Ganesh A, Godinez RI, et al. Hyperkalemic cardiac arrest after cardiopulmonary bypass in a child with unsuspected Duchenne muscular dystrophy. *Anesth Analg*. 2005;100(3):672–674.

A.6. What are the laboratory findings during an acute crisis of MH?

The laboratory values reflect changes of a hypermetabolic state and muscle tissue damage (**Table 54.2**). Hence hypercarbia,

respiratory and metabolic acidosis, hyperkalemia, elevated creatine kinase (CK), and myoglobinemia are common findings. If the hyperthermia is extreme, coagulopathy is common. In the early stage of an MH episode, metabolic acidosis, hyperkalemia, and CK elevation may be absent.

TABLE 54.2 The Laboratory Findings of Acute Malignant Hyperthermia

Metabolic and Respiratory Acidosis
Arterial blood gases
↓↓ pH
↑↑ PCO_2
Mild decreases in PO_2
Electrolytes
↑ K
Later decreased serum calcium
↑ Mg
Serum
↑ Lactate
↑ Pyruvate
↑ Creatine kinase
↑ Lactate dehydrogenase
↑ Aldolase
↑ Myoglobin
Increased INR, increased FSP, increased PT/PTT
Thrombocytopenia if DIC develops

DIC, disseminated intravascular coagulation; FSP, fibrin split product; INR, international normalized ratio; K, potassium; Mg, magnesium; P_{CO_2}, partial pressure of carbon dioxide; P_{O_2}, partial pressure of oxygen; PT/PTT, prothrombin time/partial thromboplastin time.

Larach MG, Gronert GA, Allen GC, et al. Clinical presentation, treatment, and complications of malignant hyperthermia in North America from 1987 to 2006. *Anesth Analg*. 2010;110(2):498–507.

A.7. What is the incidence of this syndrome?

The incidence of clinical MH is difficult to measure because many clinical syndromes resemble MH and often the anesthetic management is altered when initial signs suggesting MH are

detected. The incidence also depends on the prevalence in a population of genetic mutations causal for MH as well as the prevalence of use of MH trigger agents. For most conditions, the incidence is determined by coded diagnoses in the medical record. However, in the case of MH because many clinicians are not familiar with the disorder, some cases of high fever with bad patient outcome are labeled generically as "malignant hyperthermia." In one small study based on such coded diagnoses, only 25% of cases coded as MH were determined to actually represent clinical episodes of MH by an expert panel.

One of the earliest epidemiologic studies of MH was conducted in Denmark where an estimate of the incidence of fulminant MH was noted to be 1 in 260,000 general anesthetics and 1 in 60,000 anesthetics where succinylcholine was used. The incidence was even higher, that is, 1 in 5,000 anesthetics, when such signs as MMR, unexplained tachycardia, and unexplained fever were included. Two recent studies of coded hospital discharge data showed that the prevalence of MH is 1 in 100,000 hospital discharges for adults and 4 per 100,000 discharges for children.

In a particular province of Quebec, Canada, the prevalence of MH was calculated as 0.2% of the population based on a detailed genealogic study of families with MH susceptibility. Genetic studies have suggested that the prevalence of MH causative mutations is 1 in 2,000 people in France and in Japan. Incomplete penetrance results in an incidence of MH episodes far lower than anticipated by mutation prevalence. However, mortality from acute MH ranges from 6% to 10%.

Bachand M, Vachon N, Boisvert M, et al. Clinical reassessment of malignant hyperthermia in Abitibi-Témiscamingue. *Can J Anaesth*. 1997;44(7):696–701.

Brady J, Sun L, Rosenberg H, et al. Prevalence of malignant hyperthermia due to anesthesia in New York State, 2001-2005. *Anesth Analg*. 2009;109:1162–1166.

Li G, Brady JE, Rosenberg H, et al. Excess comorbidities associated with malignant hyperthermia diagnosis in pediatric hospital discharge records. *Paediatr Anaesth*. 2011;21(9):958–963.

Monnier N, Krivosic-Horber R, Payen JF, et al. Presence of two different genetic traits in malignant hyperthermia families: implication for genetic analysis, diagnosis, and incidence of malignant hyperthermia susceptibility. *Anesthesiology*. 2002;97(5):1067–1074.

Pinyavat T, Rosenberg H, Lang B, et al. Accuracy of malignant hyperthermia diagnoses in hospital discharge records. *Anesthesiology*. 2015;122(1):55–63.

Riazi S, Kraeva N, Hopkins PM. Malignant hyperthermia in the post-genomics era: new perspectives on an old concept. *Anesthesiology*. 2018;128(1):168–180.

Rosero EB, Adesanya AO, Timaran CH, et al. Trends and outcomes of malignant hyperthermia in the United States, 2000 to 2005. *Anesthesiology*. 2009;110(1):89–94.

A.8. What is the mode of inheritance of the disease? Does MH "skip" generations?

MH is inherited in humans in an autosomal dominant fashion with reduced penetrance and variable expressivity. MH is heterogeneic with up to seven gene loci implicated but only three are confirmed—*RYR1*, *CACNA1S*, and *STAC3*. A missense mutation in *STAC3* is associated with Native American myopathy and MH susceptibility; the disorder displays autosomal recessive transmission. *STAC3*-related myopathy has been described in other ethnic groups and has not been described in heterozygous family members.

Over 70% of MH cases are linked to the skeletal muscle ryanodine receptor gene *RYR1* located on chromosome 19. Less than 2% are associated with mutations in the *CACNA1S* (α1 subunit of the dihydropyridine receptor) gene. Over 400 variants have been found in *RYR1* with 48 documented as causal mutations for the syndrome.

Because MH is usually inherited in an autosomal dominant manner, the susceptibility to MH does not "skip" generations. However, because of the low penetrance, not all those with MH

mutations display the syndrome on exposure to trigger agents. *De novo* mutations have also been described.

Some MH-susceptible patients with overt myopathy are homozygous or compound heterozygous for *RYR1* mutations that are causal or potentially causal for MH. Nonmyopathic family members may also be MH susceptible.

McCarthy TV, Healey JM, Jeffron JJ, et al. Localization of the malignant hyperthermia susceptibility locus to human chromosome 19q12-13.2. *Nature*. 1990;343:562–563.

Riazi S, Kraeva N, Hopkins PM. Malignant hyperthermia in the post-genomics era: new perspectives on an old concept. *Anesthesiology*. 2018;128(1):168–180.

Sambuughin N, Holley H, Muldoon S, et al. Screening of the entire ryanodine receptor type 1 coding region for sequence variants associated with malignant hyperthermia susceptibility in the North American population. *Anesthesiology*. 2005;102:515–521.

Stewart SL, Hogan K, Rosenberg H, et al. Identification of the Arg1086His mutation in the alpha subunit of the voltage-dependent calcium channel (CACNA1S) in a North American family with malignant hyperthermia. *Clin Genet*. 2001;59:178–184.

A.9. What genetic disorder results in MH susceptibility?

In most cases, the MH-susceptible patient has a defective calcium channel located in the membrane of the sarcoplasmic reticulum (SR) of skeletal muscle. This channel is termed the ryanodine receptor because it binds the plant alkaloid ryanodine.

The channel is closely associated with other proteins and structures, such as the dihydropyridine calcium channel that mediates transfer of voltage change to the RYR1 receptor. Other proteins associated with the ryanodine receptor include triadin, *STAC3*, DHPR subunit $\beta 1\alpha$, and FKB-12 binding protein. Mutations or potentially pathogenic variants in the *RYR1* gene are found in approximately 70% of MH-susceptible patients and their families. Hundreds of additional *RYR1* variants have yet to be characterized as to effects on calcium movements. One

reason for the slow progress in deciphering the significance of these many mutations is that, unlike many other conditions, there are many private mutations that predispose to MH. No single mutation accounts for more than about 10% of MH cases. The dihydropyridine receptor gene, also involved in intracellular calcium control, has been associated with MH susceptibility in a 1% to 2% of MH-susceptible families.

The *STAC3* gene encodes a T tubule protein that is essential for excitation-contraction coupling. Native American myopathy is an autosomal recessive disorder caused by a specific *STAC3* mutation and is associated with MH susceptibility.

There are probably mutations in other genes that may contribute to MH susceptibility. A recent estimate suggests that up to 23% of MH-susceptible families do not have mutations in *RYR1*, *CACNA1S*, or *STAC3*.

Of interest is the observation that mutations associated with central core disease and multiminicore disease, two myopathies that also predisposes to MH, are located on the *RYR1* gene as well. In central core disease, the SR is depleted of calcium to a significant extent due to the increased permeability of the ryanodine receptor. With a depletion of calcium, muscle contraction is weakened when the muscle is activated.

Genetically engineered mice have been developed that include one or more of the mutations causal for MH in the mouse genome. The mouse displays signs typical of MH during exposure to MH trigger agents and also on exposure to raised environmental temperature.

Horstick EJ, Linsley JW, Dowling JJ, et al. Stac3 is a component of the excitation-contraction coupling machinery and mutated in Native American myopathy. *Nat Commun*. 2013;4:1952.

Litman RS, Griggs SM, Dowling JJ, et al. Malignant hyperthermia susceptibility and related diseases. *Anesthesiology*. 2018;128(1):159–167.

Lopez JR, Kaura V, Diggle CP, et al. Malignant hyperthermia, environmental

heat stress, and intracellular calcium dysregulation in a mouse model expressing the p.G2435R variant of RYR1. *Br J Anaesth*. 2018;121(4):953–961.

Miller DM, Daly C, Aboelsaod EM, et al. Genetic epidemiology of malignant hyperthermia in the UK. *Br J Anaesth*. 2018;121(4):944–952.

Sambuughin N, Holley H, Muldoon S, et al. Screening of the entire ryanodine receptor type 1 coding region for sequence variants associated with malignant hyperthermia susceptibility in the North American population. *Anesthesiology*. 2005;102:515–521.

A.10. What is the pathophysiology of the syndrome?

The MH syndrome results from an abnormal and uncontrolled elevation of intracellular calcium levels in skeletal muscle. The pathophysiology is as follows: The process of calcium release from the SR normally begins with depolarization of the sarcolemma, which is transmitted via the T tubules to the dihydropyridine receptor that in turn activates the calcium channel termed the ryanodine receptor to release calcium.

The elevated calcium removes the inhibition of actin and myosin interaction that leads to mechanical force generation. Calcium release occurs via a channel within the SR called the ryanodine receptor. Reuptake of calcium returns the intracellular cytoplasmic concentration of calcium to normal and muscle relaxation takes place. Reuptake is mediated via sarcoplasmic/endoplasmic reticulum calcium ATPase (SERCA) pumps.

There are a variety of intermediate proteins that also regulate the intra-SR concentration of calcium such as calsequestrin, a calcium-binding protein. Genetically engineered mice that do no express calsequestrin have been shown to develop clinical signs of MH on exposure to trigger anesthetics. It is believed that in the absence of the calcium buffer, intracellular calcium levels increase significantly but only on exposure to MH triggers. Association of variants in the calsequestrin gene with human MH has not been confirmed.

The control of calcium release is highly regulated because when muscle contraction takes place, a variety of energy-consuming steps are required resulting in adenosine triphosphate (ATP) breakdown and heat production.

During an MH episode, the ryanodine receptor calcium channel is locked in an open position leading to an uncontrolled leak or release of calcium as well as increased extracellular calcium entry with elevation of intracytoplasmic calcium levels and continuous muscle activation as well as ATP breakdown. The SR calcium pump is unable to sufficiently resequester the calcium. ATP breakdown during this process aggravates heat production further.

Energy-consuming processes take place through glycolysis as well as oxidative phosphorylation. Eventually, ATP levels are insufficient to maintain sarcolemmal integrity and potassium leaks from the cell resulting in hyperkalemia. Myoglobinemia occurs for the same reason, as does an increase of a number of enzymes, including CK.

Eltit JM, Ding X, Pessah IN, et al. Nonspecific sarcolemmal cation channels are critical for the pathogenesis of malignant hyperthermia. *FASEB J*. 2013;27(3):991–1000.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1114–1120.

Kraeva N, Zvaritch E, Frodis W, et al. CASQ1 gene is an unlikely candidate for malignant hyperthermia susceptibility in the North American population. *Anesthesiology*. 2013;118(2):344–349.

Protasi F, Paolini C, Dainese M. Calsequestrin-1: a new candidate gene for malignant hyperthermia and exertional/environmental heat stroke. *J Physiol*. 2009;587(pt 13):3095–3100.

A.11. What laboratory tests can further substantiate the susceptibility of the patient to MH?

The most accurate diagnostic test for MH is the exposure of biopsied skeletal muscle to halothane, caffeine, and, more

recently, ryanodine or chlorocresol. In this test, about 2 g of muscle is harvested from the thigh under regional, or in the case of a child at least 8 years old, nontriggering general anesthesia. Strips or fascicles of muscle weighing 100 to 200 mg are suspended in a water bath at 37°C, and exposure is made to either halothane, caffeine, ryanodine, or chlorocresol in specific graded concentrations. The isometric contracture, not contraction, response to muscle is measured via strain gauge following specific guidelines. The threshold and height of the contracture is measured and a diagnosis of MH is made based on the contracture threshold and strength exceeding specific values.

The test is highly sensitive, close to 100%, but as many as 20% of positives are false positives. Nevertheless, the value of the test resides in ruling out MH susceptibility. Patients with MH-causal mutations and negative, that is, malignant hyperthermia non-susceptible (MHN) contracture tests have been described. Although these may be false-negative contracture tests, it may be possible that the patient is MHN phenotype due to unknown genetic or epigenetic factors that counteract the causal mutation. Caution dictates that such patients would nonetheless be treated as MH susceptible.

Because the test is invasive and costly and requires strict adherence to specific requirements, there are only five testing centers in North America. There are over 20 in Europe. Two slightly different versions of the test exist, the North American and the European versions. The main difference is in the concentration of drugs used during exposure of the muscle and the threshold for determining a positive response.

The patient and his or her history must be carefully evaluated by the biopsy center director prior to recommending the test in order to enhance its positive predictive value.

Molecular Genetic Testing for MH Susceptibility

The era of DNA testing for MH susceptibility began in 1990 when a single missense mutation in the *RYR1* gene was shown to be causal for MH in pigs. In humans, several genes have been associated with MH; however, the *RYR1* gene is probably responsible for most cases of MH. At present, 48 mutations in the *RYR1* gene have been found in humans that are causal for MH based on strict criteria related to in vitro calcium release or clinical MH in several generations and families. Unfortunately, no mutation accounts for more than a small percentage of all patients with MH susceptibility. The chief advantage of genetic testing is all that is required is a blood sample and the specimen may be shipped to the laboratory. The main limitation of genetic testing is the sensitivity of <75% as well as the frequent finding of variants of unknown significance in both *RYR1* and *CACNA1S*.

Undoubtedly, the sensitivity will improve as more mutations are identified and tested for their ability to alter the structure and function of the ryanodine receptor.

Patients should consider genetic testing if

1. They have had a positive contracture test.
2. A family member has had a positive contracture test.
3. They have suffered a very likely MH episode but have not had a contracture test.
4. A family member has been found to have a causal mutation.

In those patients who are tested and a causal mutation identified, those with the mutation are MH susceptible (high specificity). The absence of a confirmed or probable pathogenic variant does *not* rule out MH susceptibility as they may harbor another as yet undescribed mutation.

At present, there are five clinical testing laboratories in the United States that perform molecular genetic testing for patients suspected to be MH susceptible (https://www.mhaus.org/testing/genetic-testing/genetic-testing-

centers/). The decision to undergo genetic testing is complex because the test, although requiring only a blood sample, costs approximately $2,000 for examining *RYR1* and *CACNA1S*. However, once a mutation is found, the cost for screening family members is approximately $200 each. This compares to an approximate cost of $6,000 for the caffeine halothane contracture test.

The pros and cons of testing should be discussed with either an MH expert or a genetic counselor.

Allen GC, Larach MG, Kunselman AR. The sensitivity and specificity of the caffeine-halothane contracture test: a report from the North American Malignant Hyperthermia Registry. The North American Malignant Hyperthermia Registry of MHAUS. *Anesthesiology*. 1998;88:579–588.

European Malignant Hyperthermia Group. Diagnostic mutations. https://www.emhg.org/diagnostic-mutations. Accessed May 31, 2019.

European Malignant Hyperthermia Group. Testing for MH. https://www.emhg.org/testing-for-mh. Accessed May 31, 2019.

Lichtman AD, Oribabor C. Malignant hyperthermia following systemic rewarming after hypothermic cardiopulmonary bypass. *Anesth Analg*. 2006;102(2):372–375.

Malignant Hyperthermia Association of the United States. CHCT—muscle biopsy testing centers. https://www.mhaus.org/testing/muscle-biopsy-chct/chct-muscle-biopsy-testing-centers/. Accessed May 31, 2019.

Malignant Hyperthermia Association of the United States. Genetic testing centers. https://www.mhaus.org/testing/genetic-testing/genetic-testing-centers/. Accessed May 31, 2019.

Miller DM, Daly C, Aboelsaod EM, et al. Genetic epidemiology of malignant hyperthermia in the UK. *Br J Anaesth*. 2018;121(4):944–952.

Riazi S, Kraeva N, Hopkins PM. Malignant hyperthermia in the post-genomics era: new perspectives on an old concept. *Anesthesiology*. 2018;128(1):168–180.

A.12. What is neuroleptic malignant syndrome (NMS)?

The NMS is characterized by altered mental status, hyperthermia, rigidity, rhabdomyolysis, acidosis, and tachycardia, features that mimic MH. However, NMS is

precipitated by a variety of neuroleptic drugs including haloperidol, the atypical antipsychotics, phenothiazines, and other centrally acting drugs.

This syndrome differs from MH in that central dopamine antagonism or depletion is thought responsible for the clinical picture, although NMS is an idiosyncratic reaction. Other factors such as antimuscarinic effect, acute inflammation, and hypovolemia are often associated with NMS. If a patient with NMS requires intubation and mechanical ventilation, nondepolarizing muscle relaxants usually result in partial or complete resolution of rigidity unlike MH. The mainstay of treatment are supportive care, benzodiazepines, and, if necessary, a dopamine agonist such as bromocriptine. Patients also respond symptomatically to dantrolene therapy. A recent report identified *RYR1* mutations in a small percentage of patients manifesting NMS.

A variety of drug-induced hyperthermic syndromes resemble MH such as the serotonin syndrome. The drug interaction resulting in potentially lethal serotonin toxicity is the administration of a monoamine oxidase (MAO)-A inhibitor, such as intravenous methylene blue, to a patient chronically taking a selective serotonin reuptake inhibitor (SSRI) antidepressant, or administration of a medication with SSRI activity, such as meperidine, to a patient taking an MAO-A or nonspecific MAO inhibitor. Ecstasy and other methylenedioxymethamphetamine (MDMA) agonists also produce hyperthermia. Again, the signs may resemble MH, but the pathophysiology is very different; unlike MH, severe serotonin toxicity consistently presents *after* discontinuation of general anesthesia.

Anesthesiologists may encounter NMS in patients who are sedated with haloperidol in the intensive care unit (ICU) and on infrequent occasions when patients are given dopamine agonist

agents such as metoclopramide and promethazine.

Gillman PK. CNS toxicity involving methylene blue: the exemplar for understanding and predicting drug interactions that precipitate serotonin toxicity. *J Psychopharmacol*. 2011;25(3):429–436.

Gillman PK. Neuroleptic malignant syndrome: mechanisms, interactions, and causality. *Mov Disord*. 2010;25(12):1780–1790.

Rosebush PI, Garside S, Mazurek MF. Recognizing neuroleptic malignant syndrome. *CMAJ*. 2004;170(11):1645.

Strawn JR, Keck PE Jr, Caroff SN. Neuroleptic malignant syndrome. *Am J Psychiatry*. 2007;164(6):870–876.

B. Preoperative Evaluation and Preparation

B.1. How would you prepare this patient for anesthesia and surgery?

Preoperative preparation should include a detailed medical history, assessment of the patient's physical status, evaluation of laboratory findings including CK, and specific investigations to determine the susceptibility of the patient to MH. Three possible scenarios are as follows:

- The caffeine halothane contracture test result is normal. The patient should be considered not susceptible to MH and the anesthetic should be nonrestrictive.
- The caffeine halothane contracture test is abnormal, implying MH susceptibility. Or, a mutation associated with MH or a probable pathogenic *RYR1* variant is identified. In this case, trigger-free anesthetic agents should be employed and all preparations should be made to quickly treat the syndrome if it develops.
- The caffeine halothane contracture test is not available. This is very frequently the case because this test is done in only a few centers in the United States. In such situations, the patient should be treated as MH susceptible, and all

appropriate steps should be followed.

Frei D, Stowell KM, Langton EE, et al. Administration of anaesthetic triggering agents to patients tested malignant hyperthermia normal and their relatives in New Zealand: an update. *Anaesth Intensive Care*. 2017;45(5):611–618.

Rosenberg H, Pollock N, Schiemann A, et al. Malignant hyperthermia: a review. *Orphanet J Rare Dis*. 2015;10:93.

B.2. Is dantrolene prophylaxis indicated?

If a nontriggering anesthetic is administered with appropriate monitoring to an MH-susceptible patient, dantrolene prophylaxis is not necessary.

With the judicious use of trigger-free anesthetics, MH is extremely unlikely. MH cases without trigger agents have been reported; however, because many syndromes may mimic MH, it is uncertain if each of the cases was really MH.

Dantrolene can cause side effects, such as nausea, vomiting, pain at the injection site, thrombophlebitis, and depression of the twitch response. In patients with preexisting muscle weakness, dantrolene may cause respiratory insufficiency in the postoperative period.

Carr AS, Lehman J, Cunliffe M, et al. Incidence of malignant hyperthermia reactions in 2,214 patients undergoing muscle biopsy. *Can J Anaesth*. 1995;42(4):281–286.

B.3. What laboratory tests would you obtain before surgery?

Chest radiograph and electrocardiogram (ECG) should be ordered if dictated by his scoliosis or other associated medical illness. Otherwise, there is no routine laboratory testing indicated for strabismus surgery in this child. Serum CK is of value as a baseline test and should be obtained.

B.4. Is outpatient surgery appropriate for this patient?

With the use of trigger-free anesthetics and appropriate monitoring, surgery normally performed in an outpatient setting is acceptable. The anesthesia provider and nursing team should be informed well in advance of the day of surgery to confirm preparedness to care for an MH-susceptible patient. Even when planning a trigger-free anesthetic, dantrolene for treatment of an acute MH episode should be available. Postoperative admission to the hospital solely on the basis of MH susceptibility is not warranted. When MH occurs, it is usually in the immediate postoperative period and usually not beyond 2 hours postoperatively. Therefore, it is prudent to keep the patient longer than usual in the postanesthesia care unit (PACU) in monitored setting and a little longer in the ambulatory discharge area.

All ambulatory surgery and office-based surgery settings should have a plan for managing an MH episode and transferring the patient to a hospital while continuing to assess and treat the episode and communicating key items to the receiving emergency department (ED) or ICU team.

Larach MG. A primer for diagnosing and managing malignant hyperthermia susceptibility. *Anesthesiology*. 2018;128(1):8–10.

Larach MG, Dirksen SJ, Belani KG, et al. Special article: creation of a guide for the transfer of care of the malignant hyperthermia patient from ambulatory surgery centers to receiving hospital facilities. *Anesth Analg*. 2012;114(1):94–100.

Pollock N, Langton E, McDonnell N, et al. Malignant hyperthermia and day stay surgery. *Anaesth Intensive Care*. 2006;34(1):40–45.

B.5. In anticipation of general anesthesia, what preparations would you make?

A satisfactory preparation for administering anesthesia to this patient should include measures to prevent and treat an acute crisis of MH. The following should be available:

Equipment

- Remove or disable vaporizers. Place a conspicuous warning on the anesthesia workstation that the patient is MH susceptible.
- Fresh circuit, reservoir bag, and soda lime
  - Flush machine and ventilator by flowing 10 L oxygen per minute for at least 10 minutes
  - For newer anesthesia work stations, the washout period may be prolonged up to 60 minutes. The manufacturers' guidelines for machine preparation should be followed. The use of activated charcoal filters greatly reduces the length of time required to prepare an anesthetic workstation for an MH-susceptible patient. After a 90-second flush with high flow oxygen, placement of activated charcoal filters on the inspiratory port immediately reduces residual breathing circuit vapor concentration to <5 ppm.
- Routine American Society of Anesthesiologists (ASA) monitors including
  - Pulse oximeter
  - Capnometer
  - Core temperature monitor using one of the following sites: distal esophagus or nasopharynx. For procedures where the patient will have a bladder catheter, bladder temperature may be monitored.
  - ECG and blood pressure monitors

Items to have available

Cooling aids

- Hypothermia blanket
- Crushed ice
- Cold 0.9% saline for intravenous infusion (e.g., 30 mL per kg): This is the most rapid, reliable technique of lowering

body temperature if the temperature is greater than 39°C or rapidly increasing.

Drugs

- Sodium bicarbonate, mannitol, furosemide, dantrolene (intravenous), sterile water, antiarrhythmics, insulin, 50% dextrose, and calcium chloride
- ***Avoid intravenous verapamil or diltiazem for treatment of arrhythmia during an MH episode*** because of interaction with dantrolene possibly resulting in cardiac arrest. On the other hand, in a patient taking oral verapamil or diltiazem who is suspected of having an acute MH episode, do ***NOT*** withhold dantrolene treatment.

Beebe JJ, Sessler DI. Preparation of anesthesia machines for patients susceptible to malignant hyperthermia. *Anesthesiology*. 1988;69(3):395–400.

Birgenheier N, Stoker R, Westenskow D, et al. Activated charcoal effectively removes inhaled anesthetics from modern anesthesia machines. *Anesth Analg*. 2011;112(6):1363–1370.

Gunter JH, Ball J, Than-Win S. Preparation of the Dräger Fabius anesthesia machine for the malignant-hyperthermia susceptible patient. *Anesth Analg*. 2008;107:1936–1945.

C. Intraoperative Management

C.1. What anesthetic techniques and agents would you employ?

Potent inhalation agents and succinylcholine (excluding nitrous oxide) are to be avoided. Local or regional anesthesia with intravenous sedation as needed may be preferable if the surgeon and anesthesia provider are confident with these techniques. General anesthesia may be induced with propofol, benzodiazepine, or other intravenous hypnotic, and the patient be ventilated with 100% oxygen. Fentanyl or other opioid may be added to ensure adequate depth of anesthesia. Topical

anesthesia of the larynx and vocal cords is optional. The trachea is intubated with or without the use of an intermediate-acting nondepolarizing muscle relaxant. Anesthetic maintenance is achieved using oxygen with or without nitrous oxide, a narcotic, and a nondepolarizing relaxant as required. Total intravenous anesthesia (TIVA), with a continuous infusion of propofol and injections of analgesics as indicated, is most often employed for nontriggering general anesthetics expected to last more than 30 minutes.

Vital signs are monitored with very close attention to capnography.

C.2. Should body (core) temperature be monitored during general anesthesia lasting more than a short time?

Definitely. Although temperature elevation is often not the first sign of MH, it is one of the common early signs of the syndrome. Therefore, core temperature, esophageal, rectal, urinary bladder, or nasopharyngeal temperature should be monitored for all procedures lasting more than about 30 minutes. Temperature monitoring is also important in detecting hypothermia.

Sessler DI. Temperature monitoring and perioperative thermoregulation. *Anesthesiology*. 2008;109(2):318–338.

C.3. What anesthetic agents are contraindicated?

In general, the anesthetic agents to be avoided include potent inhalation agents and the depolarizing muscle relaxant succinylcholine. Of the agents commonly employed today, the following have been implicated in triggering MH:

- Inhalation agents—halothane enflurane, isoflurane, desflurane, and sevoflurane
- Muscle relaxants—succinylcholine

Larach MG. A primer for diagnosing and managing malignant hyperthermia

susceptibility. *Anesthesiology*. 2018;128(1):8–10.

Litman RS. Susceptibility to malignant hyperthermia: evaluation and management. https://www.uptodate.com/contents/malignant-hyperthermia-diagnosis-and-management-of-acute-crisis?search=malignant%20hyperthermia%20treatment&source=search_result&sele Accessed May 31, 2019.

C.4. If the surgeon wants to use local anesthesia for a procedure, what agents will you recommend?

Both ester and amide local anesthetics are considered safe for use in MH-susceptible patients.

D'Ambrosio J, Adragna MG. Guidelines for the use of local anesthetics in the dental treatment of patients who are susceptible to malignant hyperthermia. *Spec Care Dentist*. 1988;8(2):61–63.

Maccani RM, Wedel DJ, Melton A, et al. Femoral and lateral femoral cutaneous nerve block for muscle biopsies in children. *Paediatr Anaesth*. 1995;5(4):223–227.

C.5. What is the significance of masseter muscle spasm occurring after succinylcholine administration?

Rigidity of the jaw muscles after administration of succinylcholine is referred to as MMR or trismus. MMR presages clinical MH in up to 30% of cases. Even in the absence of clinical MH, myoglobinuria following succinylcholine-induced MMR is common postoperatively. MMR probably occurs in individuals of all ages; however, MMR is more common in children, particularly following gas anesthesia induction

MMR has been reported in 1% of children after halothane/succinylcholine induction and in adults after succinylcholine administration. Should MMR occur, elective surgery should be postponed, the patient observed in an ICU setting for 24 hours seeking myoglobinuria specifically as well as observing for early signs of MH. The patient should be followed until CK levels normalize.

In the case of emergency surgery, the anesthetic should be converted to a "nontriggering" technique and the patient observed for early signs of MH. Dantrolene and other MH treatment procedures should be made ready.

The patient and/or family should be advised to be evaluated for MH susceptibility.

The incidence of MMR in children has decreased as a result of recommendations that the use of succinylcholine in children be reserved for emergency situations.

Other causes of succinylcholine-induced MMR include any form of myotonia or periodic paralysis.

Hudig K, Pollock N, Bulger T, et al. Masseter muscle rigidity and the role of DNA analysis to confirm malignant hyperthermia susceptibility. *Anaesth Intensive Care*. 2019;47(1):60–68.

Litman RS, Smith V, Larach MG, et al. Consensus statement of the Malignant Hyperthermia Association of the United States on unresolved clinical questions concerning the management of patients with malignant hyperthermia. *Anesth Analg*. 2019;128(4):652–659.

Parness J, Bandschapp O, Girard T. The myotonias and susceptibility to malignant hyperthermia. *Anesth Analg*. 2009;109(4):1054–1064.

C.6. Twenty minutes into the procedure with sevoflurane anesthesia, the patient developed increasing tachycardia with ventricular premature beats and mottled skin. What emergency measures would you take?

Although tachycardia may arise from other more common causes, such as a light plane of anesthesia and/or hypovolemia, its association with dysrhythmia in this patient—who is MH susceptible—raises the suspicion that an MH crisis may be starting. End-expiratory CO_2 should be monitored, and if rising despite increasing minute ventilation, the diagnosis of MH should be strongly considered. Because time is of the essence, the following steps should be taken; this constitutes a critical

emergency. Use of a cognitive aid such as a checklist or poster is highly recommended.

- Stop all potent inhalational anesthetics and surgery (if possible).
- Hyperventilate the patient with a high fresh gas flow of 100% oxygen. It is recommended that one increase ventilation using mechanical ventilation, particular in settings of limited manpower.
- Obtain help and assistance through the MH hotline of the Malignant Hyperthermia Association of the United States (MHAUS): 1-800-MH-HYPER.
- Administer specific drug therapy—start dantrolene sodium (DS) early while muscle perfusion is still present. An initial intravenous dose of 2.5 mg per kg should be followed by repeated doses of 1 to 2 mg per kg to a total of 10 mg per kg depending on the patient's response. More dantrolene may be administered if clinically indicated.
- If available, place activated charcoal filters on the inspiratory and expiratory ports of the breathing circuit.
- Initiate aggressive cooling immediately for rapidly increasing temperatures and for those higher than 39°C. Methods for cooling include the following: surface cooling with the patient on a cooling blanket and packed in ice and cold intravenous 0.9% saline or Plasmalyte A. Cooling should be stopped when the patient's temperature falls to lower than 38°C, to prevent inadvertent hypothermia.
- Treat acidosis with sodium bicarbonate (2 mEq per kg initial dose and titrate as necessary).
- Treat hyperkalemia with intravenous calcium chloride or calcium gluconate, hyperventilation, sodium bicarbonate, insulin, and 50% dextrose.
- Treat arrhythmias with standard antiarrhythmics and avoid verapamil or diltiazem if dantrolene has been given. If

hyperkalemia is suspected, do not give lidocaine or procainamide.

- Arterial line and a Foley catheter should be inserted in all cases of fulminant MH. Central venous catheterization should be considered for unstable patients.
- Maintain urine output with mannitol or furosemide. Each 20 mg bottle of Dantrium or Revonto contains 3 g mannitol. In comparison, each 250 mg bottle of Ryanodex contains only 125 mg mannitol.
- Follow CK levels every 12 hours.
- Check electrolytes, hemoglobin/hematocrit, platelet count, and coagulation parameters.
- After the MH episode, register the patient and the event with the North American MH Registry (https://anest.ufl.edu/namhr/).

Hardy JB, Gouin A, Damm C, et al. The use of a checklist improves anaesthesiologists' technical and non-technical performance for simulated malignant hyperthermia management. *Anaesth Crit Care Pain Med*. 2018;37(1):17–23.

C.7. What modalities would you monitor closely during management of the crisis?

The modalities that should be monitored closely include the following:

- End-tidal CO_2 and minute ventilation
- Arterial blood gases/electrolytes/coagulation
- Core temperature

The following should be monitored for ongoing evaluation and management:

- CK levels
- Myoglobin levels—urine and serum
- Urine output

C.8. What steps should be taken to avoid major morbidity

from MH?

All sites where general anesthesia is administered should have 36 vials of dantrolene or 3 bottles of Ryanodex available within about 10 minutes.

All patients undergoing general anesthesia for more than 30 minutes should have core temperature monitored

It is highly recommended that ORs and procedure areas where general anesthesia is employed conduct an MH drill each year. This drill should involve all OR and procedure area personnel going through the steps of alerting the team, obtaining dantrolene, mixing dantrolene, simulating blood draw, cooling the patient, and discussing the episode with family members.

In addition, nonhospital sites should ensure that a hospital is designated to receive a patient who is experiencing an MH episode. The facility should have a plan as to who will accompany the patient, what drugs and monitors will accompany the transport personnel, and the local hospital has dantrolene as well as familiarity with treating the syndrome.

C.9. How does the new formulation of dantrolene (Ryanodex) compare with the existing formulation of dantrolene (Dantrium or Revonto)?

Present formulations of dantrolene (Dantrium and Revonto) are lyophilized, freeze dried, and dispensed as DS 20 mg in a 70-mL vial and contain 3,000 mg of mannitol. It should be reconstituted by adding 60 mL of sterile water without a bacteriostatic agent, and the vial needs to be shaken until clear. Warming the sterile water to 40°C immediately prior to mixing can speed up the process and also help drawing the drug in a syringe because the solution is fairly viscous. One may require 4 to 7 vials to start the treatment and may go up to 36 vials in an adult achieving maximum dosage. This can be a tedious and time-consuming process.

Recent formulation of dantrolene (Ryanodex) is a nanocrystalline dantrolene sodium suspension (DSS) that allows for a much larger dose of 250 mg to be dispensed in a vial that requires only 5 mL of sterile water to dissolve it in solution. It offers the advantage of rapid reconstitution and administration. In one animal study, the time for preparation for DSS (less than 60 seconds) was 10- to 15-fold shorter compared with DS (658 to 1,062 seconds), and the time taken to inject was a 100-fold faster. It contains only 125 mg of mannitol; hence, mannitol needs to be given separately. Because the diluent is in small amounts of water, fluid load is not as significant as in case of existing formulations. This becomes especially significant in pediatric patients.

The cost of DSS (required supply of 3 vials) is close to $7,000 in United States. It has a shelf life of 24 months. DS has a shelf life of 36 months and costs less than half as much (required supply of 36 vials). The cost of DSS may be substantially reduced when DSS is purchased for several locations within the same organization.

Rosenberg H, Pollock N, Schiemann A, et al. Malignant hyperthermia: a review. *Orphanet J Rare Dis*. 2015;10:93.

Schütte JK, Becker S, Burmester S, et al. Comparison of the therapeutic effectiveness of a dantrolene sodium solution and a novel nanocrystalline suspension of dantrolene sodium in malignant hyperthermia normal and susceptible pigs. *Eur J Anaesthesiol*. 2011;28(4):256–264.

D. Postoperative Management

D.1. What complications may follow this syndrome?

Disseminated intravascular coagulation syndrome is a major complication of MH especially when the patient's temperature exceeds 41°C. Other complications include renal failure, hyperkalemia, compartment syndrome, and neurologic injury.

As a result of massive muscle breakdown, the patient may be weak for days and also complain of muscle cramps and pain.

Brandom BW, Larach MG, Chen MS, et al. Complications associated with the administration of dantrolene 1987 to 2006: a report from the North American Malignant Hyperthermia Registry of the Malignant Hyperthermia Association of the United States. *Anesth Analg*. 2011;112(5):1115–1123.

Rosenberg H, Pollock N, Schiemann A, et al. Malignant hyperthermia: a review. *Orphanet J Rare Dis*. 2015;10:93.

D.2. What would be your follow-up in this case?

The vigorous therapy started in the OR should be continued in the immediate postoperative period into the PACU or the ICU. Dantrolene administration should be continued for at least 24 hours after an episode is controlled at a dose of 1 mg per kg every 4 to 6 hours titrated to signs of MH. Serum CK should be followed until consistently trending downward.

Other laboratory values that should be followed until normalized include

- Arterial blood gases
- Electrolytes
- Coagulation profile

Body temperature should be monitored along with other vital signs. Recrudescence of MH occurs in about 20% of treated cases and therefore the patient should be watched in an ICU setting for at least 36 hours following an episode.

Burkman JM, Posner KL, Domino KB. Analysis of the clinical variables associated with recrudescence after malignant hyperthermia reactions. *Anesthesiology*. 2007;106:901–906.

D.3. What would you advise the patient and the family?

The patient and his family should be warned of the dangerous nature of this syndrome and should be advised to carry an identification band at all times. The pedigree of the family should be prepared, and the members should be investigated for

susceptibility to this syndrome and issued medical identification bracelets or pendants accordingly. While not changing his future anesthetic management, molecular genetic testing would be recommended for the patient; if an MH causal mutation is discovered, this will facilitate noninvasive confirmation of MH susceptibility in other family members.

The MHAUS has been active since 1981 and offers current information and advice on patient management as well as identification bracelets and a variety of material for health care professionals. The following are some useful contact information:
Emergency hotline: 1-800-MH-HYPER
Address: MHAUS, 39 East State Street, P.O. Box 1609, Sherburne, NY 13815
Phone: 1-800-98-MHAUS
Internet: www.mhaus.org

In addition, the patient and his family should consult with one of the MH diagnostic centers or with an MHAUS hotline consultant to discuss further evaluation. A complete listing is available through MHAUS.

The patient should be registered with the North American MH Registry.

Forms may be obtained through MHAUS.

The website for the North American MH Registry is https://anest.ufl.edu/namhr/; the phone number is 888-274-7899. The Registry is located at the University of Florida.

D.4. What precautions should an MH-susceptible patient take outside of the operating room (OR)?

In general, MH-susceptible patients should be cognizant of their response to heat and exercise. As for any patient, excess exposure to heat and humidity, especially with exercise should be limited or avoided. Although it is true that cases of what

appears to be “awake” MH have been reported without trigger anesthetics, these are rare. At present, there is no way to predict which previously asymptomatic patients may have an adverse response to environmental conditions. Even family members with the same MH-causal mutation may respond differently to vigorous exercise, heat, or infection.

Litman RS, Smith V, Larach MG, et al. Consensus statement of the Malignant Hyperthermia Association of the United States on unresolved clinical questions concerning the management of patients with malignant hyperthermia. *Anesth Analg*. 2019;128(4):652–659.

Tobin JR, Jason DR, Challa VR, et al. Malignant hyperthermia and apparent heat stroke. *JAMA*. 2001;286(2):168–169.

Zvaritch E, Gillies R, Kraeva N, et al. Fatal awake malignant hyperthermia episodes in a family with malignant hyperthermia susceptibility: a case series. *Can J Anaesth*. 2019;66(5):540–545.

Suggested Resources

Websites of the Malignant Hyperthermia Association of the United States: www.mhaus.org
www.nmsis.org
Website of the European MH Group: www.emhg.org

55 Postoperative Residual Neuromuscular Weakness and Prolonged Apnea

Mary So, Danielle McCullough, and David J. Kopman

A healthy 35-year-old, 65-kg female was scheduled for an elective abdominal hysterectomy. Anesthesia was induced with propofol (2.0 mg per kg) and rocuronium (1.2 mg per kg). Anesthesia, which lasted 90 minutes, was maintained with desflurane 6.0% end-tidal and was supplemented with fentanyl as needed. No reversal was given at the end of surgery because tidal volumes were deemed to be adequate. The train-of-four count (TOFC) using facial nerve stimulation was four with no detectable fade. Upon arrival in the postanesthesia care unit (PACU), the patient was tachypneic, had uncoordinated, floppy arm movements, and appeared to be agitated and in distress. Arterial oxygen saturation on room air was 89%.

A. Medical Diseases and Differential Diagnosis

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2. How is residual neuromuscular blockade (NMB) diagnosed?
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B. Intraoperative Management

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12. What are the limitations of acetylcholinesterase antagonists?

13. Is there anything wrong with administering neostigmine when the TOFC is less than 3?
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15. Is there any way to rapidly antagonize a profound nondepolarizing block?

C. Postoperative Management

1. What is the incidence of residual NMB in the PACU?
2. Does undetected postoperative residual neuromuscular block (PORB) have clinical consequences?

A. Medical Diseases and Differential Diagnosis

A.1. What is the differential diagnosis for postoperative hypoventilation?

The differential diagnosis for postoperative hypoventilation includes the following:

- Residual anesthetic agent
- Residual narcotic
- Residual muscle relaxant
- Hypercarbia
- Occurrence of some medical complication during anesthesia, such as stroke or embolism

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Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2592–2593.

A.2. How is residual neuromuscular blockade (NMB) diagnosed?

When residual NMB is clinically suspected, it is diagnosed by testing the TOFC using a PNS. This patient showed clear signs of residual neuromuscular weakness upon arrival in the PACU. TOF stimulation at the ulnar nerve showed a TOFC of only 2 at the adductor pollicis (thumb). A diagnosis of residual blockade

was made and the patient received neostigmine 0.05 mg per kg plus an appropriate dose of glycopyrrolate (0.01 mg per kg). Seven minutes later, the TOFC was 4 with no evidence of fade on palpation of the thumb, and all signs of residual block had abated.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1354–1372.

A.3. What is the order of recovery of voluntary muscle groups from nondepolarizing muscle relaxants?

Onset and recovery of muscular blockade depend on blood supply to the muscle group in question. Peripheral muscles (e.g., adductor pollicis) tend to have poor blood supply compared to central muscles (e.g., diaphragm) leading to a slower onset and offset of nondepolarizing muscle relaxants. Muscles of the upper airway/pharynx are an exception to this "rule", however, because they exhibit a fast onset of blockade but are slower to recover than peripheral muscles. When the TOFC at the orbicularis oculi or corrugator supercilii muscles shows recovery from nondepolarizing block, the response at the adductor pollicis may be almost nonexistent. Thus, facial nerve stimulation may give the clinician a false sense of security about the adequacy of neuromuscular recovery at the end of a case.

Similarly, in the intubated patient breathing spontaneously, a normal tidal volume and maintenance of an acceptable P_{CO_2} do not necessarily indicate adequate neuromuscular recovery. The diaphragm is the first muscle to recover from nondepolarizing block and requires significantly higher plasma levels of relaxants to maintain paralysis. The muscles that protect the upper airway are far more sensitive to nondepolarizing relaxants and cannot be clinically tested in the intubated patient. Thus, a patient who is able to maintain adequate respiratory exchange while intubated may experience airway obstruction due to

inadequate pharyngeal muscle recovery when extubated.

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McGrath CD, Hunter JM. Monitoring of neuromuscular block. *Contin Educ Anaesth Crit Care Pain*. 2006;6(1):7–12. doi:10.1093/bjaceaccp/mki067.

Thilen SR, Hansen BE, Ramaiah R, et al. Intraoperative neuromuscular monitoring site and residual paralysis. *Anesthesiology*. 2012;117:964–972.

A.4. What is the mechanism of action of succinylcholine, and how is it metabolized? What are the side effects of succinylcholine?

Succinylcholine is a depolarizing neuromuscular blocker. It is composed of two linked acetylcholine (ACh) molecules, which are capable of binding to the ACh receptor at the neuromuscular junction. This activates the receptor, depolarizing the membrane and causing the characteristic fasciculations (i.e., muscle contractions) seen when using this drug. Succinylcholine is metabolized by butyrylcholinesterase (BChE), also known as PChE.

The most common untoward side effect seen after succinylcholine administration is muscle pain occurring in the first 24 to 48 hours postoperatively. Women and patients undergoing ambulatory surgery appear most susceptible to this phenomenon. The reported incidence of succinylcholine-induced myalgia is variable but probably occurs in 25% to 50% of patients. Discomfort is typically characterized as being similar to the muscle soreness that occurs after heavy or unusual exercise. It has been postulated that the etiology of the phenomenon is related to muscle damage caused by asynchronous contractions during the initial muscle depolarization that precedes paralysis. Defasciculating doses of

nondepolarizing relaxants (10% of the ED95) given 2 to 5 minutes prior to succinylcholine have been shown to reduce the incidence of myalgia by as much as 50%. Pretreatment with nonsteroidal anti-inflammatory drugs has also been shown to reduce the incidence of muscle pain following succinylcholine administration.

Succinylcholine may also be associated with various cardiac dysrhythmias including bradycardia, tachycardia, and junctional and ventricular dysrhythmias. Stimulation of nicotinic receptors at sympathetic and parasympathetic ganglion and muscarinic receptors at the sinus node are believed to be involved in this phenomenon. Infants and children may be more likely to manifest clinically significant bradycardia following succinylcholine administration secondary to their relatively high degree of resting vagal tone as compared to adults; however, pretreatment with atropine is no longer recommended in this patient population. Junctional rhythms following succinylcholine administration are also relatively common. The postulated mechanism of action is muscarinic stimulation of the sinus node that results in diminished sinus activity and the subsequent emergence of the atrioventricular node as the dominant pacemaker. Various mechanisms have been postulated to explain ventricular dysrhythmias that sometimes occur after succinylcholine administration including potassium release from skeletal muscle, succinylcholine mediated sensitivity to catecholamines, and profound sinus and atrioventricular node slowing.

The most serious complication associated with succinylcholine administration is severe and potentially lethal levels of hyperkalemia in at-risk individuals. When succinylcholine is administered to an otherwise healthy patient during the induction of anesthesia, plasma potassium levels typically increase by 0.5 mEq per L as potassium ions move

from the intracellular to extracellular space. The increase is transient and is typically tolerated well by most patients. In at-risk patients, however, the efflux of potassium from the intracellular space can be in excess of 3.5 mEq per L, enough to induce malignant dysrhythmias and cardiac arrest. The list of susceptible patients includes those with congenital muscular dystrophies, upper or lower motor neuron defects, prolonged chemical denervation (e.g., muscle relaxants, magnesium, clostridial toxins), direct muscle trauma or inflammation, extensive burns, and disuse atrophy. In the event that succinylcholine is inadvertently given to an at-risk patient and an exaggerated hyperkalemic response is suspected, prompt treatment with calcium chloride (1 to 2 g), hyperventilation, sodium bicarbonate (1 mEq per kg), regular insulin, and dextrose should be initiated to prevent severe dysrhythmias and cardiac arrest.

Succinylcholine also causes increases in intraocular, intragastric, and intracranial pressures (ICP). The increase in intraocular pressure (IOP) caused by succinylcholine begins rapidly after drug administration. Peak pressures may rise as much as 5 to 15 mmHg before returning to baseline levels about 6 minutes after drug dosing. The etiology of this phenomenon is unclear, but detachment of the intraocular muscles from the globe fails to prevent the pressure rise, which is suggestive of an intraocular mechanism. It has been suggested that succinylcholine use should be avoided in the setting of open-eye injuries, although there is scant evidence that its administration has led to extrusion of intraocular contents or blindness. The increase in intragastric pressure (IGP) caused by succinylcholine is likely related to fasciculations of the abdominal skeletal musculature. A defasciculating dose of a nondepolarizing muscle relaxant given prior to succinylcholine administration can prevent any increase in IGP.

Succinylcholine can also cause a transient increase in ICP. The increase in ICP after succinylcholine administration correlates with muscle fasciculations, increased electroencephalogram (EEG) activity, and elevated cerebral blood flow. Prior administration of a nondepolarizing muscle relaxant can attenuate or even prevent this pressure increase. The use of succinylcholine in the setting of intracranial hypertension is probably best limited to emergency situations where the benefits of rapid airway control outweigh the risks of a transient increase in ICP.

Lastly, it should be remembered that succinylcholine is a potent trigger of malignant hyperthermia (MH). Its use should be restricted to settings where prompt recognition and treatment of MH are possible.

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Martyn JA, Richtsfeld M. Succinylcholine-induced hyperkalemia in acquired pathologic states: etiologic factors and molecular mechanisms. *Anesthesiology*. 2006;104:158–169.

A.5. If succinylcholine were the only muscle relaxant used during the case and the patient did not exhibit a response to train-of-four (TOF) stimulation, what is the likely diagnosis? How would you confirm it?

The most likely diagnosis is atypical BChE. In the given patient, stimulation of the ulnar nerve with a PNS resulted in no response of the muscles of the hand, confirming the diagnosis of prolonged response to succinylcholine. Extreme prolongation in the duration of effect is usually a manifestation of an atypical BChE genotype. Following a 1.0 mg per kg dose of succinylcholine, patients homozygous for the most common

atypical genotypes will exhibit apnea for an hour or more; it may take as much as 3 hours for adequate respiratory efforts to return. However, the duration of apnea is highly dependent on the BChE variant in question and may be shorter or longer than the aforementioned figures.

Traditionally, identification of the human BChE variant has been performed by biochemical analysis. These tests, which have been used for decades, consist of the measurement of plasma cholinesterase activity with different substrates and of testing the degree of inhibition of this activity with a well-known inhibitor, such as dibucaine, fluoride, or R02-0683. These tests have identified multiple genes that can reside at the same allelic site, such as the atypical, silent, fluoride-resistant, J, K, H, and Newfoundland variants. However, biochemical testing often leads to equivocal results. More recently, molecular biologic techniques have been applied to identifying a patient's exact genotype.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:792–831.

A.6. What are acetylcholinesterase and serum cholinesterase? What is the clinical significance of heterozygosity for atypical pseudocholinesterase (PChE)?

Acetylcholinesterase is a relatively specific enzyme that hydrolyzes ACh faster than it does other choline esters. It is found in red blood cells, the central nervous system, and at the neuromuscular junction. It is responsible for hydrolyzing and inactivating the ACh produced during normal neuromuscular transmission. It does not hydrolyze succinylcholine.

Serum cholinesterase, also called *cholinesterase*, *PChE*, *BChE*, and *nonspecific cholinesterase*, hydrolyzes many choline esters, including succinylcholine. It is found in many human

tissues but not in the red blood cell. It is synthesized in the liver. Its physiologic function is unknown, but it may hydrolyze choline esters, such as propionylcholine and butyrylcholine, which may be formed by bacterial action in the gut and by the enzyme systems responsible for the formation of ACh.

A patient who is heterozygous for atypical PChE will exhibit a prolonged response to depolarizing NMB. Only after a strong, sustained response to indirect tetanic stimulation at the wrist can be demonstrated should sedation be terminated and an attempt made to wean the patient off controlled ventilation. Once the diagnosis of an atypical response to succinylcholine is ascertained, treatment is entirely supportive and symptomatic. Because the duration of residual block is hard to predict, the patient should remain intubated, artificially ventilated, and sedated.

Patients recovering from prolonged succinylcholine-induced block usually exhibit a “dual” or “phase II” block during recovery (fade on repetitive stimulation). Although neostigmine or edrophonium can under certain circumstances antagonize this block, this approach is risky when dealing with prolonged succinylcholine apnea. If significant plasma levels of succinylcholine are still present, the administration of an acetylcholinesterase inhibitor may be counterproductive.

The patient should be informed that she had a prolonged episode of muscular weakness and that the presumptive cause was an atypical reaction to succinylcholine. She should also be encouraged to have this diagnosis confirmed through laboratory testing. If an atypical genotype is confirmed, she should encourage her family members to be tested as well. Finally, the patient should be assured that this diagnosis has no adverse health consequences but that in the future when surgery is planned, her anesthesiologist needs to be informed of this diagnosis.

The dibucaine number (DN) is the percentage of BChE enzyme activity that is inhibited by dibucaine. The "normal" variant of BChE is 80% inhibited by dibucaine; therefore, a "normal" DN is 80. Together, the DN and the BChE enzyme activity results can help identify individuals at risk for prolonged paralysis following the administration of succinylcholine. Decreased BChE enzyme activity in conjunction with a DN less than 30 suggests high risk for prolonged paralysis. Normal to decreased BChE enzyme activity in conjunction with a DN 30 to 79 suggests variable risk. The relation between the DN and the duration of succinylcholine NMB is shown in **Table 55.1**.

TABLE 55.1 Relation between Dibucaine Number and Duration of Succinylcholine Neuromuscular Blockade

Type of Pseudocholinesterase	Genotype	Frequency	Dibucaine Number[a]	Response to Succinylcholine or Mivacurium
Homozygous typical	EuEu	Normal	70–80	Normal
Heterozygous	EuEa	1/480	50–60	Slightly prolonged
Homozygous atypical	EaEa	1/3,200	20–30	Markedly prolonged

[a]The dibucaine number indicates the percentage of enzyme inhibited.

Cerf C, Mesguish M, Gabriel I, et al. Screening patients with prolonged neuromuscular blockade after succinylcholine and mivacurium. *Anesth Analg*. 2002;94:461–466.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:792–831.

Levano S, Ginz H, Siegemund M, et al. Genotyping the butyrylcholinesterase in patients with prolonged neuromuscular block after succinylcholine. *Anesthesiology*. 2005;102:531–535.

Levano S, Keller D, Schobinger E, et al. Rapid and accurate detection of atypical and Kalow variants in the butyrylcholinesterase gene using denaturing high performance liquid chromatography. *Anesth Analg*. 2008;106:147–151.

Massoulié J, Bon S. The molecular forms of cholinesterase and acetylcholinesterase in vertebrates. *Ann Rev Neurosci*. 1982;5:57–106.

Pantuck EJ. Plasma cholinesterase: gene and variations. *Anesth Analg*.

1993;77:380–386.

Taylor P, Schumacher M, MacPhee-Quingley K, et al. The structure of acetylcholinesterase: relationship to its function and cellular disposition. *Trends Neurosci*. 1987;10:93–95.

A.7. What is the incidence of atypical cholinesterase activity?

The incidence of atypical cholinesterase activity varies with the population studied, but it is approximately 1 of 2,800 in the general population of the United States with a 1:1 male/female ratio.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:792–831.

A.8. What are some factors that can lower PChE levels?

Reduced PChE activity may be associated with the following:

- Abnormal genotype
- Normal physiologic variation (e.g., pregnancy). However, until BChE activity is reduced to <30% of normal, only modest increases in the duration of succinylcholine are to be expected.
- Liver disease
- Malnutrition
- End-stage renal disease
- Burns
- Plasmapheresis
- Noncompetitive cholinesterase inhibitors (e.g., pesticides, certain nerve gases)
- Other drugs including: neostigmine, oral contraceptives, monoamine oxidase inhibitors, echothiophate, cytotoxic drugs, tetrahydroaminacrine, metoclopramide, and hexafluorenium

Davis L, Britten JJ, Morgan M. Cholinesterase. Its significance in anaesthetic practice. *Anaesthesia*. 1997;52:244–260.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:792–831.

B. Intraoperative Management

B.1. How is the choice among muscle relaxants made?

A muscle relaxant can be chosen based on onset characteristics, duration of action, and method of metabolism (**Table 55.2**). Muscle relaxants can be characterized as short, intermediate, and long duration. Metabolism may or may not be dependent on liver and kidney function (e.g., patients with hepatic dysfunction may have PChE deficiency). When surgical relaxation is not necessary, then NMB may be given solely to provide optimal intubating conditions by paralyzing the larynx, pharynx, and muscles of the jaw. Succinylcholine is useful for its rapid onset and recovery times, especially when performing a rapid sequence induction or facilitating motor nerve monitoring during the procedure.

If a rapid sequence induction is indicated, either succinylcholine or rocuronium may be used for NMB. Succinylcholine has a more rapid onset and is usually the preferred agent if there are no contraindications to its use (e.g., immobility, history of MH, hyperkalemia). In patients with hepatic or renal dysfunction, one can consider using cisatracurium. This nondepolarizing NMB agent undergoes Hofmann elimination and therefore is not affected by renal or hepatic dysfunction.

TABLE 55.2 Characteristics of Commonly Used Muscle Relaxants

					Elimi
ED95 under N_2O/O_2	Dose for Intubation	Clinical Duration	Metabolism	Kidne	

Drug	(mg/kg)	(mg/kg)	Time (sec)	(min)	(%)	(%)
Ultrashort acting						
Succinylcholine	0.5	1.0	60	5–10	Plasma cholinesterase (98–99)	<2
Short acting						
Mivacurium	0.08	0.2–0.25	120	12–15	Plasma cholinesterase (95–99)	<5
Intermediate acting						
Vecuronium	0.05	0.1–0.2	120	45–60	Liver (30–40)	40–50
Rocuronium	0.3	0.6–1.0	90	45–55	None	<10
Cisatracurium	0.05	0.15–0.2	120	45–60	Hofmann elimination (77)	16
Long acting						
α-Tubocurarine	0.5	0.5–0.6	150	100–120	None	80
Pancuronium	0.07	0.08–0.12	150	100–120	Liver (10–20)	85
Pipecuronium	0.05	0.08–0.10	180	100–120	10	>90
Doxacurium	0.025	0.05–0.08	240	120–150	None	>90

From Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:792–831.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:792–831.

B.2. What factors can alter sensitivity to nondepolarizing neuromuscular blockers?

In any group of healthy patients, there exists a wide variability in the sensitivity to the effects of neuromuscular blocking agents (NMBAs). The potency of these drugs is expressed as the agent's ED50 or ED95 (i.e., the dose that will produce 50% or 95% depression of a single twitch [T1] in an average individual). The coefficient of variation (the standard deviation as a percentage of the mean value) for the ED95 of most agents approximates 20% to 25%. Thus, if the ED95 for drug X is 1.0 mg per kg, in 5% of normal individuals, the ED95 may be <0.60 mg per kg. Because of the shape of the dose-response curve of nondepolarizing relaxants, this modest difference in drug

requirement may have large consequences as to the depth of block. In these individuals, a plasma level that produces only 50% block of T1 in the average subject may produce >90% instead.

Similarly, the duration of effect of administered relaxants is quite variable. For example: Following a 1.2 mg per kg dose, the clinical duration of rocuronium (time to 25% T1 recovery) in a sample size of only 12 averaged 67 minutes; however, the range in responses went from 39 to 118 minutes. Following a dose two times the ED95 of a blocker of intermediate duration (e.g., vecuronium), 30% of individuals will still need pharmacologic antagonism 2 hours later.

In the aged or in patients with renal or hepatic disease, this variability is even more pronounced. This is especially true of aminosteroid blockers, such as vecuronium or rocuronium, when compared to atracurium or cisatracurium.

Arain SR, Kern S, Ficke DJ, et al. Variability of duration of action of neuromuscular-blocking drugs in elderly patients. *Acta Anaesthesiol Scand*. 2005;49:312–315.

Heier T, Feiner JR, Wright PM, et al. Sex-related differences in the relationship between acceleromyographic adductor pollicis train-of-four ratio and clinical manifestations of residual neuromuscular block: a study in healthy volunteers during near steady-state infusion of mivacurium. *Br J Anaesth*. 2012;108:444–451.

Kopman AF, Kahn NA, Neuman GG. Precurarization and priming: a theoretical analysis of safety and timing. *Anesth Analg*. 2001:93:1253–1256.

B.3. What are the characteristics of nondepolarizing block?

The distinguishing feature of nondepolarizing block is fade on repetitive stimulation. For example, consider a situation in which the amplitude of twitch height (T1) is reduced by 50% with a nondepolarizing blocker when stimuli are delivered at 0.10 Hz (1 every 10 seconds). If the rate of stimulation is

increased to 1 Hz, the height of T1 may fall to <20% of control, and at 2 Hz to about 10% of control. This fade is most easily appreciated subjectively when tetanic stimuli (rates ≥30 Hz) are delivered.

Lee C, Katz RL. Fade of neurally evoked compound electromyogram during neuromuscular block by d-tubocurarine. *Anesth Analg*. 1977;56:271–275.

B.4. What is a TOF stimulus?

A "train-of-four" consists of four stimuli delivered at half-second intervals (2 Hz). The TOF ratio is the height of the fourth indirectly elicited response divided by the amplitude of the first response. This ratio in unparalyzed individuals normally approximates a value of 1.0 when measured by mechanomyography (MMG), electromyography (EMG), or kinemyography but may exceed a value of 1.10 when measured by acceleromyography (AMG) (see section B.11). As the depth of block increases, this ratio becomes smaller and eventually the fourth, then the third, and so on responses "drop out." If only two responses to a TOF stimulus are present, we speak of a TOF count of 2.

Ali HH, Utting JE, Gray C. Stimulus frequency in the detection of neuromuscular block in humans. *Br J Anaesth*. 1970;42:967–978.

B.5. Why is the TOF ratio of clinical importance?

The TOF fade is a far more sensitive index of residual block than single twitch depression. In addition, the TOF ratio is useful because each TOF sequence serves as its own control. It is not necessary to know the amplitude of the evoked response prior to administration of NMB or to worry about baseline drift over time. Traditionally, the TOF ratio is measured at the hand by noting the response of thumb adduction to stimulation of the ulnar nerve. While clinicians are much more interested in the neuromuscular function of the diaphragm, masseter, and

laryngeal adductors, correlation with adductor pollicis muscle function has served as a useful clinical surrogate.

Ali HH, Utting JE, Gray TC. Quantitative assessment of residual antidepolarizing block. I. *Br J Anaesth*. 1971;43:473–477.

Kopman AF. Surrogate endpoints and neuromuscular recovery. *Anesthesiology*. 1997;87:1029–1031.

B.6. How do we define adequate recovery of neuromuscular function?

Once the TOF ratio at the adductor pollicis has recovered to a value of 0.70, tests of mechanical respiratory reserve, such as vital capacity and peak expiratory flow rate, have usually recovered to within 90% of control. Clinically, this means that a patient may exhibit spontaneous respiration but may require pressure support or have upper airway obstruction when extubated.

Studies done in the 1970s suggested that a TOF ratio of 0.70 was synonymous with adequate neuromuscular recovery, and this was the accepted standard for the next two decades. However, by the late 1990s, this assumption was questioned. Work in awake volunteers demonstrated that at a TOF ratio of 0.70, grip strength was decreased by more than 40%. At a TOF ratio of 0.70, the vast majority of subjects had difficulty apposing their incisor teeth and could not sip water from a straw because they could not make a tight seal around the straw with their lips. All individuals had double vision at TOF ratio <0.90. It was clear that these health volunteers were not “street ready” until their TOF ratios reached or exceeded a value of 0.90. In addition, other volunteer studies revealed even more alarming data. At a TOF ratio of 0.70, there is a decreased ventilatory response to hypoxia (via a mechanism at the carotid body), and the swallowing mechanism is disorganized. Partial paralysis (a TOF of 0.70) causes pharyngeal dysfunction, and there is an

increased risk for aspiration with mechanical adductor pollicis TOF ratios <0.90. Pharyngeal function is not normalized until an adductor pollicis TOF ratio of >0.90 is reached. Thus, the current standard for adequate neuromuscular recovery is a TOF of 0.90 or better.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1354–1372.

Heier T, Caldwell JE, Feiner JR, et al. Relationship between normalized adductor pollicis train-of-four ratio and manifestations of residual neuromuscular block: a study using acceleromyography during near steady-state concentrations of mivacurium. *Anesthesiology*. 2010;113:825–832.

Kopman AF, Yee PS, Neuman GG. Relationship of the train-of-four fade ratio to clinical signs and symptoms of residual paralysis in awake volunteers. *Anesthesiology*. 1997;86:765–771.

B.7. Are there useful and/or trustworthy clinical tests of neuromuscular recovery?

The first commercially available PNS did not appear until the mid-1960s, and units capable of delivering TOF stimuli did not arrive for another decade. Even today, devices that can quantify or measure the TOF ratio in real time are not widely distributed. Thus, clinicians have been reluctant to abandon clinical tests of neuromuscular recovery first suggested half a century ago, including tidal volume, negative inspiratory force, grip strength, the 5-second head lift, the ability to protrude the tongue, and so on. Unfortunately, most of these tests share one fundamental weakness. They require an awake and cooperative patient. Ideally, we would like to know the state of neuromuscular recovery prior to awakening the patient and certainly prior to tracheal extubation.

The most widely cited test, the 5-second head lift, is clearly not a sensitive test of residual block. At a TOF ratio of 0.50, the majority of patients may still pass this test. Other widely mentioned tests are no better and may actually be very

misleading. Traditional "bedside" tests of residual muscle weakness lack sensitivity and must be considered unreliable.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1354–1372.

Heier T, Caldwell JE, Feiner JR, et al. Relationship between normalized adductor pollicis train-of-four ratio and manifestations of residual neuromuscular block: a study using acceleromyography during near steady-state concentrations of mivacurium. *Anesthesiology*. 2010;113:825–832.

B.8. How accurate are subjective estimates of the TOF ratio, and what purpose do peripheral nerve stimulator (PNS) monitors serve?

Visual or tactile estimations of the TOF ratio are notoriously inaccurate. Once the TOF ratio exceeds a value of 0.40 to 0.50, a majority of experienced anesthesiologists are unable to detect the presence of any fade at all. Thus, failure to detect fade may indicate a true value anywhere from 0.50 to 1.0. Accurate assessment of the TOF ratio requires an objective or quantitative monitor.

Because subjective estimates of the TOF ratio are so unreliable, one may ask does intraoperative TOF stimulation serve any purpose. The answer is a resounding yes. The only satisfactory method of determining the degree of neuromuscular block is to stimulate a motor nerve with an electric current and observe the contraction of the muscles innervated by that nerve. The TOFC (e.g., the number of evoked responses at the thumb that can be detected) gives a useful estimate of the depth of neuromuscular block. A rough rule of thumb follows: A TOFC of 1 = 5% recovery, TOFC of 2 = 15% recovery, TOFC of 3 = 25% recovery, and TOFC of 4 (with fade) = ≥35% recovery. This information allows the clinician to determine whether the patient can be given reversal and the appropriate dose.

Kopman AF. Tactile evaluation of train-of-four count as an indicator of

reliability of antagonism from vecuronium- or atracurium-induced neuromuscular blockade. *Anesthesiology*. 1991;75:588–593.

Viby-Mogensen J, Jensen NH, Engbaek J, et al. Tactile and visual evaluation of the response to train-of-four nerve stimulation. *Anesthesiology*. 1985;63:440–443.

B.9. What is double burst stimulation (DBS)?

Because of the limitations in subjective interpretation of TOF fade, other patterns of stimulation have been investigated. A somewhat more sensitive test is the response to DBS; however, this test should not replace more quantitative measures of NMB recovery. This sequence consists of a very brief tetanic pulse (3 stimuli at 50 Hz), a 0.75-second pause, and another brief tetanic pulse. The observer feels two strong twitches. Most observers lose the ability to detect DBS fade at a TOF ratio of about 0.60.

Engbaek J, Ostergaard D, Viby-Mogensen J. Double burst stimulation (DBS): a new pattern of nerve stimulation to identify residual neuromuscular block. *Br J Anaesth*. 1989;62:274–278.

B.10. What is the posttetanic count (PTC)?

As the level of NMB is progressively increased, the TOFC eventually falls to zero. Because posttetanic potentiation is a prominent feature of nondepolarizing block, it is still possible to get additional information about the depth of block once the TOF response disappears. The following sequence is employed: a 5-second 50-Hz tetanus, a 3-second pause, and then 20 single-twitch stimuli at 1 Hz. The number of responses elicited is referred to as the PTC. Generally, when the count approximates a value of 10, the first response to TOF stimulation appears.

Viby-Mogensen J, Howardy-Hansen P, Chraemmer-Jørgensen B, et al. Posttetanic count (PTC): a new method of evaluating an intense nondepolarizing block. *Anesthesiology*. 1981;55:458–461.

B.11. How can the TOF ratio be measured quantitatively?

Prior to the current decade, the vast bulk of clinical research on

neuromuscular function was done by measuring either evoked mechanical force (MMG) or summated electrical action potentials (EMG) at the adductor pollicis. Although these techniques represent gold standards for reliability, they are unfortunately cumbersome to use in daily practice. In addition, at present, there are no commercially available free-standing MMG or EMG monitors designed for use in the operating room. However, using a different method of measurement, AMG, it is now possible to obtain a real-time display of the TOF ratio using a small handheld device, which is relatively easy to set up and has a user-friendly interface. The rationale for AMG is based on Newton's second law of motion, which states that force is equal to mass times acceleration. Presumably, the mass of the thumb remains constant so that acceleration is directly proportional to force. For measurement of acceleration, a piezoelectric ceramic wafer is fixed to the thumb. When an evoked mechanical response of the thumb is elicited, an electrical signal proportional to the acceleration is generated in the ceramic transducer. This signal can then be digitized, processed, and electronically displayed in real time. Thus, it is now finally possible for the clinician to accurately and easily determine the extent of neuromuscular block (the TOF ratio) in real time. An excellent review of the pros, cons, and limitations of AMG may be found in the following references.

Claudius C, Viby-Mogensen J. Acceleromyography for use in scientific and clinical practice: a systematic review of the evidence. *Anesthesiology*. 2008;108:1117–1140.

Fuchs-Buder T, Schreiber JU, Meistelman C. Monitoring neuromuscular block: an update. *Anaesthesia*. 2009;64(suppl 1):82–89.

Hemmerling TM, Le N. Brief review: neuromuscular monitoring: an update for the clinician. *Can J Anaesth*. 2007;54:58–72.

Loughnan T, Loughnan AJ. Overview of the introduction of neuromuscular monitoring to clinical anaesthesia. *Anaesth Intensive Care*. 2013;41(suppl 1):19–24.

Stewart PA, Freelander N, Liang S, et al. Comparison of electromyography and kinemyography during recovery from non-depolarising neuromuscular blockade. *Anaesth Intensive Care*. 2014;42:378–384.

B.12. What are the limitations of acetylcholinesterase antagonists?

Nondepolarizing NMBAs are competitive in nature. Molecules of an NMBA compete with molecules of Ach for access to nicotinic binding sites or receptors at the myoneural junction. The NMBA-receptor or Ach-receptor binding is evanescent in duration (millisecond). Thus, the relative concentration of NMBA versus Ach determines which molecule is most likely to succeed in the contest for receptor access. Anticholinesterases such as neostigmine affect antagonism by preventing Ach degradation and thus increasing the concentration of Ach in the synaptic cleft. However, there is a ceiling to this effect. Once the cholinesterase enzyme is completely inhibited, the addition of additional neostigmine or edrophonium will have no further effect. In contrast, there is no limit to the concentration of NMBA that may exist at the receptor if excessive doses of relaxant are administered. In practical terms, the maximum depth of block that can be rapidly antagonized by anticholinesterases approximately corresponds to the reappearance of the fourth response to TOF stimulation. To achieve rapid (within 10 minutes) reversal to a TOF ratio of 0.7 in more than 87% of patients, three or four tactile responses should be present at the time of neostigmine administration. It is not possible within 30 minutes to achieve a TOF ratio of 0.9 in all patients, regardless of the number of tactile responses present at neostigmine administration.

Beemer GH, Goonetilleke PH, Bjorksten AR. The maximum depth of an atracurium neuromuscular block antagonized by edrophonium to effect adequate recovery. *Anesthesiology*. 1995;82:852–858.

Kirkegaard H, Heier T, Caldwell JE. Efficacy of tactile-guided reversal from

cisatracurium-induced neuromuscular block. *Anesthesiology*. 2002;96:45–50.

B.13. Is there anything wrong with administering neostigmine when the TOFC is less than 3?

As noted earlier, when the TOFC is only 1 or 2, anticholinesterases cannot be counted on to achieve satisfactory reversal in a timely manner. The peak effect of the antagonist is followed by a plateau phase that represents the balance between diminishing anticholinesterase activity and spontaneous recovery. The latter becomes the major determinant at profound levels of NMB. However, even at a TOFC of 1 to 2, it may be possible to achieve a TOF ratio >0.40 within 10 minutes. The problem for the clinician is that further recovery may be quite slow, and unless an objective monitor of neuromuscular function is being used, the clinician is likely to have the false impression that adequate recovery has been achieved as subjective detection of fade at TOF ratios >0.40 is highly unreliable.

Kopman AF, Kopman DJ, Ng J, et al. Antagonism of profound cisatracurium and rocuronium block: the role of objective assessment of neuromuscular function. *J Clin Anesth*. 2005;17:30–35.

B.14. Is reversal of blockade always necessary?

If a quantitative monitor of neuromuscular function is used, the answer to this question is simple. If the TOF ratio approximates a value of 0.90 or better, anticholinesterase administration is pointless and is best avoided. Neostigmine, edrophonium, atropine, etc., all have their own side effects and should not be administered unnecessarily. Similarly, if the TOFC is less than 4 or 4 with obvious fade, then anticholinesterase administration is indicated. However, objective monitors are still not widely available. What should be done when the TOFC is 4 with no detectable fade?

Many clinicians base the decision of whether to reverse or not on the time interval since the last dose of relaxant.

Unfortunately, this is often an unreliable way to proceed. Two hours after a single dose of an intermediate-duration blocker, 30% of individuals may have TOF ratios <0.90, and 10% will still not have returned to a value of 0.70. Therefore, in the absence of objective evidence that the TOF ratio is >0.85 to 0.90, an antagonist should be administered. However, when no fade to TOF stimulation can be subjectively detected, the dose of neostigmine can be safely reduced to only 0.02 mg per kg.

Caldwell JE. Reversal of residual neuromuscular block with neostigmine at one to four hours after a single intubating dose of vecuronium. *Anesth Analg*. 1995;80:1168–1174.

Fuchs-Buder T, Meistelman C, Alla F, et al. Antagonism of low degrees of atracurium-induced neuromuscular blockade: dose-effect relationships for neostigmine. *Anesthesiology*. 2010;112:34–40.

B.15. Is there any way to rapidly antagonize a profound nondepolarizing block?

A radically new approach to reversal presented itself with the introduction of sugammadex. This drug was recently approved by the U.S. Food and Drug Administration for use to reverse the effects of NMB induced by rocuronium bromide and vecuronium bromide. Sugammadex is a γ-cyclodextrin (**Fig. 55.1**).

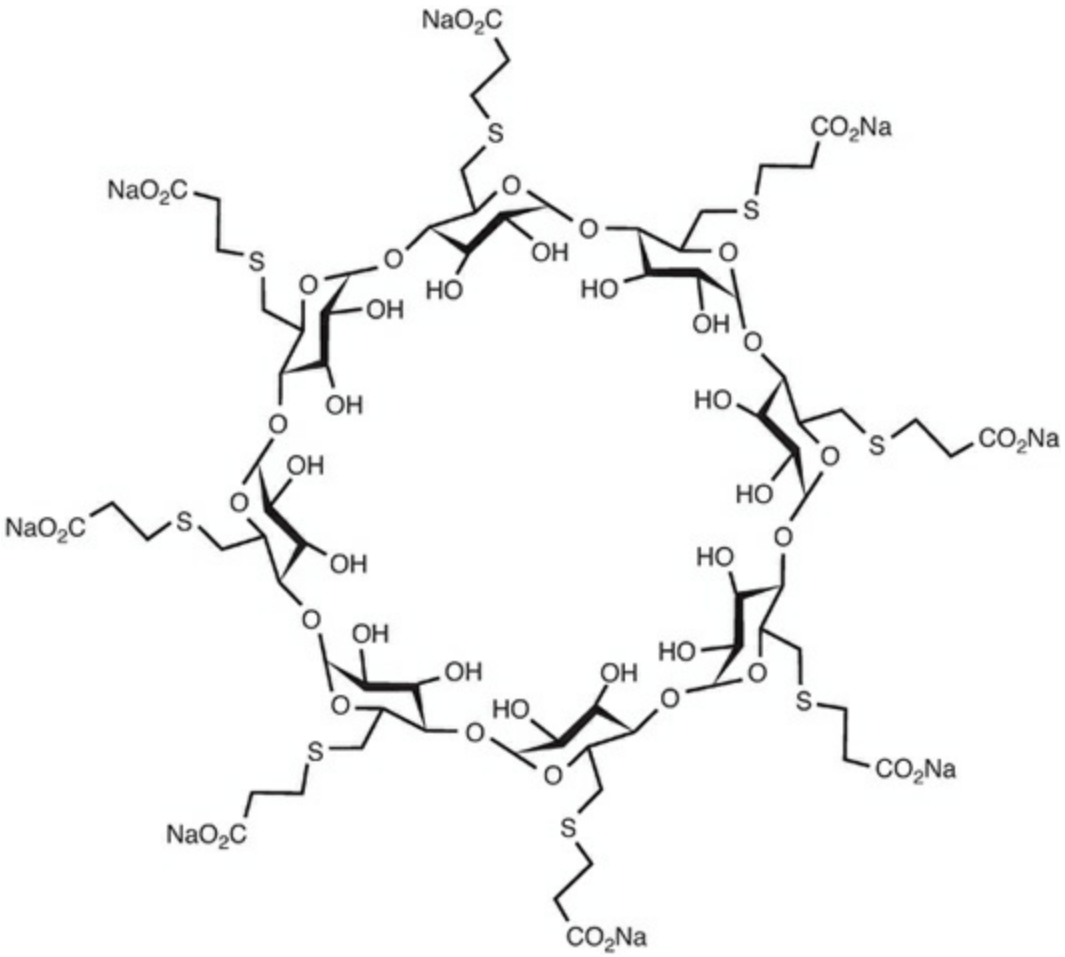


FIGURE 55.1. Structure of sugammadex, a synthetic γ-cyclodextrin. (*Reprinted with permission from Naguib MMB. Sugammadex: another milestone in clinical neuromuscular pharmacology*. Anesth Analg. *2007;104[3]:575–581*.)

It has a three-dimensional (3D) appearance similar to a doughnut with a hydrophobic interior and hydrophilic exterior. The hydrophobic core acts by strongly binding with monoquaternary aminosteroid blocking agents (e.g., rocuronium and vecuronium) thus "trapping" the drug (**Fig. 55.2**). The resulting sugammadex–rocuronium complex is water soluble and excreted renally. The complex formed creates a concentration gradient for molecules in the neuromuscular junction to move out and be further excreted. It forms a very "tight" bond utilizing hydrogen bonds, van der Waals forces, and hydrophobic interactions so molecule dissociation from the "trap" is not a concern. (Note: Sugammadex is not an effective

antagonist of benzylisoquinolinium-based relaxants such as cisatracurium.)

FIGURE 55.2. X-ray crystal structure of sugammadex (green) and rocuronium (blue) with encapsulation of a rocuronium molecule by a sugammadex molecule at 1:1 ratio. (*Reprinted with permission from Gijsenbergh F, Ramael S, Houwing N, et al. First human exposure of Org 25969, a novel agent to reverse the action of rocuronium bromide*. Anesthesiology. *2005;103:695–703*.)

Sugammadex can be used to rapidly reverse intubating doses of steroidal NMB in "cannot intubate" or "cannot ventilate" situations or when surgery concludes more quickly than anticipated. Sixteen milligrams per kilogram is given for rapid reversal of steroidal NMB when there are no posttetanic twitches. After sugammadex is given, it takes approximately 4 minutes to fully recover from a 1.2 mg per kg dose of rocuronium. This is faster than spontaneous succinylcholine recovery, which takes approximately 7 minutes. Four milligram per kilogram of sugammadex is given when there are 1 to 2 posttetanic twitches, and 2 mg per kg is given when there are 2+ twitches (i.e., the TOFC is 2 or more). Randomized controlled trials have demonstrated that TOFC recovery with similar density of blockade is faster with sugammadex than with both neostigmine–glycopyrrolate and edrophonium–atropine. Sugammadex dose is determined by actual body weight, even in the morbidly obese patient. Hepatic dysfunction does not alter drug kinetics as the molecular complex is cleared by the kidneys.

There is no need for anticholinergic drugs because sugammadex does not affect acetylcholinesterase. Because most

of the common side effects (e.g., tachycardia) when giving reversal come from anticholinergic effects, patients treated with sugammadex exhibit none of these undesirable signs and symptoms. Instead, most common side effects include postoperative nausea and vomiting (PONV), dry mouth, headache, hypotension and parosmia (abnormal smell). Rare but significant side effects of sugammadex include anaphylaxis and bradycardia. Sugammadex also sequesters (oral) hormonal contraceptives, and patients need to be advised to use alternative forms of contraception for 7 days after sugammadex administration.

de Boer H, Driessen JJ, Marcus MA, et al. Reversal of rocuronium-induced (1.2 mg/kg) profound neuromuscular block by sugammadex: a multicenter, dose-finding and safety study. *Anesthesiology*. 2007;107:239–244.

Geldner G, Niskanen M, Laurila P, et al. A randomised controlled trial comparing sugammadex and neostigmine at different depths of neuromuscular blockade in patients undergoing laparoscopic surgery. *Anaesthesia*. 2012;67:991–998.

Lemmens HJ, El-Orbany MI, Berry J, et al. Reversal of profound vecuronium-induced neuromuscular block under sevoflurane anesthesia: sugammadex versus neostigmine. *BMC Anesthesiol*. 2010;10:15.

Naguib MMB. Sugammadex: another milestone in clinical neuromuscular pharmacology. *Anesth Analg*. 2007;104(3):575–581.

Naguib MMB, Brull SJ. Sugammadex: a novel selective relaxant binding agent. *Expert Rev Clin Pharmacol*. 2009;2:37–53.

Sacan O, White PF, Tufanogullari B, et al. Sugammadex reversal of rocuronium-induced neuromuscular blockade: a comparison with neostigmine-glycopyrrolate and edrophonium-atropine. *Anesth Analg*. 2007;104(3):569–574.

C. Postoperative Management

C.1. What is the incidence of residual NMB in the PACU?

Numerous reports since 2000 make clear that even with agents of intermediate duration, undetected residual weakness in the

postoperative period is not a rare event. Large studies from Europe, where routine reversal with cholinesterase inhibitors were not administered, report that 20% to 40% of patients arrived in their PACU with TOF values <0.70.

As might be expected when a TOF ratio of 0.90 is set as the standard of adequate antagonism, the incidence of PORB approaches 40%. The incidence of PORB is highly variable from institution to institution and very dependent on individual practice patterns. Diligent intraoperative monitoring and routine antagonism of residual block can result in dramatic reductions in the incidence of PORB. In a study from France between 1995 and 2004, quantitative measurement and reversal of neuromuscular block in the operating room of one institution increased from 2% to 60% and from 6% to 42%, respectively. During the same time, the incidence of residual neuromuscular block, defined as a TOF ratio less than 0.9, decreased from 62% to 3%. Unfortunately, the lessons vividly demonstrated by these authors are far from universally understood or applied. A recent survey of North American and European clinical practices indicates that even in the year 2009, 10% of clinicians rarely or never monitor neuromuscular function with even the simplest of PNS, and the routine administration of antagonists is even less common.

Naguib M, Kopman AF, Lien CA, et al. A survey of current management of neuromuscular block in the United States and Europe. *Anesth Analg*. 2010;111:110–119.

Todd MM, Hindman BJ, King BJ. The implementation of quantitative electromyographic neuromuscular monitoring in an academic anesthesia department. *Anesth Analg*. 2014;119:323–331.

Yip PC, Hannam JA, Cameron AJ, et al. Incidence of residual neuromuscular blockade in a post-anaesthetic care unit. *Anaesth Intensive Care*. 2010;38:91–95.

C.2. Does undetected postoperative residual

neuromuscular block (PORB) have clinical consequences?

In North America, an excess of 20 million patients each year receive an anesthetic. The size of the subgroup that receives a nondepolarizing blocking agent is unknown but obviously still numbers in the millions. As indicated previously, the exact incidence of PORB probably varies greatly from institution to institution. Nonetheless, even if it is as low as 5% overall (highly optimistic), the number of individuals who arrive in the PACU with suboptimal neuromuscular recovery is substantial. In truth, the majority of patients who arrive in the PACU with TOF ratios <0.90 do not experience complications. However, not all individuals are so fortunate. Undetected PORB is clearly associated with potentially adverse respiratory events and increased morbidity. A recent prospective case-controlled study of critical respiratory events (CREs) (e.g., episodes of hypoxia, signs of airway obstruction, need for reintubation) in a university hospital's PACU is instructive. Sixty-one patients with CREs were identified. Their mean TOF ratio as measured by AMG was 0.62. The TOF value in 42 matched controls was 0.98. The same authors in a separate study were also able to demonstrate a lower frequency of residual NMB in the PACU (4.5%) (TOF ratio ≤0.9) in cases where intraoperative AMG was employed compared with the cases where conventional PNS were used (30%). During transport to the PACU, fewer AMG patients developed arterial oxygen saturation values, measured by pulse oximetry, of less than 90% (0%) or airway obstruction (0%) compared with (subjective monitoring) control patients (21.1% and 11.1%, respectively). The incidence, severity, and duration of hypoxemic events during the first 30 minutes of PACU admission were less in the AMG group (all $P < .0001$). These findings add credence to the hypothesis that incomplete neuromuscular recovery is an important contributing factor in

the development of adverse respiratory events in the PACU.

Brull SJ, Murphy GS. Residual neuromuscular block: lessons unlearned. Part II: methods to reduce the risk of residual weakness. *Anesth Analg*. 2010;111:129–140.

Butterly A, Bittner EA, George E, et al. Postoperative residual curarization from intermediate-acting neuromuscular blocking agents delays recovery room discharge. *Br J Anaesth*. 2010;105:304–309.

Kopman AF, Brull SJ. Is postoperative residual neuromuscular block associated with adverse clinical outcomes? What is the evidence? *Curr Anesthesiol Rep*. 2013;3:114–121.

Kumar GV, Nair AP, Murthy HS, et al. Residual neuromuscular blockade affects postoperative pulmonary function. *Anesthesiology*. 2012;117:1234–1244.

Murphy GS, Brull SJ. Residual neuromuscular block: lessons unlearned. Part I: definitions, incidence, and adverse physiologic effects of residual neuromuscular block. *Anesth Analg*. 2010;111:120–128.

Murphy GS, Szokol JW, Marymount JH, et al. Intraoperative acceleromyographic monitoring reduces the risk of residual neuromuscular blockade and adverse respiratory events in the postanesthesia care unit. *Anesthesiology*. 2008;109:389–398.

56 Burns

Shreyajit R. Kumar, Anup Pamnani

A 45-year-old man, who was smoking in bed, sustained 40% second- and third-degree burns over his face, neck, chest, and upper extremities. He had a history of hypertension, angina, and angioplasty of the right coronary artery 1 year ago. He has smoked 3 packs of cigarettes per day for 20 years, and he drinks alcohol daily. He is scheduled for tangential excision of eschar on the third postburn day. His blood pressure is 190/100 mmHg with a heart rate of 120 beats per minute, and he weighs 110 kg.

A. Medical Disease and Differential Diagnosis

1. How do you classify the burn injury?
2. How do you express the extent of the burn injury?
3. Should the "rule of nines" be used in children?
4. What functions does the skin perform?
5. What pathophysiologic changes accompany major thermal injury?
6. What is the prognosis for this patient? What major factors affect his prognosis?
7. What are the common causes of death in burn patients?
8. Does this patient have a smoke inhalation burn? How do you make the diagnosis?

9. What is carbon monoxide poisoning? How do you diagnose and treat carbon monoxide poisoning?
10. What resuscitative measure would you institute immediately in this patient with 40% burns?
11. What fluid formula would you use?
12. What cardiovascular changes typify the burn injury?
13. What changes occur in hepatic function? What are the anesthetic implications of such changes?
14. What are Curling ulcers? How can they be prevented?
15. What complications are associated with electrical burns?

B. Preoperative Evaluation and Preparation

1. What preoperative preparations would you order? What are particular concerns in this patient?
2. What are the various operative and management options available for severely burned patients?
3. What are the advantages and disadvantages of early tangential excision split-thickness skin grafting (TE/STSG)?
4. What is this patient's mean arterial blood pressure? How do you calculate it?
5. Are you concerned about this patient's blood pressure? What treatment would you institute?
6. This patient was ventilated with respirator settings of tidal volume, 800 mL; respiratory rate, 20 breaths per minute; fraction of inspired oxygen (F_{IO_2}), 60%; and positive end-expiratory pressure, 10 cm H_2O. Arterial blood gas analyses showed the following: pH, 7.24; P_{O_2}, 56 mmHg; P_{CO_2}, 60 mmHg; and oxygen saturation, 80%. How would you interpret these arterial blood gas analysis results? What are the possible causes of high P_{CO_2} and low P_{O_2}?
7. How do you calculate oxygen content and oxygen delivery? What factors govern the oxygen delivery to the tissues?

C. Intraoperative Management

1. What monitors would you use in the operating room?
2. What information can be obtained from an arterial line and a pulmonary artery catheter? How are these calculations performed?
3. If the patient had not been intubated, how would you proceed with the anesthetic induction?
4. Why is awake intubation considered the safest?
5. What anesthetic agents would you use? Discuss inhalation versus intravenous agents.
6. Why are you concerned about the patient's body temperature? What is normothermia for a burned patient?
7. How is temperature best maintained?
8. What derangements occur with hypothermia?
9. What muscle relaxant would you use?
10. Why is succinylcholine contraindicated in burned patients? For how long should it be avoided?
11. What other adverse effects are associated with succinylcholine?
12. How are the doses of nondepolarizing muscle relaxants affected by burn injury?
13. How are the muscle relaxants such as succinylcholine, atracurium, cisatracurium, vecuronium, pancuronium, rocuronium, and curare metabolized and eliminated? Which of them has significant histamine release?

D. Postoperative Management

1. How would you monitor this patient during transport?
2. What is meant by diffusion hypoxia? How do you prevent it?
3. Why do patients often shiver in the recovery room on emergence from anesthesia?
4. Discuss the causes of oliguria in the recovery room.

A. Medical Disease and Differential Diagnosis

A.1. How do you classify the burn injury?

Burns classification is based on both depth and degree of tissue injury. First-degree burns are superficial and confined to epidermal injury. Second-degree burns are partial thickness, involving the epidermis and dermis. Third-degree burns are full thickness and characterized by irreversible destruction of all dermal and epidermal elements. Fourth-degree burns involve injury to underlying tissue structures—muscle, fascia, tendon, and bone (**Table 56.1**).

TABLE 56.1 Classification of Burn Depth

Classification	Burn Depth	Outcome
Superficial		
First degree	Confined to epidermis	Heals spontaneously
Partial thickness		
Second degree		
Superficial dermal burn	Epidermis and upper dermis	Heals spontaneously
Deep dermal burn	Epidermis and deep dermis	Requires excision and grafting for rapid return of function
Full thickness		
Third degree	Destruction of epidermis and dermis	Wound excision and grafting required
		Some limitation of function and scar formation
Fourth degree	Muscle, fascia, bone	Complete excision required, limited function

Reprinted with permission from MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. *Anesthesiology*. 1998;89:749–779.

MacLennan N, Heimbach DM, Cullen BF. Anaesthesia for major thermal injury. *Anesthesiology*. 1998;89:749–770.

Townsend CM Jr, Beauchamp D, Evers MB, et al, eds. *Sabiston Textbook of Surgery: The Biological Basis of Modern Surgical Practice*. 20th ed. Philadelphia, PA: Elsevier Saunders; 2017:505–532.

A.2. How do you express the extent of the burn injury?

Extent of burn injury is expressed as a total body surface area (TBSA) percentage. Burn size is estimated by the "rule of nines" (**Fig. 56.1**). In adults, each upper extremity and the head and neck are 9% of TBSA. The lower extremities and anterior and posterior trunk are 18% each, and the perineum is approximately 1% of the TBSA. The burn proportions are additive, yielding a TBSA burn.

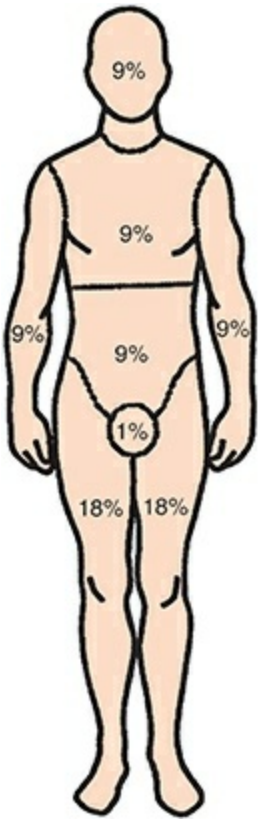


FIGURE 56.1. The rule of nines for determining the percentage of body surface area burned in adults. (*Adapted with permission from MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury*. Anesthesiology. *1998;89:749–770*.)

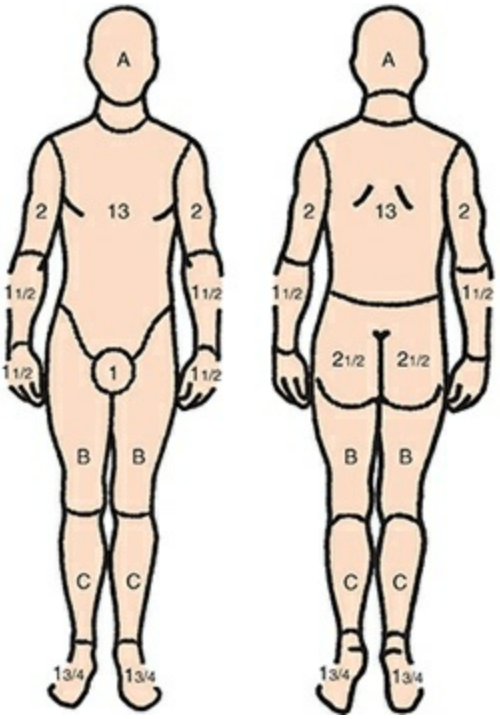
MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. *Anesthesiology*. 1998;89:749–770.

Townsend CM Jr, Beauchamp D, Evers MB, et al, eds. *Sabiston Textbook of Surgery: The Biological Basis of Modern Surgical Practice*. 20th ed. Philadelphia, PA: Elsevier Saunders; 2017:505–532.

A.3. Should the "rule of nines" be used in children?

The "rule of nines" will not estimate TBSA burns in children

because the head and neck comprise a relatively larger portion of the body surface area and a smaller surface area in the lower extremities. The Lund and Browder chart represents a precise method, accounting for the changing proportions of the TBSA from infancy to adulthood (**Fig. 56.2**).



Relative percentages of areas affected by growth

	AGE IN YEARS					
AREA	0	1	5	10	15	Adult
A: half of head	9½	8½	6½	5½	4½	3½
B: half of thigh	2¾	3¼	4	4¼	4½	4¾
C: half of leg	2½	2½	2¾	3	3¼	3½

FIGURE 56.2. Diagram and table for determining the percentage of body surface area burned in children. (*Adapted with permission from MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury.* Anesthesiology. *1998;89:749–770.*)

MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. *Anesthesiology*. 1998;89:749–770.

Townsend CM Jr, Beauchamp D, Evers MB, et al, eds. *Sabiston Textbook of Surgery: The Biological Basis of Modern Surgical Practice*. 20th ed. Philadelphia, PA: Elsevier Saunders; 2017:505–532.

A.4. What functions does the skin perform?

The skin is the largest organ of the body with a surface area and is the primary immune barrier, protecting against microorganism invasion. The skin provides thermal regulation, fluid and electrolytes homeostasis, vitamin D metabolism, and sensation (touch, temperature, pain).

Herndon DN, ed. *Total Burn Care*. 5th ed. Philadelphia, PA: Saunders Elsevier; 2018:93–114.

A.5. What pathophysiologic changes accompany major thermal injury?

The pathophysiologic alterations that accompany major thermal injury are complex. Destruction of the skin—the largest organ of the body—has a profound systemic impact. Thermal regulation, fluid and electrolyte homeostasis, and protection against bacterial infection are all lost. Inflammatory mediators released from burn injury result in a leaky capillary syndrome; fluid and albumin are sequestered from the intravascular compartment into the burn wound, causing hemoconcentration and hypoalbuminemia. Increased secretion of antidiuretic hormone may cause oliguria or anuria.

The metabolic rate is markedly increased after the burn injury. Depending on the size of the burn, the increase in metabolic rate can be doubled or tripled with a proportionate increase in oxygen consumption and carbon dioxide (CO_2) production. This hypermetabolic state will continue for weeks or months until full tissue repair is complete.

Cardiac output (CO) is often decreased in patients with major burns. This decrease is partially due to a rapid reduction in circulating blood volume as well as an upregulation of circulating myocardial-depressant factor.

Changes in vascular integrity occur in other areas remote from the injury site. The entire vascular compartment becomes permeable to circulating macromolecules, manifesting as edema. Severe pulmonary edema can be life-threatening. Airway edema is the impetus for early intubation.

Pulmonary function is significantly altered. A reduction occurs in functional residual capacity, lung capacity, and chest wall compliance. Increases occur of the alveolar–arterial oxygen

gradient (P_{AO_2}–Pa_{O_2}) and minute ventilation (as high as 40 L per minute; normal, 6 L per minute).

Brunicardi FC, Andersen DK, Billiar TR, eds. *Schwartz's Principles of Surgery*. 11th ed. New York: McGraw-Hill; 2019:251–271.

Herndon DN, ed. *Total Burn Care*. 5th ed. Philadelphia, PA: Saunders-Elsevier; 2018:103–115.

MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. *Anesthesiology*. 1998;89:749–770.

A.6. What is the prognosis for this patient? What major factors affect his prognosis?

The prognosis for this patient is very poor. Statistical survival based on TBSA alone predicts a less than 50% chance of survival. Other factors that affect his prognosis are age, size and depth of burn, associated pulmonary injury, and preexisting medical disease. In this patient with a history of angioplasty for coronary artery disease, hypertension, heavy smoking, and obesity, the risk of myocardial infarction is greatly increased.

A.7. What are the common causes of death in burn patients?

The major early cause of death is asphyxia. The most common cause of long-term mortality is septic complications. Hypovolemic shock is no longer common in the United States due to enhanced early goal-directed resuscitation.

A.8. Does this patient have a smoke inhalation burn? How do you make the diagnosis?

This patient probably sustained a smoke inhalation burn. Smoke inhalation should be highly suspected in patients who were burned in an enclosed space, received burns of the face, were burned while under the influence of alcohol or drugs, or lost consciousness at the time of the accident.

A patient with smoke inhalation often exhibits no physical

signs or symptoms during the first 24 hours after the burn—the "lucid period." The early symptoms and signs of respiratory tract injury include burned nasal mucosa/lips/mouth, singed nasal hair, and/or soot in the sputum. The posterior pharynx may appear red and edematous. Radiographic findings are usually negative immediately after injury. Laboratory tests include blood gas analysis, carboxyhemoglobin concentration, xenon scans, and fiberoptic bronchoscopy.

Brunicardi FC, Anderson DK, eds. *Schwartz's Principles of Surgery*. 11th ed. New York: McGraw-Hill; 2019:251–271.

Herndon DN, ed. *Total Burn Care*. 5th ed. Philadelphia, PA: Saunders Elsevier; 2018:184–195.

A.9. What is carbon monoxide poisoning? How do you diagnose and treat carbon monoxide poisoning?

Carbon monoxide is the leading cause of hypoxia in survivors of burn injuries; it is liberated from the incomplete combustion of carbon-containing substrates (wood, coal, and gasoline). Carbon monoxide has a 250 times greater affinity for hemoglobin than oxygen, displacing oxygen from its hemoglobin-binding sites. CO-oximetry is necessary for diagnosis of carbon monoxide poisoning because the arterial blood gas Pa_{O_2} will be falsely normal.

Expeditious oxygen therapy will displace carbon monoxide from hemoglobin moieties. The standard half-life of carbon monoxide elimination is 4 to 6 hours at room air. This is reduced to 40 to 80 minutes with 100% oxygen and 15 to 30 minutes with hyperbaric oxygen therapy.

Brunicardi FC, Anderson DK, eds. *Schwartz's Principles of Surgery*. 11th ed. New York: McGraw-Hill; 2019:251–271.

Herndon DN, ed. *Total Burn Care*. 5th ed. Philadelphia, PA: Saunders Elsevier; 2018:174–184.

A.10. What resuscitative measure would you institute immediately in this patient with 40% burns?

Early and aggressive fluid resuscitation will combat the distributive, third-spacing hypovolemia. Liberal fluid administration will ensure end-organ perfusion and adequate urine output. If an upper airway burn is involved, endotracheal intubation is indicated to prevent edematous airway compromise.

A.11. What fluid formula would you use?

The Parkland formula will guide the initial resuscitation in hypovolemic shock after burn injury. It has been adopted as the standard of practice at most burn centers due to its simplicity, reduced cost, and equivalent outcome when compared to other calculations for fluid administration.

Other formulas differ widely in the colloid/crystalloid ratio and in the rate of fluid administration. Although much controversy still surrounds the use of "the solution" for resuscitation in burn shock, scientific investigation supports the need for both crystalloid and colloid solutions (**Table 56.2**). Current sentiment supports the Parkland calculation as a resuscitation "starting point." Emphasis should then be placed on factors used to guide resuscitation; urine output of 0.5 to 1.0 mL/kg/hr is the important parameter.

TABLE 56.2 Fluid Resuscitation for Adults with Major Burns

Crystalloid Regimens		
Parkland	Lactated Ringer's	4 mL/kg/% burn
Modified Brooke	Lactated Ringer's	2 mL/kg/% burn
Colloid Regimens		
Evans	Normal saline	1 mL/kg/% burn
	Colloid	1 mL/kg/% burn
	5% Dextrose	2,000 mL/24 hr

Brooke	Lactated Ringer's	1.5 mL/kg/% burn
	Colloid	0.5 mL/kg/% burn
	5% Dextrose	2,000 mL/24 hr

Parkland Formula

First 24 hours

- *Electrolyte solution (lactated Ringer's)*—4 mL/kg/percentage of body area with second- and third-degree burn
- *Administration rate*—half the solution given in the first 8 hours, one-quarter in the second 8 hours, and one-quarter in the third 8 hours
- *Urine output*—maintain at 0.5 to 1.0 mL/kg/hr

Second 24 hours

- *Glucose in water*—to replace evaporated water loss and maintain serum sodium concentration of 140 mEq per L
- *Colloid solutions (e.g., albumin)*—amount proportional to burn
  - *30% to 50% burn*: 0.3 mL/kg/percentage of burn
  - *50% to 70% burn*: 0.4 mL/kg/percentage of burn
  - *Larger than 70% burn*: 0.5 mL/kg/percentage of burn
- *Urine output*—maintain at 0.5 to 1.0 mL/kg/hr

Blumetti J, Hunt JL, Arnoldo BD, et al. The Parkland formula under fire: is the criticism justified? *J Burn Care Res*. 2008;29(1):180–186.

Brunicardi FC, Anderson DK, eds. *Schwartz's Principles of Surgery*. 11th ed. New York: McGraw-Hill; 2019:227–326.

Herndon DN, ed. *Total Burn Care*. 5th ed. Philadelphia, PA: Saunders Elsevier; 2018:77–87.

A.12. What cardiovascular changes typify the burn injury?

Microvascular destruction of capillary membranes results in acute fluid sequestration from intravascular compartment to interstitial spaces. Decreased plasma volume leads to depressed CO and hypotension. Catecholamine release triggers vasoconstriction, which may further compromise tissue

perfusion. Ventricular dysfunction is attributed to myocardial-depressant factor present in lymphatic fluid.

Herndon DN, ed. *Total Burn Care*. 4th ed. Philadelphia, PA: Saunders Elsevier; 2012:361–369.

Townsend CM Jr, Beauchamp D, Evers MB, et al, eds. *Sabiston Textbook of Surgery: The Biological Basis of Modern Surgical Practice*. 20th ed. Philadelphia, PA: Elsevier Saunders; 2017:505–532.

A.13. What changes occur in hepatic function? What are the anesthetic implications of such changes?

Decreased circulating volume during the initial burn phase may result in shock liver and restrict hepatic detoxification capacity. Albumin levels will decrease, which may increase the free fraction levels of benzodiazepines and phenytoin. In contrast, a rise in the acute-phase reactant α_1-acid-glycoprotein, increases the binding of pH basic drugs, such as lidocaine, propranolol, and muscle relaxants.

Herndon DN, ed. *Total Burn Care*. 5th ed. Philadelphia, PA: Saunders Elsevier; 2018:259–268.

Jeevendra Martin JA, Fukushima Y, Chon JY, et al. Muscle relaxants in burns, trauma, and critical illness. *Int Anesthesiol Clin*. 2006;44:123–143.

A.14. What are Curling ulcers? How can they be prevented?

A Curling ulcer is a gastric or duodenal stress ulcer resulting from a systemic thermal injury. Without treatment, the incidence is as high as 80%. Atrophy of the small bowel mucosa occurs within 12 hours of injury and is proportional to burn extent. Additional decreases in intestinal blood flow exacerbate the gastric injury. Curling ulcers can be prevented prophylactically with antacids, H_2-antagonists, and early enteral feeding.

Townsend CM Jr, Beauchamp D, Evers MB, et al, eds. *Sabiston Textbook of Surgery: The Biological Basis of Modern Surgical Practice*. 20th ed.

Philadelphia, PA: Elsevier Saunders; 2017:505–532.

A.15. What complications are associated with electrical burns?

Electrical burns result in small skin area necrosis, with large amounts of damage to deep tissue structures—muscles, tendons, blood vessels, and nerves. Thus, the fluid losses are greater than predicted from Parkland calculation. The total injury is determined by the duration of current flow, the resistance of the tissue, and the area of contact. Muscle necrosis may cause myoglobinuria and acute tubular necrosis. Thrombotic phenomena may manifest late. Cardiac conduction abnormalities, ectopy, and congestive heart failure may all be secondary to electrical injury.

Herndon DN, ed. *Total Burn Care*. 5th ed. Philadelphia, PA: Saunders Elsevier; 2018:396–403.

B. Preoperative Evaluation and Preparation

B.1. What preoperative preparations would you order? What are particular concerns in this patient?

A thorough medical history and physical examination should be conducted, with a focus on this patient's salient risk factors. In this patient, hypertension, ischemic heart disease, angioplasty of left main coronary artery, and the history of heavy smoking and heavy alcohol consumption are of particular concern. The following laboratory tests should be ordered—complete blood count, basic metabolic profile, venous lactate, coagulation profile, liver function tests, electrocardiogram (ECG), urinalysis, chest radiograph, and arterial blood gas. With respect to this patient's left main coronary artery disease, cardiac enzymes would be beneficial. Any concern about a tenuous cardiac status should prompt involvement by a cardiologist.

Urine output, central venous pressure (CVP), pulmonary artery occlusion pressure (PAOP), CO, and cardiac index will all be beneficial in guiding fluid resuscitation.

B.2. What are the various operative and management options available for severely burned patients?

Early tangential excision of burn tissue and early wound closure, primarily by skin grafting, has significantly improved mortality among the severely burned population. Eschar, or burned skin, is an active medium for bacterial propagation, and topical antibiotic creams—silver sulfadiazine—should be applied for infection control.

Early removal of injured tissue prevents wound infection and decreases systemic inflammatory response. A widely adopted strategy involves a 48-hour period of initial resuscitation to achieve hemodynamic stability, followed by TE/STSG. The extent of escharotomy is limited to 20% of TBSA and repeated every 2 days until excision is complete.

Brunicardi FC, Anderson DK, eds. *Schwartz's Principles of Surgery*. 11th ed. New York: McGraw-Hill; 2019:251–271.

Townsend CM Jr, Beauchamp D, Evers MB, et al, eds. *Sabiston Textbook of Surgery: The Biological Basis of Modern Surgical Practice*. 20th ed. Philadelphia, PA: Elsevier Saunders; 2017:505–532.

B.3. What are the advantages and disadvantages of early tangential excision split-thickness skin grafting (TE/STSG)?

The expeditious escharotomy—within 2 days—will remove the bacterial load, reduce the risk of bacteremia and sepsis, and shorten the recovery phase and overall hospital length of stay. Very early excision—within 24 hours—has the disadvantage of a major operative stress during the resuscitative phase of the injury. The patient is not optimized, and there is an increase in anesthetic risk.

Herndon DN, ed. *Total Burn Care*. 5th ed. Philadelphia, PA: Saunders Elsevier; 2018:386–396.

Townsend CM Jr, Beauchamp D, Evers MB, et al, eds. *Sabiston Textbook of Surgery: The Biological Basis of Modern Surgical Practice*. 20th ed. Philadelphia, PA: Elsevier Saunders; 2017:505–532.

B.4. What is this patient's mean arterial blood pressure? How do you calculate it?

This patient's mean arterial pressure (MAP) can be calculated from his blood pressure of 190/100 mmHg; his MAP is 130 mmHg. The equation is MAP = two-thirds of diastolic pressure + one-third of the systolic pressure. An equivalent calculation is MAP = diastolic pressure + one-third of the pulse pressure; the pulse pressure is the difference between systolic and diastolic pressure.

B.5. Are you concerned about this patient's blood pressure? What treatment would you institute?

We are concerned with this patient's extreme blood pressure, given his history of angina and coronary disease requiring left main coronary angioplasty. We would like to maintain his blood pressure in the normal range.

β-Blockers (labetalol, metoprolol), calcium channel blockers (nicardipine), angiotensin-converting enzyme inhibitors (enalapril), and hydralazine are all intravenous vasodilators that may be used.

This tachycardic patient—heart rate 120 beats per minute—would benefit from β-blockade with labetalol or Lopressor. Reduction of afterload and tachycardia will decrease overall myocardial oxygen demand and reduce his risk of infarction.

Adequacy of volume resuscitation should be assessed. Measuring CVP, PAOP, CO, cardiac index, and systemic vascular resistance will aide in treatment initiation.

B.6. This patient was ventilated with respirator settings of

tidal volume, 800 mL; respiratory rate, 20 breaths per minute; fraction of inspired oxygen (FIO_2), 60%; and positive end-expiratory pressure, 10 cm H_2O. Arterial blood gas analyses showed the following: pH, 7.24; PO_2, 56 mmHg; PCO_2, 60 mmHg; and oxygen saturation, 80%. How would you interpret these arterial blood gas analysis results? What are the possible causes of high PCO_2 and low PO_2?

Arterial blood gas analysis demonstrates an uncompensated respiratory acidosis with a substantial hypoxic Alveolar–arterial (A–a) gradient. This patient was hypoventilated given the high PCO_2 of 60 mmHg (normal PCO_2 is 35 to 45 mmHg).

The etiology of this patient's hypercapnia may be a hypermetabolic state with marked increase in CO_2 production.

The most common cause of hypoxemia with an increased A–a gradient is a ventilation/perfusion mismatch. Atelectasis, pneumonia, pulmonary edema, or malposition of endotracheal tube with single-lung ventilation will increase dead space or shunt fractionation, resulting in ventilation/perfusion mismatch.

B.7. How do you calculate oxygen content and oxygen delivery? What factors govern the oxygen delivery to the tissues?

The oxygen content of arterial blood (CaO_2) is the sum of two components, the oxygen dissolved in plasma and the oxygen bound to hemoglobin (Hgb). It is expressed as:

$$CaO_2 \text{ (mL per dL)} = 1.31 \times \text{Hgb (g per dL)} \times SaO_2 (\%) + 0.003 \times PaO_2$$

Normal arterial oxygen content: CaO_2 = 20.73 mL per 100 mL

Oxygen delivery (DO_2) is directly proportional to the CO and

arterial oxygen content:

$$DO_2 = CO \times CaO_2 = CO \times ([1.31 \times Hgb\ (g\ per\ dL) \times SaO_2\ (\%)] + 0.003 \times PaO_2)$$

Thus, the three main factors that govern the oxygen delivery to tissues are CO, hemoglobin, and arterial oxygen saturation.

Criner GJ, Barnette RE, D'Alonzo GE, eds. *Critical Care Study Guide: Text and Review*. 2nd ed. New York: Springer; 2010:493–494.

C. Intraoperative Management

C.1. What monitors would you use in the operating room?

All standard monitors, noninvasive blood pressure, ECG (leads II and V_5), pulse oximetry, capnography, and temperature, should be used in this patient. A Foley catheter is essential for assessing urine output and volume status. An indwelling arterial line may be helpful if the standard blood pressure cuff interferes with the surgical field. A pulmonary artery catheter with CVP monitoring will be beneficial in this severely burned patient with ischemic heart disease.

C.2. What information can be obtained from an arterial line and a pulmonary artery catheter? How are these calculations performed?

The arterial line displays beat-to-beat continuous blood pressure measurements. This is most useful in fluctuating hypotensive or hypertensive situations. During dysrhythmias such as atrial fibrillation or ventricular tachycardia, variations in ventricular response or blood pressure will be recognized instantly. The morphology of the waveform can also provide information about arterial resistance (i.e., a narrow waveform is suggestive of both a reduced stroke volume and an increased systemic vascular resistance), stroke volume (area under the curve), and preload

(pulse pressure variation, particularly in response to mechanical positive pressure ventilation). In addition, it serves as ready vascular access for blood sampling (e.g., arterial blood gas analyses, electrolytes, hematocrit, and blood sugar levels).

A pulmonary artery catheter allows the measurement of PAOP, a surrogate of left atrial pressures. Left atrial pressure reflects left ventricular end-diastolic pressure, which is helpful in assessing the preload status of the left ventricle. CVP, although useful as a rough estimate of preload, does not correlate with left ventricular end-diastolic pressure when either isolated right-sided or left-sided cardiac dysfunction occurs. The multilumen pulmonary artery catheters are capable of measuring CVP and CO through the thermodilution method. It also permits sampling of mixed venous blood. These measurements permit calculation of many hemodynamic variables.

$$\text{Cardiac index (CI)} = \frac{\text{CO}}{\text{Body surface area}} \quad \text{(normal 2.8 to 4.2 L/min/m}^2\text{)}$$

$$\text{Stroke volume (SV)} = \frac{\text{CO}}{\text{Heart rate}} \quad \text{(normal 60 to 80 mL per beat)}$$

$$\text{Stroke index (SI)} = \frac{\text{CI}}{\text{Heart rate}} \quad \text{(normal 40 to 65 mL/beat/m}^2\text{)}$$

$$\text{Systematic vascular resistance (SVR)} = \frac{\text{Mean BP} - \text{CVP}}{\text{CO}} \times 80 \quad \text{(normal 900 to 1,400 dynes/sec/cm}^5\text{)}$$

$$\text{Pulmonary vascular resistance (PVR)} = \frac{\text{Mean PAP} - \text{PCWP}}{\text{CO}} \times 80 \quad \text{(normal 150 to 250 dynes/sec/cm}^5\text{)}$$

Mixed venous blood samples are needed for shunt calculations:

$$\frac{Q_s}{Q_t} = \frac{(Cc\text{O}_2 - Ca\text{O}_2)}{(Cc\text{O}_2 - C\bar{v}\text{O}_2)}$$

$Cc\text{O}_2$ = pulmonary capillary oxygen content
$Ca\text{O}_2$ = artery oxygen content
$C\bar{v}\text{O}_2$ = mixed venous oxygen content

A low mixed venous oxygen level (<30 mmHg) is suggestive

of inadequate tissue perfusion.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2746–2773.

C.3. If the patient had not been intubated, how would you proceed with the anesthetic induction?

This patient has a facial burn, which portends a difficult intubation. Burns on the face may cause severe airway and facial edema; careful assessment of the mouth opening, pharynx, and larynx is warranted. The safest way to secure the airway is to perform an awake intubation with topical anesthesia and mild sedation; it can be achieved by either direct or fiberoptic-guided intubation. If prolonged postoperative intubation is anticipated, the nasotracheal route is more easily secured, provides optimal patient comfort, and permits better oral hygienic care. Phenylephrine drops will achieve nasal mucosa vasoconstriction. Alternatively, a tracheostomy should be considered early in those patients with acute lung injury who will require prolonged mechanical ventilation.

C.4. Why is awake intubation considered the safest?

Awake intubation is the safest modality to secure an airway because when the patient is breathing spontaneously, the patient retains airway protective reflexes, is at lower risk for upper airway obstruction, and is less likely to have oxygen desaturation. This precludes the need for mask ventilation and avoids the risk of stomach distention.

When the patient is breathing spontaneously and maintains adequate oxygenation, the anesthesiologist has more time to do laryngoscopy. Identifying the passage of air from the glottis may be helpful in blind intubation.

C.5. What anesthetic agents would you use? Discuss inhalation versus intravenous agents.

For the severely burned patient, once the airway is secured, a high-dose narcotic muscle relaxant technique would be preferred because this technique confers intraoperative hemodynamic stability and optimal postoperative analgesia.

The narcotics, such as morphine, meperidine (Demerol), fentanyl, or sufentanil, do not interfere with myocardial contractility, whereas potent inhalation agents will depress the myocardium. If inhalation agents are chosen, the concentration should be carefully titrated to prevent hemodynamic embarrassment.

C.6. Why are you concerned about the patient's body temperature? What is normothermia for a burned patient?

Massive burn injury with loss of skin integrity will lead to considerable evaporative fluid losses and the risk of profound intraoperative hypothermia. This tendency is exacerbated by the vasodilatory effects of general anesthesia on central thermoregulatory centers and by the cool, arid operating room milieu. The infusion of large volume intravenous fluids at room temperature also contributes to the development of hypothermia.

Normothermia for a burned patient is approximately 38.5°C. The stress of thermal injury results in a resetting of the hypothalamic thermostat.

Brunicardi FC, Anderson DK, eds. *Schwartz's Principles of Surgery*. 11th ed. New York: McGraw-Hill; 2019:251–271.

Herndon DN, ed. *Total Burn Care*. 5th ed. Philadelphia, PA: Saunders Elsevier; 2018:131–157.

Townsend CM Jr, Beauchamp D, Evers MB, et al, eds. *Sabiston Textbook of Surgery: The Biological Basis of Modern Surgical Practice*. 20th ed. Philadelphia, PA: Elsevier Saunders; 2017:505–532.

C.7. How is temperature best maintained?

Hypothermia is a chief concern from loss of the insulator effect

of the skin organ. Heat losses occur through convection, conduction, evaporation, and radiation. Methods to maintain normothermia should involve active warming and prevention of heat loss. Crystalloid and blood transfusions must be administered through the blood- and/or fluid-warming device. A prewarmed forced air mattress, such as a Bair Hugger, is placed under a single-layer sterile sheet on the operating table. Warming the operating room to temperatures between 24°C (75.2°F) and 27°C (80.6°F) with a relative humidity higher than 50% is particularly effective. The nonsurgical areas of the patient's body must be covered. Heated, humidified airway circuits are most effective in minimizing the heat loss from ventilation with cold anesthetic gases.

C.8. What derangements occur with hypothermia?

Hypothermia causes many physiologic changes. Hypothermia decreases metabolism, heart rate, CO, and blood pressure. At temperatures less than 28°C (82.4°F), atrial pacing becomes irregular and ventricular ectopy increases. Ventricular fibrillation occurs between 25°C (77°F) and 30°C (86°F) in the human adult.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2746–2773.

C.9. What muscle relaxant would you use?

A nondepolarizing muscle relaxant should be used. Depolarizing relaxants, that is, succinylcholine, should be avoided. In general, the choice of muscle relaxant should be based on the duration of the operation and the presence of any coexisting diseases affecting drug elimination. Muscle relaxants without histamine release would be preferred, such as vecuronium and rocuronium.

C.10. Why is succinylcholine contraindicated in burned patients? For how long should it be avoided?

Succinylcholine is contraindicated in burned patients because it may cause a significant transient increase in serum potassium levels as high as 13 mEq per L, resulting in ventricular fibrillation and cardiac arrest. This hyperkalemic response begins approximately 5 to 15 days after the burn and persists for 2 to 3 months or longer, irrespective of degree and size of burn injury.

The exact mechanism responsible for this response is not known. It is hypothesized that the abrupt release of potassium is from the hypersensitive muscle membranes. Extrajunctional acetylcholine receptors are located on the muscle membranes of burned patients. Stimulation of these receptors may mediate a potentially lethal efflux of potassium.

The exact time for this hypersensitivity is unclear. Most authors advocate against succinylcholine use from 24 to 48 hours after the burn injury until complete healing has occurred. A hyperkalemic response has been reported in a patient after 480 days. The recommended limit now is extended to approximately 2 years after the burned skin has healed.

Gronert GA. Succinylcholine hyperkalemia after burns. *Anesthesiology*. 1999;91(1):320–322.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2746–2773.

Jeevendra Martyn JA. Succinylcholine hyperkalemia after burns. *Anesthesiology*. 1999;91(1):321–322.

Schaner PJ, Brown RL, Kirksey TD, et al. Succinylcholine-induced hyperkalemia in burned patients. 1. *Anesth Analg*. 1969;48:764–770.

C.11. What other adverse effects are associated with succinylcholine?

The adverse effects of succinylcholine are many. Its side effects are as follows:

- Hyperkalemia, particularly following burns, spinal cord injuries, and generalized major trauma: a single case report of

a marked hyperkalemic response to succinylcholine in a patient with a closed head injury without peripheral paralysis

- Increased intracranial and intraocular pressures: the practical importance of which is controversial
- Increased intragastric pressure: counterbalanced by the increase in lower esophageal pressure, which reduces or eliminates the increased risk of regurgitation
- Muscle pains: more likely to concern the patient with minor injuries who ambulates soon after surgery
- Prolonged paralysis in patients with atypical pseudocholinesterase
- Cardiac arrhythmias, particularly bradycardia after repeated doses
- Trigger for malignant hyperthermia

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2746–2773.

C.12. How are the doses of nondepolarizing muscle relaxants affected by burn injury?

In general, burn patients show great resistance to the nondepolarizing relaxants. Martyn et al. first reported that burn patients required a five times higher plasma concentration of D-tubocurarine to attain a given percentage of twitch depression compared with healthy subjects. The dose of pancuronium is increased by 2.5 times.

This increased requirement appears secondary to an upregulation of and altered affinity for junctional receptors. The burn patient also has increased plasma protein binding of nondepolarizing relaxants.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2746–2773.

Jeevendra Martin JA, Fukushima Y, Chon JY, et al. Muscle relaxants in burns, trauma, and critical illness. *Int Anesthesiol Clin*. 2006;44:123–143.

C.13. How are the muscle relaxants such as succinylcholine, atracurium, cisatracurium, vecuronium, pancuronium, rocuronium, and curare metabolized and eliminated? Which of them has significant histamine release?

See **Table 56.3**.

TABLE 56.3 The Metabolism, Elimination, and Histamine Release of Muscle Relaxants

	Elimination			
Relaxant	Kidney (%)	Liver (%)	Plasma Metabolism (%)	Histamine Release
Succinylcholine	<2	0	98	Slight
Atracurium	10–40	0	60–90	Slight
Cisatracurium	16	7	77	None
Vecuronium	40	60	0	None
Pancuronium	85	15	0	None
Rocuronium	25	70	0	None
D-Tubocurarine	80	20	0	Moderate

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2746–2773.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2746–2773.

D. Postoperative Management

D.1. How would you monitor this patient during transport?

This patient was most likely intubated, paralyzed, apneic, and still under the influence of general anesthetic. Monitoring should be directed toward respiration, oxygenation, and hemodynamics. These can be achieved by utilizing a transport monitor capable of monitoring ECG, blood pressure, CVP, and pulse oximeter.

During transport, ventilation should be controlled with positive pressure ventilation via an Ambu bag with supplemental oxygen.

D.2. What is meant by diffusion hypoxia? How do you prevent it?

In 1954, Fink et al. first reported diffusion hypoxia during recovery from nitrous oxide–oxygen anesthesia. A mild degree of hypoxia may develop for more than 10 minutes after cessation of a nitrous oxide–oxygen anesthetic if the patient is breathing room air. The arterial oxygen saturation may fall 5% to 10% and often reaches values less than 90% (Pa_{O_2} <60 mmHg). This desaturation occurs upon rapid nitrous oxide elimination. Nitrous oxide is 35 times more soluble in blood than nitrogen. Alveolar oxygen is diluted by the high nitrous oxide concentration diffusing from blood. Diffusion hypoxia can be prevented by the administration of a high fractional inspired oxygen for several minutes before allowing the patient to breathe room air.

Fink R. Diffusion anoxia. *Anesthesiology*. 1955;16:511–519.

Fink R, Carpenter SL, Holiday DA, et al. Diffusion anoxia during recovery from nitrous oxide-oxygen anesthesia. *Fed Proc*. 1954;13:354.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2746–2773.

D.3. Why do patients often shiver in the recovery room on emergence from anesthesia?

Postanesthetic shivering is commonly observed in the recovery room after emergence from inhalational general anesthetics. It is postulated that inhalation agents inhibit central hypothalamic thermoreceptors and that shivering is a thermoregulatory response to intraoperative heat loss. Shivering will produce energy to maintain normothermia. Secondarily, tremors may be

the result of anesthetic-induced disinhibition of descending spinal reflexes. Similar nonthermoregulatory tremors have been seen in women during labor after neuroaxial anesthesia.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2746–2773.

D.4. Discuss the causes of oliguria in the recovery room.

Oliguria is arbitrarily defined as the production of less than 400 mL of urine in 24 hours. It is the functional manifestation of *acute renal failure* (ARF). The syndrome of ARF may be classified into the following three groups:

- *Prerenal ARF (hypovolemic)*. A reduction of renal blood flow decreases both the filtration rate and the overall urinary flow. There is no structural damage to the kidney. Prerenal azotemia is reversible with volume expansion. However, if untreated, it can progress to the ischemic form of acute tubular necrosis.
- *Renal ARF (acute tubular necrosis)*. Ischemia or nephrotoxic substances result in structural damage to the renal tubules.
- *Postrenal ARF (obstruction of urinary outflow)*. Obstruction occurs distal to the kidney, at the level of the ureter, bladder, or urethra. Pus, tubular debris, blood clots, nephrolithiasis, tumor burden, prostatic hypertrophy, or a nonfunctioning Foley catheter can cause mechanical cessation of urinary flow.

Determining the underlying etiology of oliguria is essential because management strategies vary greatly. To identify the cause of oliguria, one must make a careful assessment of the urinary sediment. Presence of renal tubular cells, renal tubular cell casts, and pigmented granular casts is strong evidence supporting acute tubular necrosis. Normal urinary sediment is consistent with prerenal azotemia. Other data, such as CVP and PAOP, provide valuable information about the state of

hydration. Postrenal etiologies of ARF are supported by bladder ultrasonography (demonstrating an enlarged, distended bladder) or an elevated pressure on bladder manometry (supporting intraabdominal hypertension).

Perazella MA, Coca SG, Kanbay M, et al. Diagnostic value of urine microscopy for differential diagnosis of acute kidney injury in hospitalized patients. *Clin J Am Soc Nephrol*. 2008;3:1615–1619.

57 Trauma

Rohan K. Panchamia, Jaideep K. Malhotra, Ralph L. Slepian

A 31-year-old man sustained multiple stab wounds to the left upper quadrant of his abdomen and to his left hemithorax. Vital signs were as follows: blood pressure, 85/60 mmHg; heart rate, 130 beats per minute; respiratory rate, 32 breaths per minute; and temperature, 34.5°C (94.1°F). His hematocrit was 27%. He was emergently brought to the operating room for an exploratory laparotomy and possible thoracotomy.

A. Medical Disease and Differential Diagnosis

1. How is trauma classified?
2. What are the injuries associated with thoracic trauma?
3. What are the injuries associated with cardiac trauma?
4. What is the pathophysiology of acute pericardial tamponade?
5. What are the anesthetic implications for treating cardiac tamponade?
6. How is the initial assessment and management of the trauma patient performed?
7. What constitutes a primary survey, and what is its objective?
8. What constitutes a secondary survey, and what is its objective?
9. What is the definition of massive hemothorax? What are the signs and symptoms of a hemothorax?

10. What are the indications for a thoracotomy to treat a hemothorax?
11. How are pneumothoraces categorized?
12. What is an occult pneumothorax?
13. If the patient has a widened mediastinum on chest radiograph, what are your concerns?
14. What are the most commonly injured organs in blunt abdominal trauma?
15. What is a focused abdominal sonography for trauma (FAST) examination?
16. What is diagnostic peritoneal lavage (DPL)?
17. Why was DPL not performed for this patient?
18. Define shock.
19. What are the four types of shock?
20. List the signs and symptoms of shock.
21. What is the pathophysiology of hypovolemic shock?
22. How would you classify hemorrhage?
23. What is the initial treatment of hemorrhagic shock?
24. Would you choose crystalloid, colloid, or blood products to treat hemorrhagic shock?
25. Is there a place for dextran or hetastarch (Hespan) in treating hypovolemic shock?

B. Preoperative Evaluation and Preparation

1. What premedication would you order?
2. What preoperative testing would you order?

C. Intraoperative Management

1. How would you monitor this patient?
2. How would you induce anesthesia?
3. What technique could you use if single-lung ventilation was indicated?
4. What agents would you choose to maintain anesthesia?
5. What muscle relaxant would you choose?

6. What can be done to decrease the incidence of intraoperative awareness?
7. Five minutes after intubation, the peak airway pressure increased from 20 to 40 cm H_2O. What are the possible causes?
8. How would you make a diagnosis of tension pneumothorax?
9. What is the treatment of tension pneumothorax?
10. The patient's blood loss was continuing, and the hematocrit was 18%. What type of blood would you give if the type and crossmatch are not completed?
11. What precautions should be taken if more than 2 units of low titer type O uncrossmatched whole blood are given?
12. What are the complications associated with any blood transfusion?
13. What is considered a massive transfusion (MT)? What is the Assessment of Blood Consumption (ABC) score?
14. What are the complications associated with an MT?
15. Can the shift of the oxygen–hemoglobin dissociation curve be quantified?
16. How is hypothermia defined?
17. What are the adverse effects of hypothermia?
18. What is the treatment of hypothermia?
19. What are the effects of blood transfusion on the immune system?
20. What are the guidelines for transfusion of blood products?
21. What are the guidelines for the ratio of plasma/platelet transfusion to packed red blood cells in an MT?
22. If a patient were a member of the Jehovah's Witness religious sect, would you give a blood transfusion?
23. If a child is a Jehovah's Witness and suffered from hemorrhagic shock, what would you do?
24. What are the concentrated factors and hemostatic agents available for bleeding patients?

25. What is thromboelastography (TEG) and thromboelastometry? How can they guide transfusion?

D. Postoperative Management

1. What is acute respiratory distress syndrome (ARDS)? What is acute lung injury?
2. How is ARDS treated?
3. In the recovery room, you are called to see this patient because of oliguria. How would you evaluate and treat this patient?
4. If this patient had a crush injury and low urine output, what other concerns might you have? What if the patient has dark or "tea-colored" urine?

A. Medical Disease and Differential Diagnosis

A.1. How is trauma classified?

Trauma is usually separated into two distinct categories: penetrating and blunt trauma. Both can cause havoc on the body's vascular, visceral, musculoskeletal, and nervous systems.

A.2. What are the injuries associated with thoracic trauma?

Penetrating injuries associated with thoracic trauma are typically associated with stabbings and gunshot wounds. The latter causes far more destruction because of the large amount of kinetic energy transferred to the thoracic cavity from the impact of the bullet. As a result, gunshot wounds to the thorax are diffuse and much more likely to be fatal when compared to stabbings.

Blunt injuries to the chest are far more common than penetrating injuries. The most common causes of blunt injuries are deceleration injuries (as a result of motor vehicle accidents) and crush injuries. These can range from relatively minor injuries such as rib fractures to more severe ones such as lung

contusion, tracheobronchial tears, flail chest, pneumothorax, hemothorax, injuries to the great vessels, and traumatic ruptures of the esophagus or diaphragm.

Barbeito A, Shaw AD, Grichnik K, eds. *Thoracic Anesthesia*. New York: McGraw-Hill; 2012:379–402.

A.3. What are the injuries associated with cardiac trauma?

Penetrating cardiac injuries often lead to immediate cardiovascular collapse, and patients rarely survive to reach the operating room. Injuries associated with penetrating cardiac trauma include pericardial tamponade, cardiac perforation, rupture of a chamber, and fistula formation.

Blunt cardiac injuries (BCI) include cardiac contusion (most common), pericardial ruptures, rupture of a chamber, valvular tears, coronary artery injuries, and ventricular aneurysms. Screening for BCI includes electrocardiogram (ECG) and troponin I level; an echocardiogram is reserved for those with new ECG changes, elevated troponin I levels, hypotension, and/or arrhythmias. At the very least, patients with abnormal cardiac studies should be admitted for monitoring.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2017:1506–1510.

Barbeito A, Shaw AD, Grichnik K, eds. *Thoracic Anesthesia*. New York: McGraw-Hill; 2012:379–402.

Clancy K, Velopulos C, Bilaniuk J, et al. Screening for blunt cardiac injury: an Eastern Association for the Surgery of Trauma practice management guideline. *J Trauma*. 2012;73(5, suppl 4):S301–S306.

A.4. What is the pathophysiology of acute pericardial tamponade?

Acute pericardial tamponade represents a rapid increase in intrapericardial pressure exceeding intracardiac pressures. This process results in cardiac chamber compression and diminished

diastolic filling, leading to reduced cardiac output and systemic hypoperfusion, and may be followed by bradycardic arrest. Clinically unstable patients present with Beck triad (hypotension, distended neck veins, and muffled heart sounds), tachycardia, and pulsus paradoxus (>10 mmHg); some of these signs can be easily missed on a hypovolemic trauma patient. The diagnosis of cardiac tamponade can be aided with transthoracic echocardiography, demonstrating key echo findings: pericardial effusion, dilated inferior vena cava (IVC), chamber collapse during diastole, exaggerated respirophasic transvalvular flow velocities, respirophasic septal shift, and a swinging heart. It is important to understand that the hemodynamic effect of the pericardial effusion depends on the change in ventricular diastolic function in response to increased intracardial pressure and not size of the effusion per se. If the diagnosis of acute pericardial tamponade is made and the patient is unstable, immediate evacuation of the pericardium via a pericardiocentesis or a pericardial window is required (also see Chapter 12).

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2017:1506–1510.

Klein AL, Abbara S, Agler DA, et al. American Society of Echocardiography clinical recommendations for multimodality cardiovascular imaging of patients with pericardial disease: endorsed by the Society for Cardiovascular Magnetic Resonance and Society of Cardiovascular Computed Tomography. *J Am Soc Echocardiogr*. 2013;26:965–1012.

A.5. What are the anesthetic implications for treating cardiac tamponade?

The anesthetic goal for treating acute cardiac tamponade is to maintain intrinsic sympathetic tone. These patients are extremely dependent on intrinsic sympathetic tone, and therefore, maintenance of heart rate and preload are of utmost importance. A preinduction intra-arterial catheter and large-bore

intravenous access are essential. Ketamine and etomidate are considered appropriate agents for induction. A rapid sequence induction with succinylcholine or an awake intubation can be performed. If possible, preinduction sedation should be avoided. Inotropes such as epinephrine should be readily available and can be given in small doses to avoid bradycardia and hypotension. Induction should be delayed until after patient preparation and draping is completed. In the event the patient becomes hemodynamically unstable, the effusion can then be drained as quickly as possible (also see Chapter 12).

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2017:1506–1510.

Barbeito A, Shaw AD, Grichnik K, eds. *Thoracic Anesthesia*. New York: McGraw-Hill; 2012:310–312, 379–402.

A.6. How is the initial assessment and management of the trauma patient performed?

A systematic and organized approach to the assessment and management of the trauma patient has been developed by the American College of Surgeons and is taught as Advanced Trauma Life Support. Initial evaluation and management as stated by Advanced Trauma Life Support consists of five components:

- The primary survey
- Resuscitation
- The secondary survey
- Continued monitoring and reevaluation
- Definitive care

Barbeito A, Shaw AD, Grichnik K, eds. *Thoracic Anesthesia*. New York: McGraw-Hill; 2012:379–402.

A.7. What constitutes a primary survey, and what is its objective?

The assessment of the trauma patient consists of the primary and secondary survey. The function of the primary survey is to identify and treat immediately life-threatening injuries. The life-threatening injuries associated with chest trauma are the following:

- Lost airway/airway obstruction
- Tension pneumothorax
- Massive hemothorax
- Open pneumothorax
- Cardiac tamponade
- Flail chest

ATLS Subcommittee, American College of Surgeons' Committee on Trauma, International ATLS Working Group. Advanced trauma life support (ATLS®): the ninth edition. *J Trauma Acute Care Surg*. 2013;74(5):1363–1366.

Barbeito A, Shaw AD, Grichnik K, eds. *Thoracic Anesthesia*. New York: McGraw-Hill; 2012:379–402.

Chest trauma: initial evaluation. http://www.trauma.org/archive/thoracic/CHESTintro.html. Published February 2004. Accessed October 20, 2015.

A.8. What constitutes a secondary survey, and what is its objective?

The secondary survey is a more detailed examination aimed at identifying other non–life-threatening injuries, planning further laboratory and radiographic studies, and forming a workable differential diagnosis. It begins only after abnormalities identified during the primary surgery have been appropriately addressed and treated. Examples of chest injuries identified on secondary survey are the following:

- Simple pneumothorax
- Hemothorax
- Rib fractures
- Pulmonary contusion
- Tracheobronchial tree injury

- Non–life-threatening blunt myocardial injury

ATLS Subcommittee, American College of Surgeons' Committee on Trauma, International ATLS Working Group. Advanced trauma life support (ATLS®): the ninth edition. *J Trauma Acute Care Surg*. 2013;74(5):1363–1366.

Barbeito A, Shaw AD, Grichnik K, eds. *Thoracic Anesthesia*. New York: McGraw-Hill; 2012:379–402.

Chest trauma: initial evaluation. http://www.trauma.org/archive/thoracic/CHESTintro.html. Published February 2004. Accessed October 20, 2015.

A.9. What is the definition of massive hemothorax? What are the signs and symptoms of a hemothorax?

A massive hemothorax is defined as a rapid accumulation of greater than 1,500 mL of blood in the thoracic cavity. It is usually caused by rib fractures (intercostal or internal mammary vessel bleeding), lung injury, great vessel injury, cardiac injury, or diaphragmatic injury. The signs and symptoms of a hemothorax include diminished breath sounds on the affected side, hemorrhagic shock, and mediastinal shift.

Reed AP, Yudkowitz FS. *Clinical Cases in Anesthesia*. 4th ed. London: Elsevier Saunders; 2014:395–410.

A.10. What are the indications for a thoracotomy to treat a hemothorax?

Hemothorax, if severe enough, can lead to hemorrhagic shock. Therefore, timely diagnosis and treatment are of utmost importance. After a chest tube is placed, if drainage of blood is greater than 1,500 mL or one-third of blood volume, or if drainage is greater than 200 mL per hour for over 2 to 4 hours, a thoracotomy is indicated. Alternatively, if the patient is older than 60 years, then if drainage is greater than 100 mL per hour for over 4 hours, a thoracotomy is also indicated. If the patient does not meet these criteria but is still hemodynamically unstable or if ventilation is difficult, emergent surgery should be

performed.

ATLS Subcommittee, American College of Surgeons' Committee on Trauma, International ATLS Working Group. Advanced trauma life support (ATLS®): the ninth edition. *J Trauma Acute Care Surg*. 2013;74(5):1363–1366.

Reed AP, Yudkowitz FS. *Clinical Cases in Anesthesia*. 4th ed. London: Elsevier Saunders; 2014:395–410.

A.11. How are pneumothoraces categorized?

Pneumothoraces are categorized into three broad categories: simple, open, and tension pneumothorax. The principal physiologic changes are hypoxemia due to reduced vital capacity and alveolar hypoventilation and impaired venous return secondary to increased intrathoracic pressure.

Simple pneumothorax can result from both blunt and penetrating trauma to the chest. It is defined as the presence of air in the pleural space without an open chest wound and evidence of tension pneumothorax. Diagnosis can be made radiographically, via a chest radiograph or computed tomography (CT), although in many trauma situations, the patients' condition precludes obtaining conventional imaging. In such cases, diagnosis can be made by lung ultrasound. The lack of pleural sliding, lung pulse, and vertical artifacts over the anterior chest wall, coupled with the presence of a lung point, are highly sensitive and specific findings for pneumothorax. Recent studies have demonstrated that using lung ultrasound can be a faster and more sensitive test than a supine anterior-posterior chest radiograph. Definitive treatment is the placement of a chest tube or pleural pigtail if the patient is experiencing cardiopulmonary instability, and/or if the pneumothorax is sizeable, that is, greater than 10% of the pleural cavity. Of note, pigtail catheters have been shown to be equally as effective as chest tubes with decreased rate of complications.

Open pneumothorax is the result of an open wound in the

thoracic cavity that favors constant entrainment of air through the wound. Treatment entails placing an occlusive dressing on three sides over the wound, to create a "flutter valve" and allow egress of air but not entrainment of air, followed by chest tube placement.

Tension pneumothorax is the rapid buildup of air within the pleural space that cannot escape, causing an acute rise in airway pressures with resulting mediastinal shift and obstructive shock. Management is the immediate decompression of the thoracic cavity via needle thoracentesis or finger thoracostomy and then proceeding to chest tube insertion.

Barbeito A, Shaw AD, Grichnik K, eds. *Thoracic Anesthesia*. New York: McGraw-Hill; 2012:382–383.

Chang SH, Kang YN, Chiu HY, et al. A systematic review and meta-analysis comparing pigtail catheter and chest tube as the initial treatment for pneumothorax. *Chest*. 2018;153(5):1201–1212.

Kruisselbrink R, Chan V, Cibinel GA, et al. I-AIM (Indication, Acquisition, Interpretation, Medical Decision-making) framework for point of care lung ultrasound. *Anesthesiology*. 2017;127:568–582.

Pneumothorax: an overview of pneumothoraces-diagnosis & management. http://www.trauma.org/index.php/main/article/393/. Published May 9, 2009. Accessed May 2, 2015.

Wilkerson RG, Stone MB. Sensitivity of bedside ultrasound and supine anteroposterior chest for the identification of pneumothorax after blunt trauma. *Acad Emerg Med*. 2010;17:11–17.

A.12. What is an occult pneumothorax?

An occult pneumothorax is a pneumothorax that is seen on CT but was not identified previously on the chest radiograph, comprising as many as 50% of all pneumothoraces, with an overall incidence of 5% in all trauma patients.

In many cases, this type of pneumothorax is managed conservatively with serial imaging and resolves over time, without requiring placement of a chest tube. However, decompression should be considered if the patient is

symptomatic, hemodynamically unstable, or has a pneumothorax greater than 10% in size. Another indication for decompression, although controversial, is the delivery of positive pressure ventilation. Whether these patients should have a chest tube or pigtail placed preemptively is up for debate; for now, the decision should be made on a case-by-case basis.

Ball CG, Kirkpatrick AW, Feliciano DV. The occult pneumothorax: what have we learned? *Can J Surg*. 2009;52:E173–E179.

Ouellet JF, Trottier V, Kmet L, et al. The OPTICC trial: a multi-institutional study of occult pneumothoraces in critical care. *Am J Surg*. 2009;197:581–586.

A.13. If the patient has a widened mediastinum on chest radiograph, what are your concerns?

A chest radiograph revealing a widened mediastinum may indicate the presence of a thoracic aortic injury; other radiographic features suggestive of aortic injury include abnormal mediastinal contour, hemothorax, pleural cap, and tracheal deviation. However, the best screening tool is contrast-enhanced CT of the chest.

These types of injuries are often life-threatening, necessitating immediate identification and intervention. Blunt aortic injury is associated with high-speed deceleration and is the second leading cause of death in trauma patients, accounting for 16% of all trauma-related deaths. Open surgical repair requires a double-lumen tube, single-lung ventilation, and clamping of the proximal aorta while taking measures to protect the spinal cord. In patients with coexisting conditions, such as increased intracranial pressure, profound bleeding, or hypoxemia, this procedure is extremely high risk and may be contraindicated. Mainstay of treatment of an aortic transection includes control of blood pressure and ventricular ejection force (dP/dt) with β-blocker infusions and/or mixed β-blocker/α-antagonist

medications, followed by endovascular repair. At high-volume centers, endovascular repair is associated with a higher survival benefit and decreased incidence of complications, especially paraplegia, compared to open surgical repair.

Demetriades D, Velmahos GC, Scalea TM, et al. Operative repair or endovascular stent graft in blunt traumatic thoracic aortic injuries: results of an American Association for the Surgery of Trauma multicenter study. *J Trauma*. 2008;64(3):561–571.

Ekeh AP, Peterson W, Woods RJ, et al. Is chest x-ray an adequate screening tool for diagnosis of blunt thoracic aortic injury? *J Trauma*. 2008;65:1088–1092.

Neschis DG, Scalea TM, Flinn WR, et al. Blunt aortic injury. *N Engl J Med*. 2008;359:1708–1716.

A.14. What are the most commonly injured organs in blunt abdominal trauma?

In blunt abdominal trauma, the most commonly injured organs are the spleen, liver, kidneys, and bowel. Generally, blunt abdominal trauma leads to higher mortality rates than penetrating trauma. The reason is multifactorial and includes greater difficulty in diagnosis and frequent association with other injuries, such as head injury, chest trauma, and fractures.

A.15. What is a focused abdominal sonography for trauma (FAST) examination?

FAST is a rapid ultrasonography examination that is routinely performed in the setting of blunt or penetrating torso trauma. It is designed to evaluate for free fluid (blood until proven otherwise) in the peritoneum, pleural space, and around the heart; four areas are interrogated with ultrasound: the subxiphoid, right upper quadrant, left upper quadrant, and suprapubic areas. The most dependent space in supine adult patients is the hepatorenal space (Morrison pouch) and therefore is the most likely to collect fluid. One downside to the FAST

exam is the fact that usually 200 to 250 mL of fluid needs to accumulate before it can be visualized sonographically. Furthermore, it cannot evaluate the retroperitoneum and misses solid organ injuries. The utility of FAST resides in the bedside examination of the hemodynamically unstable trauma patient, determining operative management versus considering other potential sources of shock. It has largely replaced DPL as the initial screening tool for intra-abdominal injury.

Hoff WS, Holevar M, Nagy KK, et al. Practice management guidelines for the evaluation of blunt abdominal trauma: the East Practice Management Guidelines Work Group. *J Trauma*. 2002;53(3):602–615.

Richards JR, McGahan JP. Focused assessment with sonography in trauma (FAST) in 2017: what radiologist can learn. *Radiology*. 2017;283(1):30–48. doi:10.1148/radiol.2017160107.

Rozycki GS, Root HD. The diagnosis of intraabdominal visceral injury. *J Trauma*. 2010;68(5):1019–1023.

A.16. What is diagnostic peritoneal lavage (DPL)?

In abdominal trauma, DPL allows for rapid identification of a hemoperitoneum and, therefore, the discovery of an intraperitoneal injury. A minilaparotomy is performed, then a catheter is placed into the abdomen and aspirated looking for gross blood. Aspiration of 10 mL of blood is considered a positive finding, suggesting visceral or vascular injury. As previously mentioned, the FAST exam is preferred over DPL because of its noninvasive nature and less false-positives, in comparison to DPL; however; DPL may have utility in detecting hemoperitoneum in the patient who is hemodynamically unstable and either has a negative or equivocal FAST.

If less than 10 mL of blood is aspirated, then 1 L of lactated Ringer's solution or normal saline is allowed to drain into the abdomen. The lavage fluid is then allowed to return by gravity and is sent to the laboratory for analysis. Criteria for a positive peritoneal lavage are an erythrocyte count of 100,000 per μL, a

white blood cell count of 500 per μL, the presence of bile or food particles, and a fluid amylase concentration of 175 units per dL. The white blood cell level itself should not determine the need for laparotomy. The level of white blood cells also does not rise initially but requires several hours to rise. Alkaline phosphatase and amylase are contained in the small bowel and spill into the abdominal cavity after injury. These levels tend to rise early in injury. Amylase in lavage fluid has been seen as a more accurate marker than alkaline phosphatase. If the peritoneal lavage meets one or more of these criteria, the patient goes to the operating room for an exploratory laparotomy.

Roberts JR, Hedges JR, Custalow CB, et al, eds. *Roberts and Hedges' Clinical Procedures in Emergency Medicine*. Philadelphia, PA: Elsevier Saunders; 2014:852–872.

A.17. Why was DPL not performed for this patient?

DPL was not done for two reasons. First, it is felt that all penetrating wounds to the abdomen need to be surgically explored. Second, this patient was exhibiting signs of shock and obviously needed to be sent to the operating room without delay.

Before CT and ultrasonography technologies, DPL was the only diagnostic test available to rapidly evaluate the abdomen for injury. Although DPL is highly sensitive, it can also result in false-positive results, leading to unnecessary exploratory laparotomies. CT now allows for evaluation of all intraperitoneal organs, the diaphragm, and the retroperitoneum (an area inaccessible to DPL) while also allowing for identification of the specific organ injured. CT should be used in the evaluation of hemodynamically stable trauma patients.

Rozycki GS, Root HD. The diagnosis of intraabdominal visceral injury. *J Trauma*. 2010;68(5):1019–1023.

A.18. Define shock.

Shock is defined as inadequate oxygen delivery and/or tissue oxygenation to maintain normal cellular processes, for example, aerobic metabolism. End-organ hypoperfusion seems to be the final common denominator in all forms of shock.

Townsend CM Jr, Beauchamp RD, Evers BM, et al, eds. *Sabiston Textbook of Surgery*. 20th ed. Philadelphia, PA: Elsevier Saunders; 2017:44–97.

A.19. What are the four types of shock?

Shock is classified according to its cause:

- *Hypovolemic (hemorrhagic) shock*: characterized by a loss of circulatory blood and plasma volumes
- *Cardiogenic shock*: characterized by an inability of the myocardium to pump blood
- *Distributive (neurogenic, septic) shock*: leads to reduced systemic vascular resistance
- *Obstructive*: characterized by an impairment in cardiac function due to direct cardiac compression or decreased venous return.

Tisherman SA, Forsythe RM, eds. *Trauma Intensive Care*. New York: Oxford University Press; 2013:63–72.

Townsend CM Jr, Beauchamp RD, Evers BM, et al, eds. *Sabiston Textbook of Surgery*. 20th ed. Philadelphia, PA: Elsevier Saunders; 2017:44–97.

A.20. List the signs and symptoms of shock.

Tachycardia, decreased capillary refill, reduced pulse pressure, tachypnea, pallor, cool extremities, oliguria, anxiety, restlessness, and loss of consciousness may present as manifestations of shock. Hypotension tends to be a late finding; however, its absence does not rule out shock.

Tisherman SA, Forsythe RM, eds. *Trauma Intensive Care*. New York: Oxford University Press; 2013:63–72.

A.21. What is the pathophysiology of hypovolemic shock?

Cardiovascular Derangement

A number of neurohormonal responses occur in the setting of hypovolemic shock. An acute decrease in circulating blood volume activates aortic and carotid baroreceptors, leading to an outpouring of catecholamines from the sympathetic nervous system and adrenal gland, with an increase in heart rate, blood pressure, contractility, and minute ventilation. The α-adrenergic agonist is responsible for vasoconstriction, shunting blood from the skin, viscera, and muscle, thereby preserving flow to the coronary and cerebral circulations. Vasopressin and the renin–angiotensin–aldosterone system contribute to renal water retention, sodium and chloride resorption, and peripheral vasoconstriction.

Various immunologic and inflammatory mediators, such as tissue necrosis factor and nitric oxide, are released in response to tissue injury. These substances can cause myocardial depression, inappropriate vasodilatation, and end-organ dysfunction.

Acid–Base Disturbance

Metabolic acidosis is almost always seen in association with a shock state. As a result of tissue hypoperfusion, oxygen delivery to vital organs is reduced resulting in tissue hypoxia and oxygen debt. At the cellular level, there is a change from aerobic to anaerobic metabolism. This switch leads to the production of anaerobic metabolites, such as lactic acid. Sequelae include hypotension, decreased myocardial contractility, arrhythmias, encephalopathy, and worsening end-organ function.

Marx JA, Hockberger RS, Walls RM, et al, eds. *Rosen's Emergency Medicine-Concepts and Clinical Practice*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2014:67–74.

Tisherman SA, Forsythe RM, eds. *Trauma Intensive Care*. New York: Oxford University Press; 2013:63–72.

Townsend CM Jr, Beauchamp RD, Evers BM, et al, eds. *Sabiston Textbook of Surgery*. 20th ed. Philadelphia, PA: Elsevier Saunders; 2017:44–97.

A.22. How would you classify hemorrhage?

Classification of hemorrhage based on blood loss is as follows:
Class I: blood loss of up to 15% of the blood volume: normal pulse and blood pressure
Class II: blood loss of up to 30% of the blood volume: tachycardia, decreased urine output, and anxiety
Class III: blood loss of up to 40% of the blood volume: marked tachycardia, hypotension, tachypnea, oliguria, and anxiety
Class IV: blood loss of more than 40% of the blood volume: tachycardia and hypotension, tachypnea, anuria, confusion, and lethargy

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Dutton RP. Shock and trauma anesthesia. *Anest Clin North Am*. 1999;17:83–95.

A.23. What is the initial treatment of hemorrhagic shock?

From a resuscitation standpoint, the initial approach to traumatic hemorrhagic shock entails (1) restoring intravascular volume with a high ratio of blood products to maintain oxygen delivery and tissue perfusion, (2) treating the coagulopathy, and (3) managing complications related to shock and MT, that is metabolic acidosis and hypothermia. For more than a decade, trauma centers have adapted the practice of initial resuscitation with hemostatic components, such as plasma and platelets. This strategy for treating massive hemorrhage was pioneered from experience and knowledge gained during combat in Afghanistan and Iraq; it involves limiting the total volume of crystalloid administered and replacing intravascular volume with packed red blood cells and fresh frozen plasma (FFP) in a ratio approaching 1:1. The overall goal is to provide fluids with oxygen-carrying capacity and hemostatic capabilities while avoiding the acute coagulopathy associated with major trauma and blood loss, which has been shown to increase mortality rates.

Barash PG, Cahalan MK, Cullen BF, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1494–1499.

Griffee MJ, Deloughery TG, Thorborg PA. Coagulation management in massive bleeding. *Curr Opin Anaesthesiol*. 2010;23:263–268.

Seheult JN, Bahr M, Anto V, et al. Safety profile of uncrossmatched, cold-stored, low-titer, group O+ whole blood in civilian trauma patients. *Transfusion*. 2018;58:2280–2288.

A.24. Would you choose crystalloid, colloid, or blood products to treat hemorrhagic shock?

Crystalloid solutions can sustain hemodynamics and deliver adequate oxygenation in healthy patients who have lost as much as 30% of their total blood volume. Still, controversy remains over the use of crystalloid versus colloid therapy for the initial therapy of hypovolemic shock.

Proponents of crystalloid therapy believe that both intravascular and interstitial fluid losses occur in hypovolemic shock and that these can be readily replaced with crystalloids. Another benefit of crystalloids is the decrease in blood viscosity, which may enhance perfusion. A particular advantage to lactated Ringer's solution is that lactate is metabolized to bicarbonate, which may help to buffer the patient's acidosis. Finally, in this age of medical economics, the cost of crystalloid is much less than that of colloid. Because crystalloid leaves the intravascular space and enters the interstitial space, large quantities are needed, and some fear that these quantities may lead to both pulmonary and peripheral edema, although studies have not confirmed this fear.

Proponents of colloid therapy, on the other hand, argue that much less volume of fluid is needed to counteract hypovolemic shock and that early colloid therapy can prevent the complications associated with large-volume crystalloid resuscitation such as dilutional coagulopathy, hyperchloremic acidosis, and edema. Colloids maintain the oncotic pressure and

hold the interstitial fluids in the intravascular space, which is felt to possibly prevent pulmonary edema. If leaky alveolar capillary membranes are seen within the lung, colloids may worsen pulmonary edema.

The best resuscitative fluid to treat hemorrhagic shock is whole blood. It provides a balanced resuscitation, reversing shock and coagulopathy, by containing all components of blood, including 100% clotting activity. A major advantage whole blood possesses over crystalloid and colloid is that it does not promote dilutional coagulopathy. From a logistical standpoint, it requires a limited amount of processing and is feasible to use. In terms of its safety profile, the administration of uncrossmatched, cold-stored, low-titer, group O+ whole blood was shown too well tolerated, not causing any episodes of hemolysis or suspected transfusion reactions.

Choi PT, Yip G, Quinonez LG, et al. Crystalloids vs. colloids in fluid resuscitation: a systematic review. *Crit Care Med*. 1999;27:200–210.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1492–1498, 2136–2137.

Orlinsky M, Shoemaker W, Reis ED, et al. Current controversies in shock and resuscitation. *Surg Clin North Am*. 2001;81:1217–1262.

Seheult JN, Bahr M, Anto V, et al. Safety profile of uncrossmatched, cold-stored, low-titer, group O+ whole blood in civilian trauma patients. *Transfusion*. 2018;58:2280–2288.

A.25. Is there a place for dextran or hetastarch (Hespan) in treating hypovolemic shock?

Dextran and hetastarch are synthetic polysaccharide solutions with varying mean molecular weights. Dextran 40, dextran 70, and hetastarch have all been used as volume expanders. Dextrans are relatively inexpensive, increase effective blood volume, and decrease blood viscosity. Nevertheless, their negative aspects are considerable. They impair coagulation by coating platelets as well as impair typing and crossmatching by

coating red blood cells. Furthermore, anaphylactic reactions have been reported.

Kozek-Langenecker SA. Effects of hydroxyethyl starch solutions on hemostasis. *Anesthesiology*. 2005;103:654–660.

B. Preoperative Evaluation and Preparation

B.1. What premedication would you order?

None. This is a critically ill patient who is coming to the operating room for emergency surgery. Narcotics and sedatives are contraindicated because they could worsen his already tenuous hemodynamic state.

B.2. What preoperative testing would you order?

Because of the emergent nature of the trauma setting, preoperative tests and imaging studies are frequently limited. If the patient is hemodynamically unstable, any preoperative evaluation is aborted and the patient is taken directly to the operating room.

If the patient is stable, a portable chest radiograph, arterial blood gas, complete blood count, and FAST can be done in a relatively short period in the resuscitation bay before surgery. Often, these tests are obtained while the patient is being prepared for emergency surgery. This information is then combined with other primary survey adjuncts, such as oxygen saturation and ECG, to evaluate the patient and formulate an appropriate management strategy. Although it is usually not possible to clinically clear the cervical spine before surgery, it is important to know the results of any radiologic studies that have been done (e.g., in order to rule out an unstable cervical spine fracture) and to adjust the anesthetic plan accordingly.

C. Intraoperative Management

C.1. How would you monitor this patient?

Routine noninvasive monitor would include ECG, blood pressure cuff, pulse oximeter, end-tidal carbon dioxide, esophageal stethoscope, temperature probe, and Foley catheter.

Invasive monitors for this patient include an arterial line and a central venous catheter. An arterial line is useful for serial blood sampling and continuous arterial blood pressure monitoring. There is a low threshold to place a central venous line, for example, an introducer, to assist with resuscitation efforts. A pulmonary artery catheter may be indicated if the patient has a history of heart failure, myocardial dysfunction, mixed shock picture, and/or poor response to resuscitation.

C.2. How would you induce anesthesia?

Because all trauma patients are considered to have a full stomach, the best way to protect the patient's airway is to perform a rapid sequence induction with cricoid pressure, while maintaining in-line cervical spine immobilization for any patient in a cervical collar. For the patient with a suspected difficult airway, one could do an awake fiberoptic intubation. An awake fiberoptic intubation in this population can be difficult because they may be confused, uncooperative, and sometimes even combative. First, if tolerated, the patient should be preoxygenated for 3 to 5 minutes. Next, ketamine 1 to 2.5 mg per kg might be given followed by succinylcholine 1.5 mg per kg while maintaining cricoid pressure. Ketamine was chosen in this case because of its cardiovascular-stimulating effects and the patient's unstable hemodynamics. Etomidate (0.2 mg per kg) would be another appropriate choice for an induction agent.

If the patient is comatose, in severe shock, or in full arrest on admission to the resuscitation room, no drug other than oxygen

and possibly a neuromuscular blocking drug is required until the patient's blood pressure and heart rate sufficiently rebound so that anesthetics can be titrated. In awake traumatized patients who are thought to be hypovolemic, etomidate is best tolerated.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2115–2152.

C.3. What technique could you use if single-lung ventilation was indicated?

If the patient does not already have a secure airway, the airway should be secured in the manner described in the previous question. Single-lung ventilation is indicated in this situation if the patient is bleeding from one lung and protection of the other lung is required or to improve the surgical field (lower priority). Once the airway is secured, there are several ways to obtain single-lung ventilation. The easiest and safest technique would be to use an Arndt or Cohen bronchial blocker through the endotracheal tube. If those blockers are not available, one could pass an embolectomy catheter (bronchial blocker) into the trachea and then the endotracheal tube. The bronchial blocker could then be positioned under direct vision using fiberoptic bronchoscopy. Alternatively, the bronchial blocker could be placed through a bronchoscopy adapter and endotracheal tube, and its position can be confirmed by fiberoptic bronchoscopy. The point at which the bronchial blocker enters the bronchoscopy adapter can then be sealed with pliable "bone wax" (a form of sterile bees wax that is soft and kneadable).

Another method of obtaining single-lung ventilation would be to change the endotracheal tube to a double-lumen tube using a Cook exchange catheter. The major risks of this option are losing a previously secured airway and aspiration while attempting to change the tube.

C.4. What agents would you choose to maintain anesthesia?

As the patient stabilizes and the hemodynamics improve, other anesthetic agents can be carefully titrated to prevent hypotension, as follows:

- Sedatives or amnestics should be added to the anesthetic as soon as tolerated. Remember to start with small doses and check the patient's reaction to the drugs between doses.
- Opioids should be titrated to control the hemodynamic response to surgery.
- Nitrous oxide must be carefully considered because it has the capacity to accumulate in closed airspaces or because of the high possibility that this patient has an occult pneumothorax.
- Inhalational anesthetics may be used in low concentrations, so the patient's hemodynamics are not compromised.

C.5. What muscle relaxant would you choose?

Vecuronium, rocuronium, and cisatracurium are free of cardiovascular side effects and have an intermediate duration of action. They are acceptable choices. Pancuronium is a long-acting muscle relaxant with vagolytic properties that may be deleterious to the patient.

D-Tubocurarine, metocurine, atracurium, and mivacurium all have the potential to cause hypotension and therefore would not be chosen for this patient.

C.6. What can be done to decrease the incidence of intraoperative awareness?

The incidence of intraoperative awareness is commonly cited as approximately 0.2%. This is probably an overestimation. In other sources, the incidence of traumatic intraoperative recall associated with pain is less that 0.03%. The American Society of Anesthesiologists Closed Claims database states that claims

associated to recall during anesthesia constitute 1.5% of claims. An increased relative risk for recall is seen in certain types of surgery, including cardiac surgery, cesarean sections, and trauma surgery. This most likely represents intentional light anesthesia associated with higher levels of stimulation. Bispectral index monitoring may be potentially useful; the application of these monitors during a trauma resuscitation may not be easily accomplished. It has been shown that patients with a bispectral index value of 50 were able to respond to verbal commands less than 10% of the time.

Johansen JW. Update on bispectral index monitoring. *Best Pract Res Clin Anaesthesiol*. 2006;20(1):81–99.

O'Connor MF, Daves SM, Tung A, et al. BIS monitoring to prevent awareness during general anesthesia. *Anesthesiology*. 2001;94:520–522.

Rampil IJ. Monitoring depth of anesthesia. *Curr Opin Anaesthesiol*. 2001;14:649–653.

C.7. Five minutes after intubation, the peak airway pressure increased from 20 to 40 cm H_2O. What are the possible causes?

The possible causes of peak airway pressure increase are as follows:

- Tension pneumothorax
- Bronchospasm
- Endobronchial intubation
- Pulmonary edema
- Secretions
- Kink in the anesthesia circuit or endotracheal tube

Hines RL, Marschall KE, eds. *Stoelting's Anesthesia and Co-existing Disease*. 7th ed. Philadelphia, PA: Elsevier; 2018:22.

Woods BD, Sladen RN. Perioperative considerations for the patient with asthma and bronchospasm. *Br J Anaesth*. 2009;103(suppl 1):i57–i65.

C.8. How would you make a diagnosis of tension

pneumothorax?

A tension pneumothorax can be diagnosed by the absence of breath sounds on the affected side. The chest movement may be asymmetric. Neck veins will be full, and systemic hypotension can occur if the tension pneumothorax is severe. Any patient who deteriorates under anesthesia and has wounds to the upper abdomen, lower neck, or ribs should be assumed to have a tension pneumothorax until proven otherwise.

Marx JA, Hockberger RS, Walls RM, et al, eds. *Rosen's Emergency Medicine-Concepts and Clinical Practice*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2014:431–458.

C.9. What is the treatment of tension pneumothorax?

Immediate decompression of the chest is mandatory for tension pneumothorax because otherwise the patient's hemodynamics will deteriorate. The diagnosis is made clinically and not by a chest radiograph. A 16- or 18-gauge Angiocath is placed into the second intercostal space at the midclavicular plane. After the air escapes confirming your diagnosis and the lung is decompressed, a chest tube should be placed.

Marx JA, Hockberger RS, Walls RM, et al, eds. *Rosen's Emergency Medicine-Concepts and Clinical Practice*. 8th ed. Philadelphia, PA: Elsevier Saunders; 2014:431–458.

C.10. The patient's blood loss was continuing, and the hematocrit was 18%. What type of blood would you give if the type and crossmatch are not completed?

This patient should have blood transfused as soon as possible. Type O Rh-negative packed red blood cells are the universal donor. This should be started while type-specific blood is being made available. Whenever the type-specific blood is ready, one can switch to it. Usually, by the time a patient reaches the operating room from the emergency room, a partial crossmatch

can be done. This usually takes 5 to 10 minutes, after which time type-specific blood can be transfused. If, however, the transfusion begins with low titer group O *whole blood* because the patient's ABO type was unknown and is found later not to be type O, follow your blood bank's criteria for switching to type-specific blood.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1546–1576.

Roberts JR, Hedges JR, Custalow CB, et al, eds. *Roberts and Hedges' Clinical Procedures in Emergency Medicine*. Philadelphia, PA: Elsevier Saunders; 2014:496–517.

C.11. What precautions should be taken if more than 2 units of low titer type O uncrossmatched whole blood are given?

The plasma from type O *whole blood* contains anti-A and anti-B antibodies, which can cause hemolytic reactions with type A and B red blood cells if given in significant quantities. Therefore, low titer type O uncrossmatched *whole blood* (i.e. It has low titers of anti-A and anti-B antibodies.) should be given and should continue to be transfused, although this will lead to minor hemolysis of the patient's own red blood cells if they are not type O. The patient should not receive his type-specific blood until the blood bank determines that the transfused anti-A and anti-B antibody levels are sufficiently low to permit safe transfusion of type-specific blood.

Packed red blood cells have smaller volumes of plasma and are virtually free of anti-A and anti-B antibodies. Therefore, whenever type-specific blood is not yet available, type O Rh-negative uncrossmatched packed red blood cells should be given in preference to low titer O *whole blood*. Once type-specific blood is available, it can be used safely.

Cain JG. Current practices in fluid and blood component therapy in trauma.

Semin Anesth. 2001;20:28–35.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1546–1576.

Weymouth W, Long B, Koyfman A, et al. Whole blood in trauma: a review for emergency clinicians. *J Emerg Med*. 2019;56(5):491–498.

C.12. What are the complications associated with any blood transfusion?

Complications associated with blood transfusion are as follows:

Transfusion Reactions

- Transfusion-related acute lung injury (TRALI) is characterized by the onset of hypoxemia and bilateral pulmonary edema within 6 hours of a transfusion, in the absence of other causes such as heart failure. It is attributed to donor plasma human leukocyte antigen class I and II antibodies activating recipient neutrophils, leading to a lung immune response. In 2006, U.S. blood collection agencies instituted a male-only plasma donor policy because multiparous females are more likely to carry the offending antibodies. The TRALI rate decreased to about one-third of its previous level. TRALI is now the leading cause of transfusion-related mortality. The treatment of this noncardiogenic pulmonary edema is aggressive supportive care.
- Transfusion-associated circulatory overload (TACO) occurs in 1% to 6% of transfused patients and can cause pulmonary edema secondary to fluid overload. Large amounts of plasma that may be transfused during MT or coagulopathy correction increase the likelihood of TACO.
- Transfusion-related immunomodulation (TRIM) is a risk with allogenic red blood cell transfusion. Although incompletely understood, there is a decrease in immunity with an increased incidence of nosocomial infection, postoperative infection,

and cancer recurrence.

- Febrile reactions occur in approximately 1% of all transfusions. In an awake patient, this is usually no more than an annoyance that requires antipyretics and decreasing the infusion rate. Leukoreduction decreases the likelihood of a febrile reaction occurring.
- Allergic (nonanaphylactic/nonanaphylactoid) nonhemolytic reactions to properly crossmatched blood will manifest as an increase in temperature, pruritus, and urticaria. This may be difficult to diagnose in the anesthetized patient. Treatment consists of the administration of antihistamines and discontinuation of the transfusion.
- Hemolytic reactions occur when incompatible blood is administered. The risk of an ABO-incompatible transfusion is 1:33,500 for red blood cell transfusions. Mortality associated with this remains high at approximately 40%. Caused by activation of the complement system, hemolytic reactions can be life-threatening. In the awake patient, fever, chills, dyspnea, substernal, and lumbar pain are seen in addition to hypotension. Under general anesthesia, the only sign that is not masked is hypotension. Free hemoglobin can be detected in the plasma or urine is indicative of a transfusion reaction. Substances released by the hemolyzed cells can lead to disseminated intravascular coagulation (DIC) and acute renal failure (ARF). Treatment consists of immediate discontinuation of the transfusion. Hypotension should be treated with hydration, vasopressors, and inotropic agents if needed. Urinary output must be maintained by adequate hydration. Although its value is uncertain, sodium bicarbonate has been used to alkalinize the urine to improve the solubility of the hemoglobin-degradation products.
- Other reactions include posttransfusion purpura, microchimerism, and graft-versus-host disease.

Transmission of Disease

- Human immunodeficiency virus (HIV), hepatitis B virus, hepatitis C virus, and cytomegalovirus can all be transmitted by transfusion of blood products. Because the risk of disease transmission increases with each unit of blood or its components given, they must be carefully scrutinized before being administered. Currently, the incidence of posttransfusion HIV 1 and 2 infection is 1:1,476,000 per transfused unit of blood, almost similar to the risk of hepatitis C transmission, which is 1:1,149,000 per unit transfused. In comparison, the risk of hepatitis B transmission is higher, approximately 1 per 350,000 units. Nevertheless, cytomegalovirus remains the most common viral agent transmitted by transfusion; it produces clinically important infections only in immunosuppressed patients. Laboratory testing done to detect these viruses includes enzyme immunoassays and nucleic acid testing.
- Malaria, syphilis, Lyme disease, Chagas disease, West Nile virus, Creutzfeldt-Jakob disease, and other diseases may also be transmitted through transfusion of blood.
- Bacterial infection occurs in 1:75,000 transfusions. As new nonhemoglobin solutions appear on the market, less blood will be transfused and disease transmission will diminish.

Microembolization

Microembolization can occur from the transfusion of blood or its components. Stored blood forms microaggregates that are too small to be removed by the standard 170-μm blood filters. Smaller filters have been developed to remove these particles. When using blood filters of the 20- to 40-μm range, the rate of transfusion is dramatically decreased because of the increased resistance of the filters. Some early reports suggested that these microaggregates may lead to pulmonary dysfunction, but this

has never been proven.

Chestnut DH, Wong CA, Tsen LC, et al, eds. *Chestnut's Obstetric Anesthesia: Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2020:920–921, 1291.

Greer JP, Arber DA, Glader B, et al, eds. *Wintrobe's Clinical Hematology*. 13th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2014:547–586.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1546–1576.

Murphy MF, Roberts DJ, Yazer MH, eds. *Practical Transfusion Medicine*. 5th ed. Oxford: Wiley-Blackwell; 2017:153–167.

What is considered a massive transfusion (MT)? What is the Assessment of Blood Consumption (ABC) score?

The conventional definition of MT is the replacement of the patient's total blood volume (≥10 units of packed red blood cells) in 24 hours. However, this definition is considered arbitrary and retrospective; it fails to identify those at an increased risk for hemorrhagic death. In contrast, the critical administration threshold (CAT) definition of ≥3 units in 1 hour has a stronger association with mortality compared to MT; it may serve as an activation trigger for initiating an MT protocol.

The ABC score is a validated, nonlaboratory scoring system, designed to identify patients who will require MT. It looks at four parameters: (1) penetrating mechanism, (2) positive FAST, (3) arrival systolic blood pressure ≤90 mmHg, and (4) arrival heart rate ≥120. A score of 2 (positive cutoff) or greater was 75% sensitive and 86% specific for predicting MT.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1546–1576.

Nunez TC, Voskresensky IV, Dossett LA, et al. Early prediction of massive transfusion in trauma: simple as ABC (assessment of blood consumption)? *J Trauma*. 2009;66(2):346–352.

Savage SA, Zarzaur BL, Croce MA, et al. Redefining massive transfusion

when every second counts. *J Trauma Acute Care Surg*. 2013;74:396–402.

C.14. What are the complications associated with an MT?

Complications of an MT include hypothermia, acidosis, coagulopathy, DIC, fibrinolysis, citrate toxicity, hyperkalemia, hypokalemia, acid–base imbalance, and impaired hemoglobin function.

- Hypothermia is a consequence of exposure, impaired thermoregulation, and the transfusion of cold, banked blood. Therefore, it is recommended that the room temperature be increased, and all fluids and blood pass, in order to help prevent hypothermia.
- Acute coagulopathy of trauma is a combination of dilutional coagulopathy and thrombocytopenia. The coagulopathy is preexisting and/or due to the acute production of endogenous substances, for example, activated protein C. It is often exacerbated by acidosis, hypothermia, and dilution of procoagulants with aggressive crystalloid/colloid resuscitation. The optimal ratio of blood components is unknown. In cases requiring MT when there is insufficient time to obtain conventional labs or point-of-care testing to guide transfusion, it may be necessary to take the "damage control" approach of transfusing a set ratio of pRBC:FFP:platelets, such as a 1:1:1 ratio. DIC and fibrinolysis may occur in the setting of trauma. An important triggering event of DIC and fibrinolysis is shock, with its accompanying tissue ischemia, acidosis, and waste product accumulation. Therefore, early and prompt treatment of hypoperfusion is mandatory.
- Hypocalcemia may result from inadequate citrate metabolism. Citrate is present in stored blood to bind calcium and prevent clotting. Consequences of hypocalcemia include prolongation of the QT interval, decreased myocardial contractility, and

depressed procoagulant activity—calcium is clotting factor IV.

- Hyperkalemia can occur in the massively transfused patient. Plasma potassium levels of stored whole blood range between 12 and 32 mEq per L. The potassium level increases approximately 1 mEq/L/day in stored blood. A unit of whole blood would contain between 4 and 8 mEq of potassium, which is hardly enough to cause hyperkalemia. A unit of packed red blood cells contains insignificant amounts of potassium because most of the plasma is removed. However, in the shock state with hypoperfusion and acidemia, hyperkalemia may become evident.
- Hypokalemia is also a possibility after an MT. Citrate is metabolized to bicarbonate, resulting in a metabolic alkalosis that can cause hypokalemia. Furthermore, transfused red blood cells take up potassium, potentially potentiating hypokalemia.
- Acid–base imbalance is a problem after MT. Banked blood with a pH level of 6.8 is acidotic and may worsen the acidosis that accompanies shock. This acidosis is reversible with the restoration of normal perfusion. Supplemental bicarbonate should not be given based on an arbitrary number of units transfused. Nevertheless, if metabolic acidosis persists, sodium bicarbonate may be warranted, especially in the setting of renal failure and severe muscle damage. As previously stated, citrate from stored blood and lactate from Ringer's lactate solution are metabolized to bicarbonate, resulting in a metabolic alkalosis.
- Impaired hemoglobin function is a theoretic possibility after MT. The 2,3-diphosphoglycerate levels are decreased in banked blood, shifting the oxygen–hemoglobin dissociation curve to the left. A leftward shift causes oxygen to be held more tightly by the hemoglobin molecule. No studies have

documented any clinical adverse effects from this.

Drummond JC, Petrovitch CT. The massively bleeding patient. *Anesthesiol Clin North Am*. 2001;19:633–649.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1546–1576.

Shaz BH, Dente CJ, Nicholas J, et al. Increased number of coagulation products in relationship to red blood cell products transfused improves mortality in trauma patients. *Transfusion*. 2010;50(2):493–500.

C.15. Can the shift of the oxygen–hemoglobin dissociation curve be quantified?

Yes, the shift of the oxygen–hemoglobin dissociation curve is quantified by means of the P_{50} value (i.e., oxygen tension at which hemoglobin is 50% saturated). The normal P_{50} value of blood is 27 mmHg. Decreased levels of 2,3-diphosphoglycerate (normal level is 4.8 mmol per mL of erythrocytes) would cause a leftward shift of the curve, lowering the P_{50} value and reducing oxygen unloading at the tissues.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2017:169–202.

C.16. How is hypothermia defined?

Hypothermia is defined as a core body temperature of less than 35°C (95°F). Prolonged exposure to a cold operating room, evaporative heat loss from the respiratory tract, infusions of cold fluids, and loss of heat production secondary to shock, cause decreased core temperatures in trauma most patients.

Hypothermia can be avoided by covering skin surfaces not in the surgical field with warm blankets (reduce convective and radiant heat losses), humidifying inspired gases (reduce evaporative heat loss from the lung), using a warming device for fluids and blood, and increasing the room temperature.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed.

Philadelphia, PA: Elsevier; 2020:2341–2344.

Roberts JR, Hedges JR, Custalow CB, et al, eds. *Roberts and Hedges' Clinical Procedures in Emergency Medicine*. Philadelphia, PA: Elsevier Saunders; 2014:496–517.

C.17. What are the adverse effects of hypothermia?

- Shivering-induced increase in oxygen consumption by as much as 400%
- A leftward shift in the oxygen–hemoglobin dissociation curve
- Decreased blood clotting ability (10% reduction in coagulation factor activity for every 1°C drop in body temperature)
- Increased epinephrine and norepinephrine levels causing vasoconstriction
- As hypothermia becomes severe, possible decreases in both heart rate and blood pressure
- Cardiac arrhythmias that can progress to ventricular fibrillation

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2341–2344.

Sihler KC, Napolitano LM. Complications of massive transfusion. *Chest*. 2010;137:209–220.

Tanaka M, Nagasaki G, Nishikawa T. Moderate hypothermia depresses arterial baroreflex control of heart rate during, and delays its recovery after general anesthesia in humans. *Anesthesiology*. 2001;95:51–55.

C.18. What is the treatment of hypothermia?

The normal response to hypothermia is shivering, which is blocked by general anesthesia. Therefore, it is of utmost importance to prevent and treat hypothermia. Recommendations include the following:

- Increase the temperature of the operating room.
- Use a warming blanket.
- Preheat intravenous fluids.
- Pass all fluids through a warming device.

- Use low-flow anesthesia.
- Use a heat moisture exchanger in the anesthesia circuit.

C.19. What are the effects of blood transfusion on the immune system?

Blood transfusion will result in immunologic changes that can be harmful in some patients. This immunomodulation occurs from immunosuppression or the production of alloantibodies. The blood components crucial to these changes are thought to be leukocytes and plasma. In patients who have cancer, a possible harmful effect of immunosuppression is the increased cancer recurrence rate seen in patients who have had prior transfusions. Finally, clinical studies have demonstrated that perioperative transfusions are associated with an increased incidence of infection and sepsis.

Greer JP, Arber DA, Glader B, et al, eds. *Wintrobe's Clinical Hematology*. 13th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2014:547–586.

Landers DF, Hill GE, Wong KC, et al. Blood transfusion-induced immunomodulation. *Anesth Analg*. 1996;82:187–204.

Youssef LA, Spitalnik SL. Tranfusion-related immunomodulation: a reappraisal. *Curr Opin Hematol*. 2017; 24(6): 551–557.

C.20. What are the guidelines for transfusion of blood products?

The NewYork-Presbyterian Hospital Guidelines for blood product usage are as follows:

Red Blood Cell Transfusion Criteria

- Hgb <7 g/dL
- Hgb <8 g/dL (with history or risk factors for cardiovascular disease)
- Neonates requiring:
  - Mechanical ventilation with Hgb <11.5 g/dL
  - CPAP or O_2 with Hgb <9.5 g/dL

- Exchange transfusion
- Symptomatic anemia
- Greater than 15% blood volume loss

Platelet Transfusion Criteria

- Platelet count <10,000/μL
- Platelet count <50,000/μL with minor bleeding/procedure
- Platelet count <100,000/μL with ECMO/imminent procedure (<4 hours)/neurosurgery intracranial hemorrhage/pulmonary hemorrhage
- Platelet count <25,000/μL in neonates (0–28 days)
- Neonates with plt count <50,000/μL with minor bleeding, ventilatory support, risk of intracranial hemorrhage or minor surgery
- Neonates with plt count <100,000 with major bleeding or major surgery
- Bleeding with loss of one blood volume and no labs available
- Bleeding with qualitative platelet defect

Fresh Frozen Plasma Transfusion Criteria

- INR >1.6 for patients with bleeding and/or surgery
- PTT >55 with factor deficiency and bleeding and/or surgery
- Infants with active bleeding, undergoing surgery and PT or PTT >1.5 × the upper limit of reference range for age
- Bleeding with loss of one blood volume and no labs available
- TTP, HUS
- Patients receiving plasma exchange with coagulopathy or imminent procedure
- Patients treated with L-asparaginase

Cryoprecipitate Transfusion Criteria

- Acquired hypofibrinogenemia <60 mg/dL
- Fibrinogen <150 mg/dL with bleeding/procedure
- DIC

- Abnormal fibrinogen (dysfibrinogenemia)
- Uremic bleeding refractory to DDAVP and dialysis

NewYork-Presbyterian Hospital. *NYP Transfusion Guidelines*. New York: Weill Cornell Medical Center; 2016.

What are the guidelines for the ratio of plasma/platelet transfusion to packed red blood cells in an MT?

Most trauma centers have implemented MT protocols that use the strategy of "hemostatic resuscitation." These protocols are highly variable but largely involve minimizing aggressive crystalloid use, delivering early resuscitation with blood products, and providing early administration of FFP and platelets.

At present, the optimal ratio of blood product transfusion is not known. Although more studies are required, current literature shows an association toward increased survival when a ratio of FFP to packed red blood cells is 1:2 or higher during MT. In 2015, the "Pragmatic, Randomized Optimal Platelets and Plasma Ratios" study was published, which randomized 680 severely injured trauma patients to receive FFP:platelets:RBCs in a 1:1:1 or 1:1:2 fashion. The 1:1:1 cohort was found to be noninferior to 1:1:2, as there was no significant difference in mortality or adverse events between the groups.

Griffee MJ, Deloughery TG, Thorborg PA. Coagulation management in massive bleeding. *Curr Opin Anaesthesiol*. 2010;23:263–268.

Holcomb JB, Tilley BC, Baraniuk S, et al. Transfusion of plasma, platelets, and red blood cells in a 1:1:1 vs a 1:1:2 ratio and mortality in patients with severe trauma: the PROPPR randomized clinical trial. *JAMA*. 2015;313(5):471–482.

Ketchum L, Hess JR, Hiippala S. Indications for early fresh frozen plasma, cryoprecipitate, and platelet transfusion in trauma. *J Trauma*. 2006;60:S51–S58.

Teixeira PG, Inaba K, Shulman I, et al. Impact of plasma transfusion in

massively transfused trauma patients. *J Trauma*. 2009;66:693–697.

C.22. If a patient were a member of the Jehovah's Witness religious sect, would you give a blood transfusion?

Jehovah's Witnesses are best known for refusing the transfusion of blood and blood products. This belief is based on the Bible (Acts 15:28–29). In the awake and otherwise competent adult, courts have ruled that physicians cannot be held liable if they comply with a patient's directive and withhold life-saving blood administration after specific and detailed informed consent of the consequences of such an omission of treatment. The issue becomes clouded when patients are incompetent, unconscious (most Jehovah's Witnesses carry cards informing medical personnel of their religious beliefs), or minors. They believe all hope of eternal life is forfeited if they accept a transfusion. Therefore, a blood transfusion is considered a physical violation. The right of a Jehovah's Witness to refuse a blood transfusion is absolute; the courts have upheld their rights to refuse a blood transfusion. Most Jehova's Witnesses take legal steps to relieve the liability of the medical personnel. Moreover, the vast majority will carry a medical alert card that states their wishes, and they usually have made arrangements for proxy or surrogate decision makers. It is crucial an open and honest avenue of communication exist between the patient, surgeon, and anesthesiologist.

Witnesses will refuse transfusion of whole blood, packed red blood cells, white blood cells, plasma, and platelets; however, they will allow the use of cardiopulmonary bypass, dialysis, or similar equipment, as well as intraoperative blood salvage, in which the extracorporeal circulation is uninterrupted. Their religious understanding does not absolutely prohibit albumin, immune globulins, or hemophiliac preparations; those products must be decided on an individual basis. They accept all

nonblood replacements, including nonblood colloids, crystalloids, dextrans, and oxygen-carrying blood substitutes.

An anesthesiologist may refuse to care for any patient when a procedure is elective. In an emergency situation, legal and ethical requirements apply. Conversely, any competent adult also has the right to refuse any therapy, and to treat such a patient against that person's will is to commit battery.

Dasen KR, Niswander DG, Schlenker RE. Autologous and allogenic blood products for unanticipated massive blood loss in a Jehovah's Witness. *Anesth Analg*. 2000;90:553–555.

Roberts JR, Hedges JR, Custalow CB, et al, eds. *Roberts and Hedges' Clinical Procedures in Emergency Medicine*. Philadelphia, PA: Elsevier Saunders; 2014:496–512.

Waters JH, Potter PS. Cell salvage in the Jehovah's Witness patient. *Anesth Analg*. 2000;90:229–230.

C.23. If a child is a Jehovah's Witness and suffered from hemorrhagic shock, what would you do?

Care of minors presents the greatest concern and often leads to legal action against the parents under child-neglect status. Such actions are questioned by Jehovah's Witnesses who do seek good medical care for their children while claiming that consideration be given to their families' religious beliefs. Doctors can appeal to the court for permission to transfuse blood to children of this sect who are underage. In an unforeseeable emergency, blood may be given without consulting a court.

C.24. What are the concentrated factors and hemostatic agents available for bleeding patients?

Recombinant Activated Factor VII (rFVIIa, NovoSeven)

NovoSeven is approved in the United States for prophylaxis and treatment of hemorrhage in hemophiliacs with inhibitors to factor VIII or IX or congenital factor VII deficiency. Despite its

limited approval, it has been used off-label in patients with refractory traumatic hemorrhage. Although NovoSeven is extremely effective at stopping uncontrolled bleeding, it may not provide a survival benefit versus placebo, as suggested by the CONTROL study. Moreover, there have reports linking it to thromboembolic adverse events, such as an increased risk of stroke. A meta-analysis by Zangrillo et al. showed that recombinant NovoSeven was associated with a decreased need for surgical revision after cardiac surgery; however, it was also associated with an increase in perioperative stroke.

Four-Factor Prothrombin Complex Concentrate

Four-factor prothrombin complex concentrate (PCC) contains II, VII, IX, and X as well as low doses of anticoagulants protein C, protein S, and heparin. It has the advantages of requiring significantly less volume for infusion versus plasma, achieving a more rapid reversal of international normalized ratio (INR), and almost eliminating the risk of TRALI. PCC has U.S. Food and Drug Administration (FDA) approval for the reversal of vitamin K antagonists (VKA), for example, warfarin, in patients with acute major bleeding but has shown promise in treating acute coagulopathy in trauma. In fact, its administration is recommended by the European trauma guidelines in managing patients with evidence of delayed thrombin generation.

Fibrinogen Concentrates

Fibrinogen concentrate is a pasteurized collection from human plasma that is approved for the use in patients with congenital fibrinogen deficiency to treat acute bleeding episodes. It acts to replenish fibrinogen levels in the blood in place of FFP or cryoprecipitate. A Cochrane Review by Wikkelsø et al. showed no difference between fibrinogen concentrate versus blood products in regard to adverse events, bleeding, or recovery.

Tranexamic Acid

Tranexamic acid (TXA) is an antifibrinolytic that blocks the interaction of plasminogen with fibrin, effectively preventing clot breakdown and lysis. It may be used to treat hyperfibrinolysis in trauma, which in an independent predictor of mortality in trauma patients. The CRASH-2 trial, an international clinically randomized study of over 20,000 trauma patients, found TXA was associated with a significant reduction in all-cause mortality versus placebo (14.5% vs. 16%, p = 0.035). Subsequent analyses revealed the greatest benefit of TXA was only seen when given <3 hours from injury, supporting its early administration in trauma.

Hauser CJ, Boffard K, Dutton R, et al. Results of the CONTROL trial: efficacy and safety of recombinant activated factor VII in the management of refractory traumatic hemorrhage. *J Trauma*. 2010;69(3):489–500.

Napolitano LM, Cohen MJ, Cotton BA, et al. Tranexamic acid in trauma: how should we use it? *J Trauma Acute Care Surg*. 2013;74(6):1575–1586.

Rossaint R, Bouillon B, Cerny V, et al. The European guideline on management of major bleeding and coagulopathy following trauma: fourth edition. *Crit Care*. 2016;20(1):100.

Shakur H, Roberts I, Bautista R, et al. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2); a randomized, placebo-controlled trial. *Lancet*. 2010;376(9734):23–32.

Wikkelsø A, Lunde J, Johansen M, et al. Fibrinogen concentrate in bleeding patients. *Cochrane Database Syst Rev*. 2013;(8):CD008864.

Zangrillo A, Mizzi A, Biondi-Zoccai G, et al. Recombinant activated factor VII in cardiac surgery: a meta-analysis. *J Cardiothorac Vasc Anesth*. 2009;23(1):34–40.

What is thromboelastography (TEG) and thromboelastometry? How can they guide transfusion?

Rotation thromboelastometry (ROTEM®) and TEG are two different viscoelastic hemostatic assays used to assess clot

kinetics. Both assays employ a suspended pin that sits in a metal cup containing whole blood. As the blood clots, they detect the change in tensile force and use this change to assess the strength of the clot formed.

Rotation Thromboelastometry

The ROTEM® uses a rotating pin in a stationary cup to detect increases in tensile force as a clot forms or decreases as a clot lysis. It is a point-of-care test, which looks at several different parts of the coagulation cascade:

- INTEM—intrinsic pathway of the coagulation cascade
- HEPTEM—intrinsic pathway of the coagulation cascade with the addition of heparinase, which removes the effects of heparin from the results
- EXTEM—extrinsic pathway of coagulation cascade
- FIBTEM—extrinsic pathway of the coagulation cascade after the addition of cytochalasin D, which inhibits the effects of platelets on the formation of the clot
- APTEM—extrinsic pathway with the addition of aprotinin to block fibrinolysis

These tests will generate images based on a patient's coagulation status, which can be used to guide transfusion therapy (**Figs. 57.1** to **57.6**). Bolliger et al. developed a chart to guide therapy based on ROTEM® results (**Fig. 57.7**).

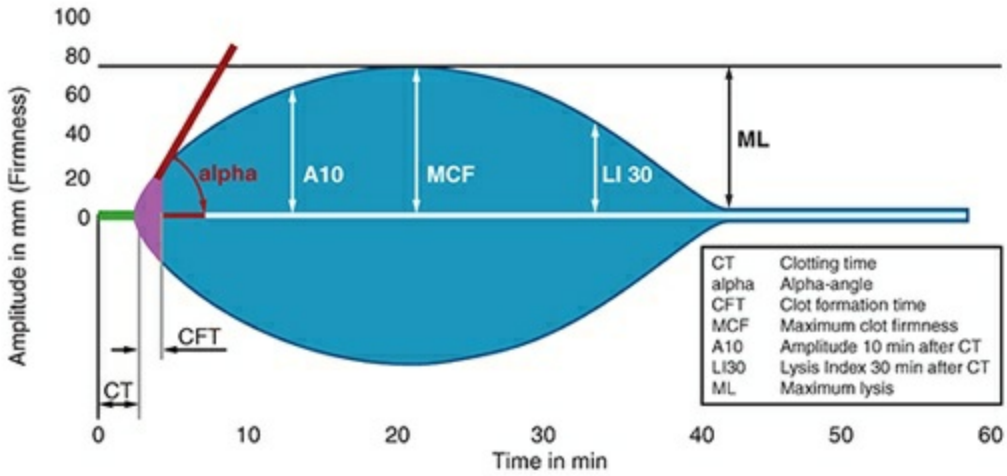

FIGURE 57.1. Basic ROTEM® image. Clot time: the measured time until clot formation starts; affected by clotting factors and anticoagulants. Clot formation time: a measure of initial rate of clot formation, the time from clot formation until the clot forms to an amplitude of 20 mm; depends on platelets and fibrinogen. *α* Angle: a measure of the initial rate of clot formation. Maximum clot firmness: the maximum tensile strength of the clot; describes quality of clot and is dependent on platelets, fibrinogen, factor XIII, and fibrinolysis. Maximum lysis: reduction of clot firmness during measurement; abnormality in the ML at 30 minutes indicated fibrinolysis. Amplitude: A5/10/15 is the amplitude of the clot at 5, 10, and 15 minutes.

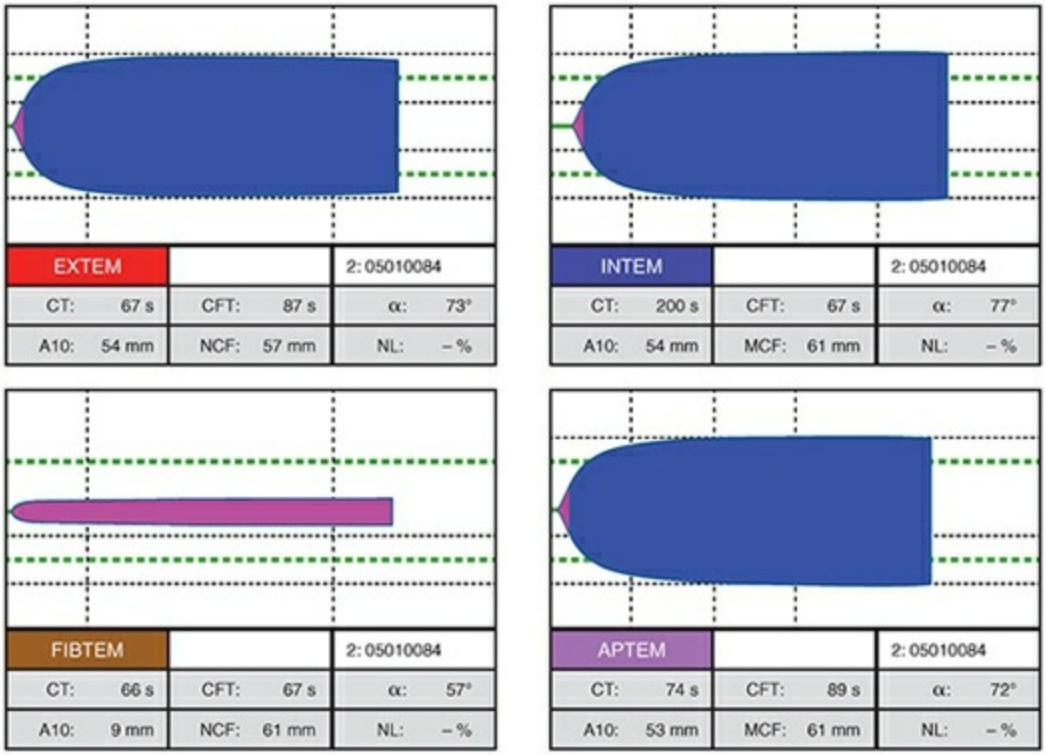

FIGURE 57.2. ROTEM® in a patient with normal coagulation parameters.

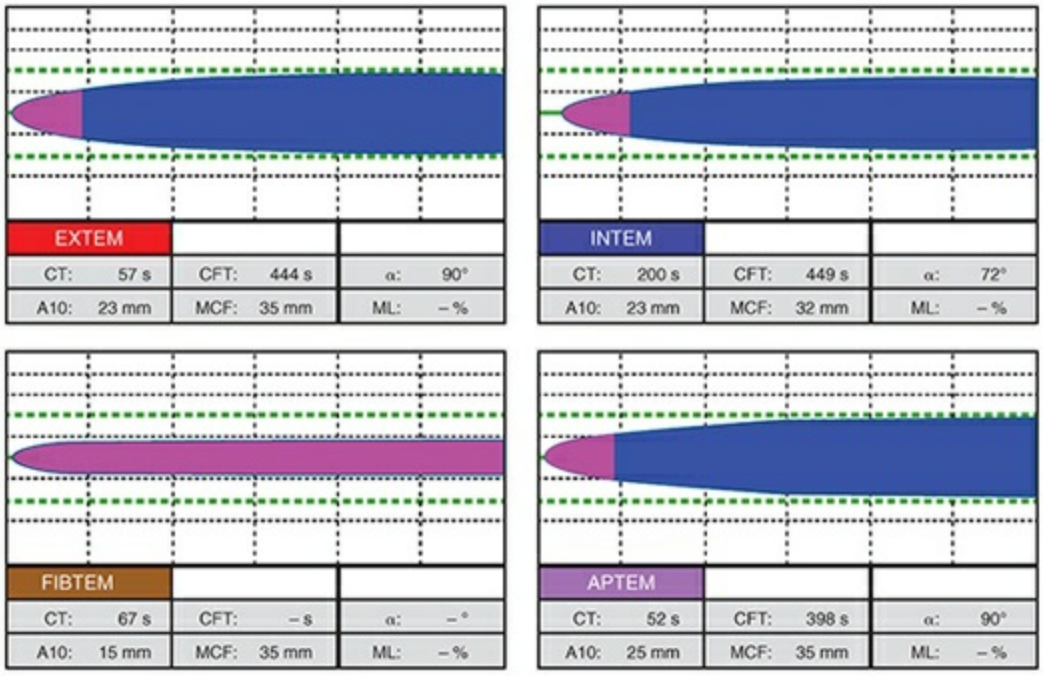

FIGURE 57.3. ROTEM® in a patient with a platelet deficiency.

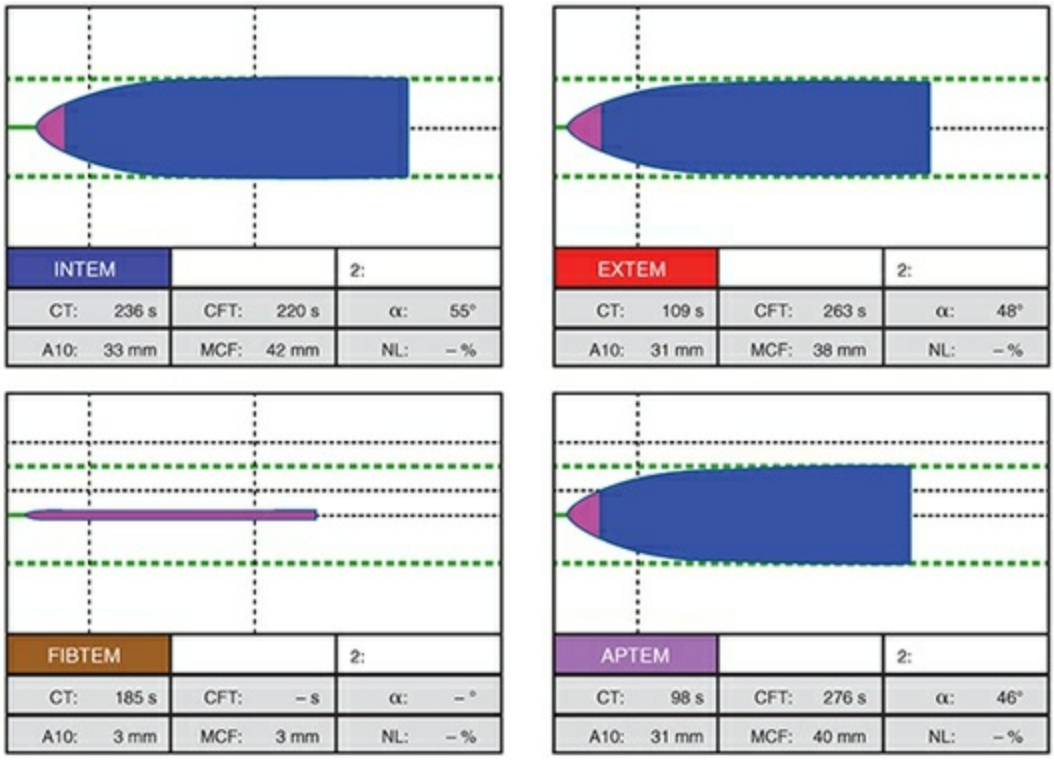

FIGURE 57.4. ROTEM® in a patient with a fibrinogen deficiency.

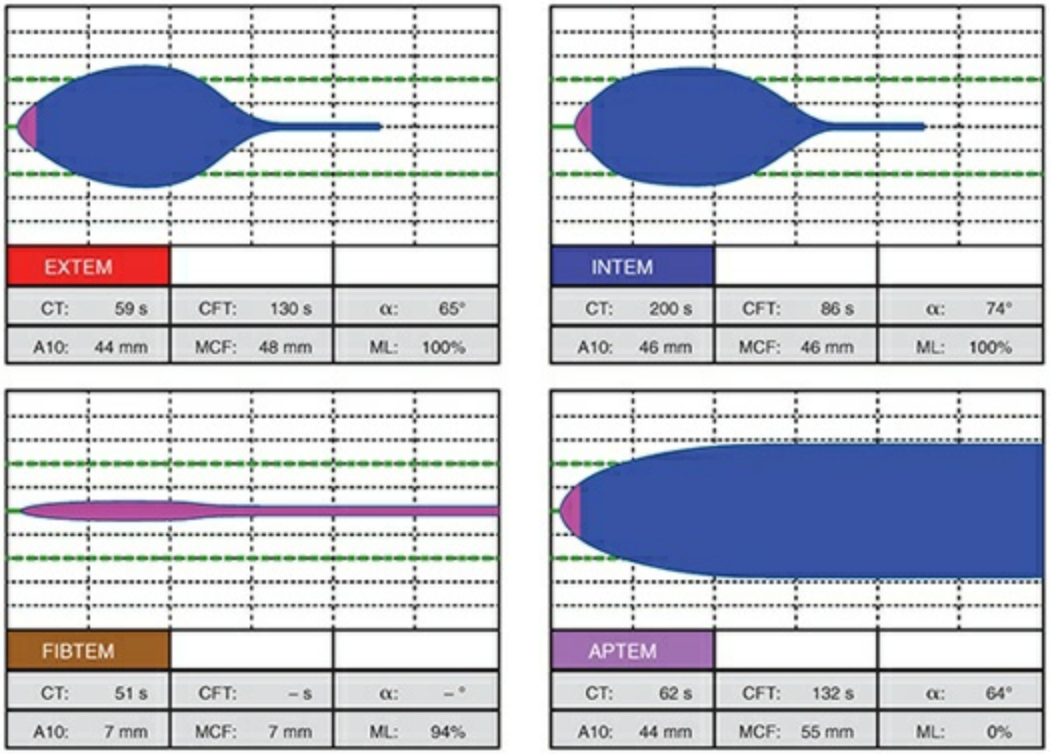

FIGURE 57.5. **ROTEM® in a patient with hyperfibrinolysis.**

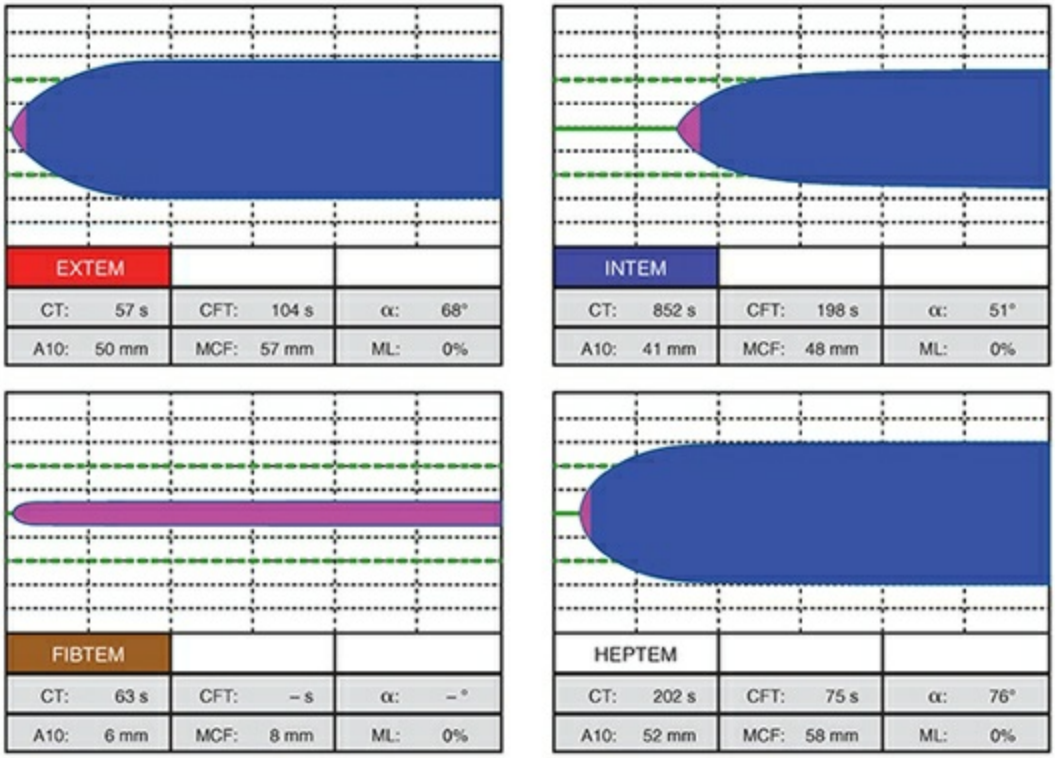

FIGURE 57.6. **ROTEM® in a patient with heparin influence.**

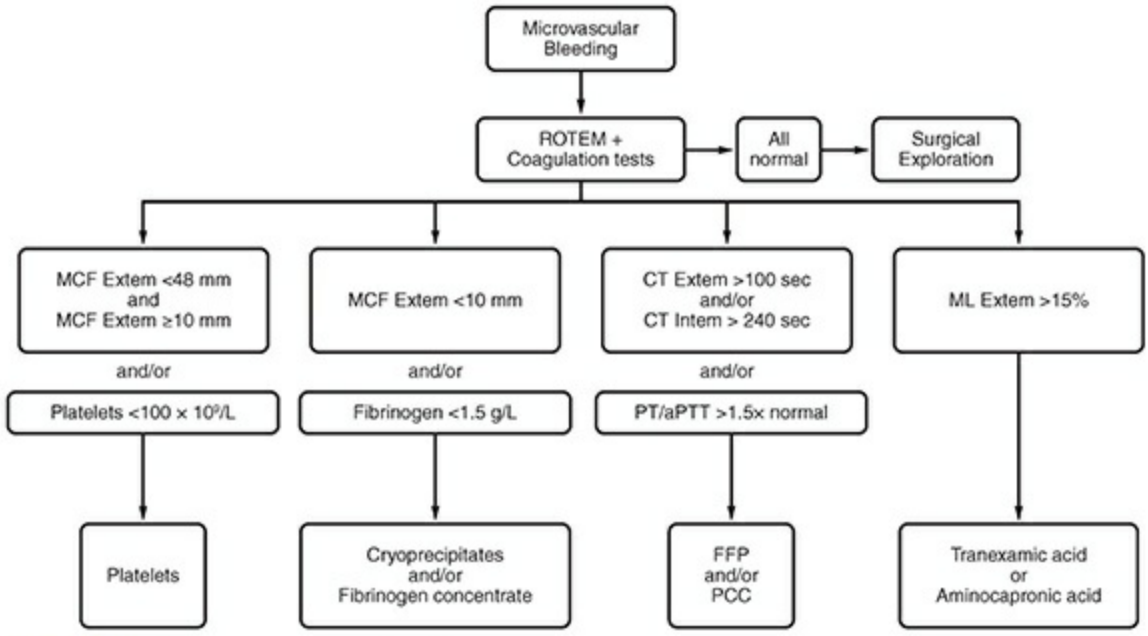

FIGURE 57.7. Guide to therapy based on ROTEM® results. aPTT, activated partial thromboplastin time; CT, computed tomography; FFP, fresh frozen plasma; MCF, maximum clot firmness; ML, maximum lysis; PCC, prothrombin complex concentrate; PT, prothrombin time. (*Reprinted from Bolliger D, Seeberger MD, Tanaka KA. Principles and practice of thromboelastography in clinical coagulation management and transfusion practice.* Transfus Med Rev. *2012;26[1]:1–13. Copyright © 2012 Elsevier. With permission.*)

FIGURE 57.7. Guide to therapy based on ROTEM® results. aPTT, activated partial thromboplastin time; CT, computed tomography; FFP, fresh frozen plasma; MCF, maximum clot firmness; ML, maximum lysis; PCC, prothrombin complex concentrate; PT, prothrombin time. (*Reprinted from Bolliger D, Seeberger MD, Tanaka KA. Principles and practice of thromboelastography in clinical coagulation management and transfusion practice.* Transfus Med Rev. *2012;26[1]:1–13. Copyright © 2012 Elsevier. With permission.*)

Thromboelastography

The TEG is based on the same principles as the ROTEM®. The difference is that instead of having a mobile pin in a stationary cup, TEG has a stationary pin in a mobile cup. A sample will generate an image (**Fig. 57.8**). The TEG values can be compared to ROTEM® values (**Table 57.1**). Some examples of the effect of different coagulation states on TEG (**Fig. 57.9**) and a guideline for transfusion therapy (**Fig. 57.10**) are shown.

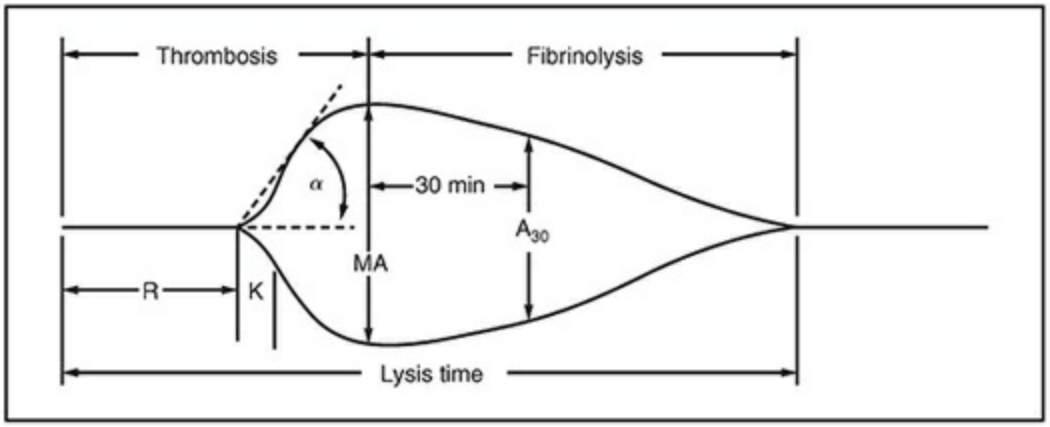

FIGURE 57.8. **Basic TEG image.**

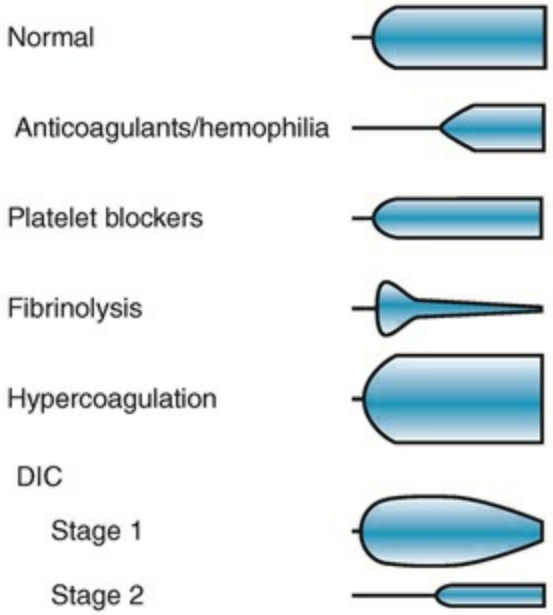

FIGURE 57.9. **Effects of different coagulation states on TEG results.**

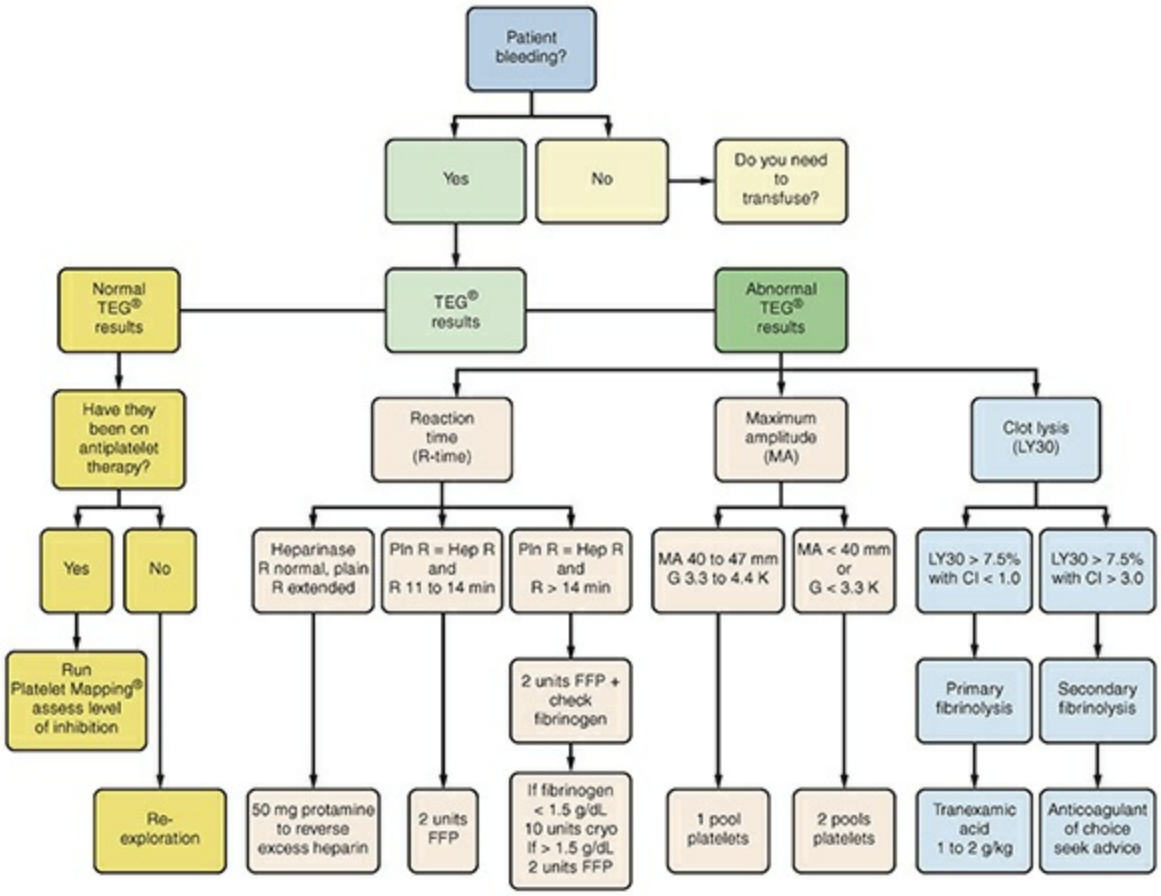

FIGURE 57.10. A guideline for transfusion based on TEG results. CI, coagulation index; FFP, fresh frozen plasma; G, clot elasticity; K, kinetics; Pln, plain.

TABLE 57.1 Thromboelastography (TEG) Values Compared to Their Rotation Thromboelastometry (ROTEM®) Equivalents

TEG	Measures	ROTEM® Equivalent
R time	Time to 2 mm amplitude	CT
K time	Time from 2 to 20 mm	CFT
α Angle	Slope between R and K	α Angle
MA	Maximum amplitude of clot	MCF
LY30	Percentage of clot lysis at 30 min after MA	ML
A30	Size of clot at 30 min after MA	A10
G	Clot elasticity	MCE
CI	Coagulation index is value determined by a manufacturer created mathematical formula which takes into account R, K, α angle, and MA to give an overall assessment of the state of coagulation.	

CFT, clot formation time; CI, coagulation index; CT, clotting time; K, kinetics; MA, maximum

amplitude; MCE, maximum clot elasticity; MCF, maximum clot firmness; ML, maximum lysis.

Bolliger D, Seeberger MD, Tanaka KA. Principles and practice of thromboelastography in clinical coagulation management and transfusion practice. *Transfus Med Rev*. 2012;26(1):1–13.

Jackson GN, Ashpole KJ, Yentis SM. The TEG vs the ROTEM thromboelastography/thromboelastometry systems. *Anaesthesia*. 2009;64(2):212–215.

Johansson PI, Stissing T, Bochsen L, et al. Thrombelastography and tromboelastometry in assessing coagulation in trauma. *Scand J Trauma Resusc Emerg Med*. 2009;17:45.

Ogawa S, Szlam F, Chen EP, et al. A comparative evaluation of rotation thromboelastometry and standard coagulation tests in hemodilution-induced coagulation changes after cardiac surgery. *Transfusion*. 2012;52(1):14–22.

TEM Systems. Result interpretation. http://www.rotem-usa.com/methodology/result-interpretation/. Accessed October 20, 2015.

D. Postoperative Management

D.1. What is acute respiratory distress syndrome (ARDS)? What is acute lung injury?

ARDS is a type of acute respiratory failure seen in patient after being exposed to direct (e.g., aspiration) or indirect (e.g., severe trauma) lung injury. Initially, when this clinical syndrome was thought to be related to the underlying shock state and its resuscitation, names such as “shock lung” and “traumatic wet lung” were applied to the subsequent acute respiratory insufficiency. It is now recognized that many types of insults will result in damage to the alveolar capillary membrane, resulting in leakage of proteinaceous fluid into the alveolar space. This injury with its resulting interstitial and alveolar edema, produces a clinical picture ranging from mild to severe pulmonary dysfunction that can be fatal.

ARDS was formerly defined as:

- The acute onset of respiratory failure
- Bilateral infiltrates on chest x-ray

- Pa_{O_2}/fraction of inspired oxygen (F_{IO_2}) ratio of 200 or less
- A pulmonary capillary wedge pressure <18 mmHg

However, this definition was reevaluated in 2012 secondary to concerns regarding its accuracy. First, the diagnosis of bilateral infiltrates on chest x-ray was found to have wide interobserver variability and thus was inconsistent. Next, the Pa_{O_2}/F_{IO_2} ratio varied greatly based on the patient's ventilator status and needed to be refined. Third, heart failure patients with elevated left atrial pressures can have ARDS, so high pulmonary capillary wedge pressures are not enough to rule out the diagnosis of ARDS. Finally, the definition was found to have low specificity when compared to autopsy results of patients with diffuse alveolar damage.

For these reasons, the Berlin definition was established, which characterizes ARDS by the following:

Oxygenation

- Mild—Pa_{O_2}/F_{IO_2} <200 mmHg or ≤300 mmHg with positive end-expiratory pressure (PEEP) or continuous positive airway pressure (CPAP) ≥5 cm H_2O
- Moderate—Pa_{O_2}/F_{IO_2} ≤100 mmHg or ≤200 mmHg with PEEP ≥5 cm H_2O
- Severe—Pa_{O_2}/F_{IO_2} ≤100 mmHg with PEEP ≥5 cm H2O

Timing—onset within 1 week of a known clinical insult, or the patient has worsening respiratory symptoms

Chest radiograph—demonstrates opacities bilaterally that are not due to pleural effusions, atelectasis, or nodules

Origin of edema—respiratory insufficiency that is not solely caused by cardiogenic causes, that is, left heart failure or volume overload

Acute lung injury—a term for a less severe form of ARDS was removed from the definition and is no longer used

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2017:1644–1645.

Bope ET, Kellerman R, eds. *Conn's Current Therapy*. Philadelphia, PA: Saunders Elsevier; 2015:333–406.

Fanelli V, Vlachou A, Ghannadian S, et al. Acute respiratory distress syndrome: new definition, current and future therapeutic options. *J Thorac Dis*. 2013;5(3):326–334.

D.2. How is ARDS treated?

The treatment of ARDS is primarily supportive. Currently, mechanical ventilation is the mainstay of supportive therapy for ARDS. The principal goal of mechanical ventilation is to allow times for the lungs to heal. Unfortunately, mechanical ventilation can cause further lung injury, known as ventilator-induced lung injury (VILI). Excessive alveolar volumes (volutrauma), high mean and peak airway pressures (barotrauma), and shearing forces caused by frequent collapse and opening of alveolar units, contribute to VILI.

Investigators have looked at protective ventilator strategies in patients with ARDS. Amato et al. used a strategy to limit peak inspiratory pressures by using low tidal volumes (<6 mL per kg) and the institution of PEEP. Their approach was associated with a lower 28-day mortality (38% vs. 71%), higher weaning rate (66% vs. 29%), and lower barotrauma rate (7% vs. 42%).

The National Heart, Lung, and Blood Institute ARDS Network reported improved survival with a low tidal volume strategy (6 mL per kg vs. 12 mL per kg). Moreover, there was a decrease in mortality of approximately 25% in the intervention group compared with the control group.

Amato MB, Barbas CS, Medeiros DM, et al. Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. *N Engl J Med*. 1998;338:347–354.

Bope ET, Kellerman R, eds. *Conn's Current Therapy*. Philadelphia, PA: Saunders Elsevier; 2015:333–406.

Brower RG, Ware LB, Berthiaume Y, et al. Treatment of ARDS. *Chest*.

2001;120(4):1347–1367.

Thomson BT, Bernard GR. ARDS Network (NHLBI) studies: successes and challenges in ARDS clinical research. *Crit Care Clin*. 2011;27(3):459–468.

D.3. In the recovery room, you are called to see this patient because of oliguria. How would you evaluate and treat this patient?

Oliguria is a decrease in urinary output to less than 0.3 to 0.5 mL/kg/hr.

ARF is a syndrome characterized by a rapid (hours to weeks) decline in glomerular filtration rate (GFR) and retention of waste products such as urea. Most cases of ARF are reversible, as the kidney is remarkable in its ability to recover from almost complete loss of function. ARF is associated with major in-hospital morbidity and mortality. The diagnosis of ARF usually hinges on changes in serum creatinine, GFR, and urine output.

Causes of renal failure can be grouped into one of three categories:

Prerenal

Prerenal failure is the most common cause of ARF. It is usually caused by a low flow state, such as hypovolemia or cardiac failure. Evaluation begins with reviewing hemodynamic trends, fluid balance, and relevant studies (e.g., echocardiogram). If hypovolemia is suspected, then treatment would consist of a fluid bolus. If the patient's cardiac output is inadequate, then inotropic support and/or diuretics could be administered. Severe renal hypoperfusion may cause ischemic acute tubular necrosis (ATN); therefore, prerenal azotemia and ischemic ATN are part of a spectrum of manifestations of renal hypoperfusion.

Renal

Intrinsic renal failure is generally due to toxic injury or ischemia resulting in glomerular and tubular damage. Ischemic ATN,

unlike prerenal azotemia, is associated with injury to renal parenchyma and does not typically resolve immediately on restoration of renal perfusion. In its more extreme form, renal hypoperfusion may result in bilateral renal cortical necrosis and irreversible renal failure. Urinalysis may show cells or casts that are indicative of ARF. Intrinsic renal failure can be minor and short-lived, or it can progress to chronic renal failure, depending on the severity of the insult.

Postrenal

Urinary tract obstruction accounts for less than 5% of cases of ARF. Urinary tract obstruction must be sought and corrected to treat possible causes of postrenal oliguria. This usually requires irrigation or changing of the Foley catheter. Consider the possibility of an intraoperative mishap causing postrenal obstruction.

Taal MW, Chertow GM, Marsden PA, et al, eds. *Brenner and Rector's The Kidney*. 9th ed. Philadelphia, PA: Saunders Elsevier; 2012:844–867.

D.4. If this patient had a crush injury and low urine output, what other concerns might you have? What if the patient has dark or "tea-colored" urine?

Leakage of myoglobin from muscles and damaged tissue secondary to a crush injury can result in rhabdomyolysis. Myoglobin at high concentrations precipitates in the nephron, appearing pigmented and causing acute renal injury. The urine may look suspicious for hematuria or have a "tea-colored" appearance. Rhabdomyolysis can be diagnosed by the presence of myoglobinuria or elevated serum creatine kinase levels. Preventing ARF in these patients is essential because the development of ARF is associated with increased mortality. The treatment is hydration with large volumes of crystalloid, resulting in goal urine outputs as high as 100 to 300 mL per

hour. In addition, alkalization of the urine, with agents such as bicarbonate, may help by decreasing the rate of precipitation. Mannitol has also been used to induce an osmotic diuresis and flush the myoglobin through the kidney. Other electrolyte abnormalities, including hyperkalemia, hyperphosphatemia, hypocalcemia, and metabolic acidosis, can develop with crush injury and the patient should be monitored.

Bosch X, Poch E, Grau JM. Rhabdomyolysis and acute kidney injury. *N Engl J Med*. 2009;361:62–72.

Gonzalez D. Crush syndrome. *Crit Care Med*. 2005;33:S34–S41.

Taal MW, Chertow GM, Marsden PA, et al, eds. *Brenner and Rector's The Kidney*. 9th ed. Philadelphia, PA: Saunders Elsevier; 2012:844–867.

58 Scoliosis

Jordan M. Ruby, Victor M. Zayas

A 14-year-old girl with scoliosis is scheduled for posterior spine fusion with segmental instrumentation. She has been told that her scoliosis is idiopathic. Her past medical history is unremarkable, but her mother states that she appears to get short of breath more easily than her friends when she plays basketball.

A. Medical Disease and Differential Diagnosis

1. What is scoliosis?
2. What is the most common type of scoliosis?
3. What are the other types of scoliosis?
4. How is the severity of scoliosis assessed, and why is the severity important?
5. What are the nonoperative treatment options of scoliosis?
6. What abnormalities in pulmonary function tests (PFTs) are most commonly seen in scoliosis? What is the cause of these abnormalities?
7. What is the most common arterial blood gas abnormality seen in scoliosis? What are possible causes for this abnormality?
8. What abnormalities of ventilatory drive may be associated with scoliosis?
9. How may the cardiovascular system be affected in patients

with scoliosis?

10. What is the relationship between scoliosis and malignant hyperthermia?

B. Preoperative Evaluation and Preparation

1. What should the anesthesiologist know about the nature of the spinal curve?
2. What aspects of the history are most important?
3. What aspects of the physical examination are most important?
4. Why is a preoperative neurologic assessment important?
5. What tests would you order preoperatively?
6. What is an enhanced recovery after surgery (ERAS) pathway? How has it been applied to the recovery for pediatric patients undergoing posterior spinal instrumentation and fusion?
7. How will the surgical procedure influence the anesthetic management?

C. Intraoperative Management

1. What monitoring would you use?
2. What is the incidence of neurologic complications in scoliosis surgery, and which patients are at highest risk?
3. What monitoring techniques are used to minimize neurologic complication?
4. What are somatosensory evoked potentials (SSEPs), and how are they used?
5. How reliable are SSEPs for predicting spinal injury?
6. What are motor evoked potentials (MEPs), and how are they used?
7. How is spinal cord monitoring affected by anesthetic agents? What other factors affect spinal cord monitoring?
8. What is the optimal anesthetic technique for scoliosis surgery?
9. What should be done if the SSEPs or MEPs become abnormal during surgery?
10. How is the “wake-up” test performed? What complications can

occur during this test?

11. Four hours into the surgical procedure, the surgeon reports some bubbling in the thoracic portion of the wound. Shortly thereafter, end-tidal carbon dioxide decreases abruptly from 35 to 18 mmHg, heart rate increases from 80 to 120 beats per minute, blood pressure begins to fall, and arterial saturation decreases to 90%. On auscultation through esophageal stethoscope, you hear a loud gurgling murmur. What is your diagnosis?
12. How common is significant air embolism during scoliosis surgery?
13. What should be done if an air embolus is suspected?
14. What complications occur related to positioning the patient?
15. What is transfusion-related acute lung injury (TRALI)? How do you distinguish it from transfusion-associated circulatory overload (TACO)?
16. What techniques can be used to minimize transfusion requirements?

D. Postoperative Management

1. When would you extubate the patient?
2. What should be done to optimize pulmonary status?
3. What laboratory tests should be ordered postoperatively?
4. What fluid therapy would you use postoperatively?
5. What complications may occur following scoliosis surgery?
6. Upon arrival to the recovery room, you notice that the urine appears to be tea colored. What is your diagnosis, and how should this be managed?
7. How would you manage this patient's pain, nausea, and vomiting postoperatively?

A. Medical Disease and Differential Diagnosis

A.1. What is scoliosis?

The spine normally curves posteriorly in the thoracic region and anteriorly in the lumbar region. These physiologic curves are the thoracic kyphosis and the lumbar lordosis, respectively. The spine is not normally curved when viewed from the front or back. Scoliosis refers to a lateral curvature of the spine. Curves are classified as structural or nonstructural. A nonstructural curve, such as lumbar scoliosis from a leg length discrepancy, will resolve when the patient is supine or uses a shoe lift and does not require surgical correction. In contrast, structural scoliosis lacks normal flexibility and does not correct with bending or lying supine. In addition to the lateral curvature of the spine, the vertebrae are rotated and the rib cage may be markedly deformed (**Fig. 58.1**). As demonstrated in the computed tomography scan image in **Figure 58.2**, this thoracic deformity may lead to a significant decrease in total lung volume. Particularly, note the decrease in left lung volume relative to the right.

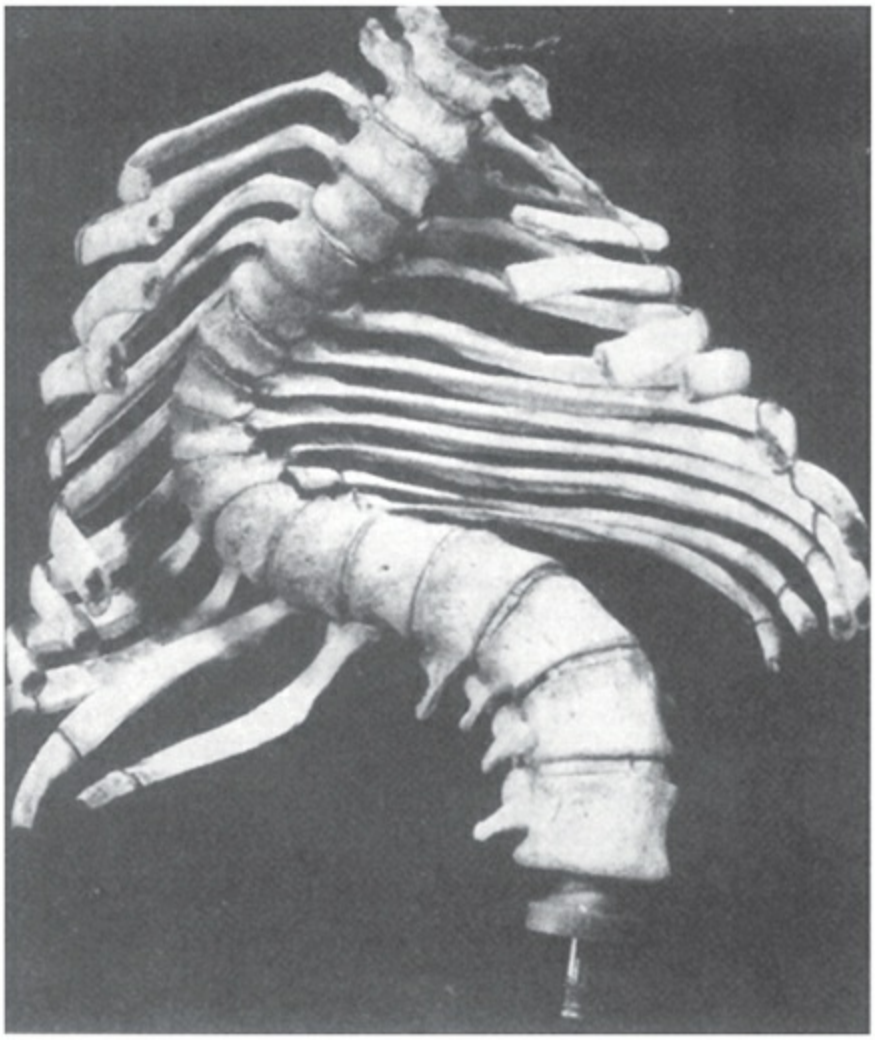

FIGURE 58.1. In addition to producing a lateral deformity of the spine, scoliosis also results in rotation of the vertebral bodies and significant rib cage deformity.

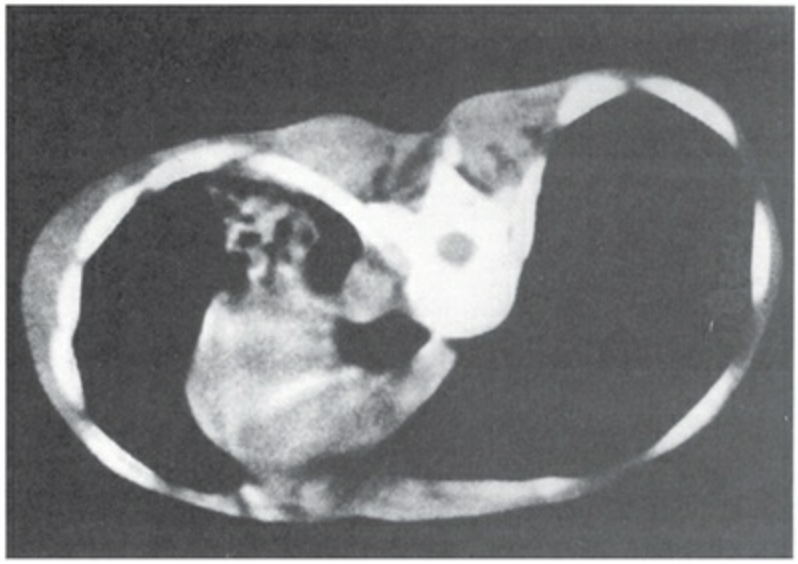

FIGURE 58.2. A computed tomography scan of the thorax demonstrating significant loss of lung volume resulting from the rib cage deformity.

Azar FM, Canale ST, Beaty JH, eds. *Campbell's Operative Orthopaedics*. 13th ed. Philadelphia, PA: Elsevier Mosby; 2017:1897–2120.

Nnadi C, ed. *Early Onset Scoliosis: A Comprehensive Guide from the Oxford Meetings*. Stuttgart, Germany: Thieme; 2015:23–25.

A.2. What is the most common type of scoliosis?

Idiopathic scoliosis is the most common type of scoliosis (70% of all cases) and occurs in infantile, juvenile, and adolescent forms. As the name implies, the cause is unknown but appears to be multifactorial, including abnormalities of collagen, brainstem function, equilibrium, hormones, and growth. Genetic factors are important in its development as evidenced by an 11% incidence of idiopathic scoliosis in first-degree relatives of affected patients. Furthermore, there is a 73% concordance of idiopathic scoliosis among monozygotic twins. Understanding the genetic basis of idiopathic scoliosis is becoming increasingly complex based on the number of associated genes identified by genome-wide association studies. However, the significance of many other genes remains indeterminate. Research is ongoing to further understand the genetic basis of idiopathic scoliosis.

The prevalence of idiopathic scoliosis in large screening

studies depends on the definition of scoliosis and the population screened. The prevalence of spinal curves greater than 10 degrees is 1.5% to 3%; greater than 20 degrees, it is 0.3% to 0.5%; and greater than 30 degrees, it is 0.2% to 0.3%. The adolescent form of idiopathic scoliosis is by far the most common in the United States. The male-to-female prevalence ratio depends in part on the age of the patient, but scoliosis requiring surgical correction is more common in women. The ratio increases with the severity of the curve, with a ratio of girls to boys at 2:1 for curves of 10 degrees, and increasing to 10:1 for curves over 30 degrees.

Azar FM, Canale ST, Beaty JH, eds. *Campbell's Operative Orthopaedics*. 13th ed. Philadelphia, PA: Elsevier Mosby; 2017:1897–2120.

Giampietro PF, Pourquie O, Raggio C, et al. Summary of the first inaugural joint meeting of the International Consortium for Scoliosis Genetics and the International Consortium for Vertebral Anomalies and Scoliosis, March 16-18, 2017, Dallas, Texas. *Am J Med Genet A*. 2018;176(1):253–256.

Kusumi K, Dunwoodie SL. *The Genetics and Development of Scoliosis*. 2nd ed. New York: Springer; 2018:139–178.

Newton PO, O'Brien MF, Shufflebarger HL, et al, eds. *Idiopathic Scoliosis: The Harms Study Group Treatment Guide*. New York: Thieme; 2011:30, 51–53.

Nnadi C, ed. *Early Onset Scoliosis: A Comprehensive Guide from the Oxford Meetings*. Stuttgart, Germany: Thieme; 2015:23–25.

A.3. What are the other types of scoliosis?

Many etiologic classifications exist for structural scoliosis. Neuromuscular scoliosis may occur as a result of diseases such as cerebral palsy, muscular dystrophy, poliomyelitis, and familial dysautonomia. This type of scoliosis is associated with significantly increased intraoperative blood loss compared with idiopathic scoliosis. Congenital scoliosis is the result of congenital anomalies such as hemivertebrae and fused vertebrae or ribs. Neurofibromatosis and Marfan syndrome are also associated with scoliosis. These underlying conditions may have

a major impact on the anesthetic plan. The classification of scoliosis is as follows:

Idiopathic

- Infantile (birth to 3 years of age)
- Juvenile (4 years of age to 10 years of age)
- Adolescent (10 years of age to skeletal maturity)

Neuromuscular

- Neuropathic
  - Upper motor neuron (e.g., cerebral palsy, spinal cord injury)
  - Lower motor neuron (e.g., poliomyelitis, myelomeningocele, spinal muscular atrophy)
  - Familial dysautonomia

Myopathic

- Muscular dystrophy
- Myotonic dystrophy

Congenital

- Hemivertebrae
- Congenitally fused ribs

Neurofibromatosis

Mesenchymal Disorders

- Marfan syndrome
- Osteogenesis imperfecta
- Arthrogryposis

Trauma

- Vertebral fracture or surgery
- Postthoracoplasty
- Postradiation

Azar FM, Canale ST, Beaty JH, eds. *Campbell's Operative Orthopaedics*. 13th ed. Philadelphia, PA: Elsevier Mosby; 2017:1897–2120.

Nnadi C, ed. *Early Onset Scoliosis: A Comprehensive Guide from the Oxford Meetings*. Stuttgart, Germany: Thieme; 2015:23–25.

A.4. How is the severity of scoliosis assessed, and why is the severity important?

In 1966, the Scoliosis Research Society standardized the method for assessing the severity of scoliosis. The most common measure of severity is Cobb angle. **Figure 58.3** illustrates how Cobb angle is measured on a spine radiograph. A perpendicular (*2*) is constructed from the bottom of the lowest vertebrae (*1*) whose bottom tilts toward the concavity of the curve, and another perpendicular (*4*) from the top of the highest vertebrae (*3*) whose top tilts toward the concavity. The angle (*5*) at which these perpendiculars intersect is Cobb angle. Numerous studies have documented that the more severe the thoracic curve (greater Cobb angle), the more profound the disturbance in pulmonary function. Surgical treatment is usually recommended for curves greater than 45 to 50 degrees. Curves greater than 60 degrees are usually associated with decreases in pulmonary function.

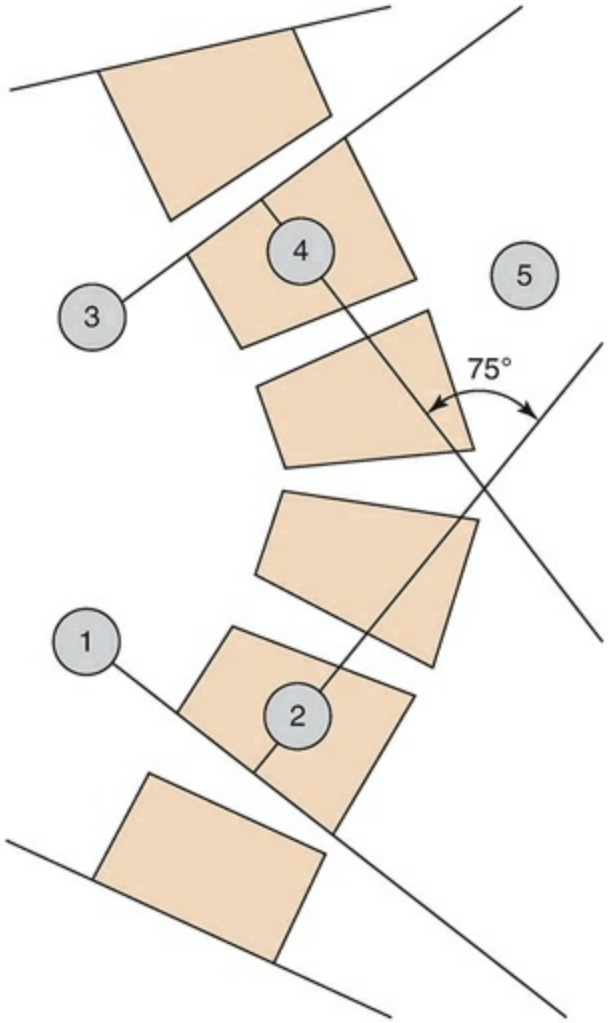

FIGURE 58.3. Measurement of the curve in scoliosis using Cobb angle. (*Reprinted with permission from Levine DB. Scoliosis*. Curr Opin Rheumatol. *1990;2[1]:190-196*.)

In a series of 79 patients with thoracic scoliosis, the mean Cobb angle was 45 degrees and vital capacity was decreased by an average of 22%. **Figure 58.4** demonstrates that forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1) decrease with increasing thoracic curve severity.

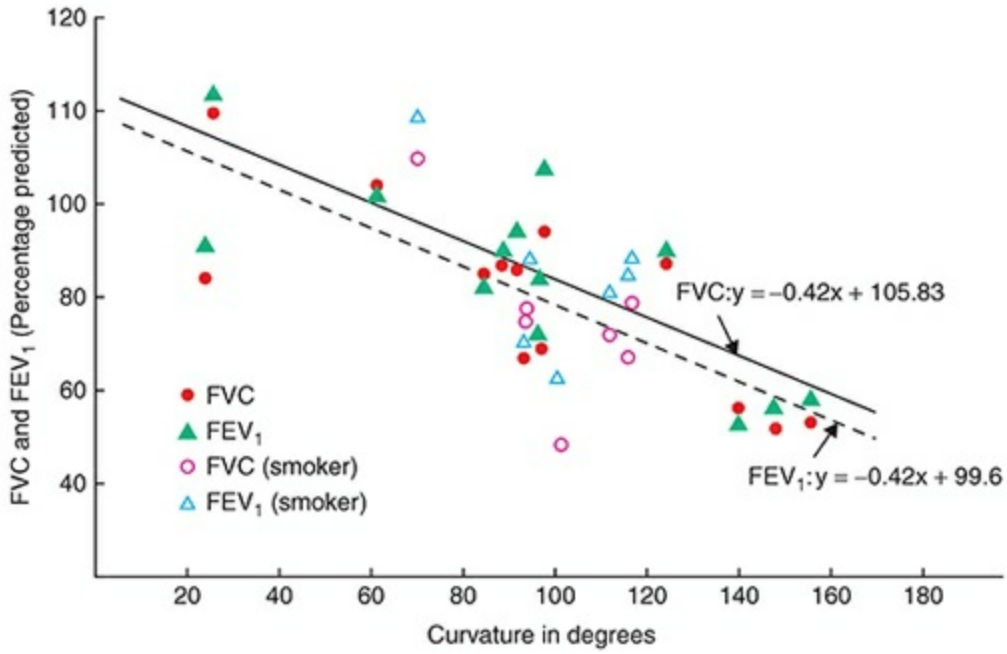

FIGURE 58.4. Relation between forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), and size of the curve in 20 patients with thoracic scoliosis. (*Reprinted with permission from Weinstein SL, Zaval DC, Ponseti IV, et al. Idiopathic scoliosis: long-term follow-up and prognosis in untreated patients*. J Bone Joint Surg Am. *1981;63:702–712*.)

Scoliosis severity and impairment of pulmonary function also increase with greater number of vertebrae involved, more cephalad location of the curve, and loss of the normal thoracic kyphosis. Severe curves have a worse prognosis because they tend to progress and, if long-standing, can cause permanent damage of the lung parenchyma, respiratory failure, cor pulmonale, and death. It is important to note that patients with neuromuscular types of scoliosis may have a much more profound decrease in pulmonary function for any given curve severity.

Azar FM, Canale ST, Beaty JH, eds. *Campbell's Operative Orthopaedics*. 13th ed. Philadelphia, PA: Elsevier Mosby; 2017:1897–2120.

Nnadi C, ed. *Early Onset Scoliosis: A Comprehensive Guide from the Oxford Meetings*. Stuttgart, Germany: Thieme; 2015:23–25.

A.5. What are the nonoperative treatment options of

scoliosis?

Those with progressive curves of greater than 25 degrees may be treated initially with rigid bracing (thoracolumbosacral orthosis [TLSO]). Compliance can be problematic due to patient comfort and social stigma. However, the importance of compliance was demonstrated in the Bracing in Adolescent Idiopathic Scoliosis Trial (BrAIST), which showed that bracing significantly decreased the progression to need surgical intervention, with the benefit increasing with more hours of brace compliance.

Similarly, infantile scoliotic curves are sometimes treated with noninvasive measures prior to proceeding with surgical correction. These noninvasive measures are noted to be most successful to halt curve progression when used prior to the development of a 60-degree curve and before 20 months of age. Serial full-body casting is used for infantile scoliosis in lieu of orthotics given the patient's rapid skeletal growth. In order to appropriately place the cast, these patients need to have general endotracheal anesthesia and be placed in a suspension table (**Fig. 58.5**). As these patients grow, they require frequent cast changes, and thus general anesthesia, every 2 to 3 months. The extent to which various anesthetic drugs affect the developing human brain has yet to be fully elucidated thereby warranting a preoperative discussion with the parents, particularly with repeated anesthetics. Care must be taken during the molding of the cast because considerable pressure can be applied to the chest and abdomen. This may result in a significant increase in peak airway pressures and arterial desaturation.

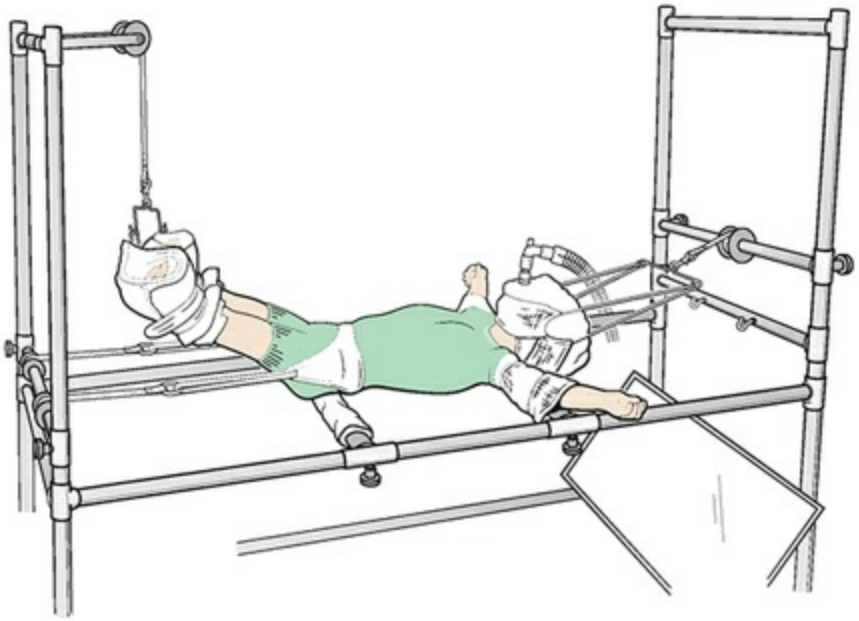

FIGURE 58.5. Example of a positioning used on a traction table for full body casting of infantile scoliosis. (*Reprinted with permission from Sanders JO, D'Astous J, Fitzgerald M, et al. Derotational casting for progressive infantile scoliosis*. J Pediatr Orthop. *2009;29:581*.)

Azar FM, Canale ST, Beaty JH, eds. *Campbell's Operative Orthopaedics*. 13th ed. Philadelphia, PA: Elsevier Mosby; 2017:1897–2120.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:727–753.

Weinstein SL, Dolan LA, Wright JG, et al. Effects of bracing in adolescents with idiopathic scoliosis. *N Engl J Med*. 2013;369(16):1512–1521.

A.6. What abnormalities in pulmonary function tests (PFTs) are most commonly seen in scoliosis? What is the cause of these abnormalities?

A restrictive pattern with decrease in lung volumes is the most common PFT abnormality in thoracic scoliosis. The greatest reduction occurs in vital capacity, which is typically reduced to 60% to 80% of predicted. Total lung capacity, functional residual capacity, inspiratory capacity, and expiratory reserve volume are also decreased. An increase in residual volume has been reported in patients with congenital scoliosis and in patients with idiopathic scoliosis 3 years following corrective

spine fusion.

During exercise, ventilation is adequate, but tidal volume is reduced and respiratory rate is increased. Maximal work capacity may also be decreased. Unless there is coexisting obstructive airway disease, the ratio of FEV_1/FVC is normal. Impaired respiratory muscle function also occurs in scoliosis, as evidenced by a decrease in inspiratory force to 70% of normal values. The decrease in inspiratory force is probably due to the inspiratory muscles working at a mechanical disadvantage because of the chest wall deformity.

These abnormalities in pulmonary function are usually the result of abnormal thoracic cage geometry producing a marked decrease in chest wall compliance rather than any abnormality in the lungs or respiratory muscles themselves. In dynamic magnetic resonance imaging, adolescent girls with idiopathic scoliosis and healthy controls showed no difference in diaphragmatic motion. The changes in chest wall compliance can be mimicked in normal volunteers by chest strapping. Exceptions include congenital and infantile scoliosis in which growth of the lungs may be impaired early in development by the thoracic deformity.

Azar FM, Canale ST, Beaty JH, eds. *Campbell's Operative Orthopaedics*. 13th ed. Philadelphia, PA: Elsevier Mosby; 2017:1897–2120.

Barrios C, Pérez-Encinas C, Maruenda JI, et al. Significant ventilatory functional restriction in adolescents with mild or moderate scoliosis during maximal exercise tolerance test. *Spine (Phila Pa 1976)*. 2005;30:1610–1615.

Chu WC, Li AM, Ng BK, et al. Dynamic magnetic resonance imaging in assessing lung volumes, chest wall, and diaphragm motions in adolescent idiopathic scoliosis versus normal controls. *Spine (Phila Pa 1976)*. 2006;31(19):2243–2249.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:727–753.

Koumbourlis AC. Scoliosis and the respiratory system. *Paediatr Respir Rev*.

2006;7:152–160.

Lazova S, Yablanski V, Vlaev E, et al. Lung function in children with scoliosis and enhanced spirometry sensitivity when using arm span index for restriction detection. *Ann Pulmonol*. 2019;3:33–38.

Nnadi C, ed. *Early Onset Scoliosis: A Comprehensive Guide from the Oxford Meetings*. Stuttgart, Germany: Thieme; 2015:23–25.

A.7. What is the most common arterial blood gas abnormality seen in scoliosis? What are possible causes for this abnormality?

It has been documented that patients with thoracic scoliosis have arterial oxygen desaturation compared to normal controls. Both arterial P_{CO_2} and pH are usually normal. Several studies have failed to show a correlation between the severity of the spinal curve and the degree of arterial oxygen desaturation.

Arterial hypoxemia is probably caused by ventilation/perfusion ($\dot{V}/\dot{Q}$) inequalities. Decreased diffusing capacity and alveolar hypoventilation may also play a role. Nevertheless, the diffusing capacity is not decreased sufficiently to be the sole cause of the hypoxemia. Similarly, alveolar ventilation at rest and during exercise is usually normal; therefore, arterial P_{CO_2} is usually normal. It has been reported that some patients have a closing capacity higher than functional residual capacity, resulting in premature airway closure during normal tidal breathing. Other studies have failed to demonstrate this finding. Some authors have reported an increase in the ratio of dead space to tidal volume (V_D/V_T), whereas other recent series have found V_D/V_T to be normal. This discrepancy may be related to the patient population studied, the severity of the scoliosis, or both. Severe and long-standing scoliosis can produce severe abnormalities, alveolar hypoventilation, carbon dioxide retention, and more severe hypoxemia. If not surgically treated, severe scoliosis increases the risk of premature death from respiratory failure after 40 years of age. A survey of

patients with respiratory failure in Sweden found that a vital capacity less than 50% of predicted and a Cobb angle greater than 100 degrees indicated an increased risk of respiratory failure.

Azar FM, Canale ST, Beaty JH, eds. *Campbell's Operative Orthopaedics*. 13th ed. Philadelphia, PA: Elsevier Mosby; 2017:1897–2120.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2071–2101.

Koumbourlis AC. Scoliosis and the respiratory system. *Paediatr Respir Rev*. 2006;7:152–160.

McPhail GL, Ehsan Z, Howells SA, et al. Obstructive lung disease in children with idiopathic scoliosis. *J Pediatr*. 2015;166(4):1018–1021.

A.8. What abnormalities of ventilatory drive may be associated with scoliosis?

The slope of the ventilatory response to carbon dioxide may be decreased in patients with scoliosis. This is probably not specific to scoliosis because this response is known to be reduced in situations in which the work of breathing is increased even in the absence of a chest wall deformity. Patients with mild scoliosis have been reported to exhibit abnormal ventilatory patterns in response to hypoxemia and hypercarbia. This pattern tends to minimize the work of breathing, a higher respiratory rate, and lower tidal volume.

It has also been demonstrated that during maximal exercise, patients with mild-to-moderate scoliosis exhibit a significantly decreased ventilatory capacity, reduced exercise tolerance, and oxygen consumption despite normal pulmonary function testing at rest.

Barrios C, Pérez-Encinas C, Maruenda JI, et al. Significant ventilatory functional restriction in adolescents with mild or moderate scoliosis during maximal exercise tolerance test. *Spine (Phila Pa 1976)*. 2005;30:1610–1615.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2071–2101.

Koumbourlis AC. Scoliosis and the respiratory system. *Paediatr Respir Rev*. 2006;7:152–160.

McPhail GL, Ehsan Z, Howells SA, et al. Obstructive lung disease in children with idiopathic scoliosis. *J Pediatr*. 2015;166(4):1018–1021.

A.9. How may the cardiovascular system be affected in patients with scoliosis?

Patients with scoliosis may develop elevated pulmonary vascular resistance and pulmonary hypertension. This may result in right ventricular hypertrophy and eventually right ventricular failure. A 50-year study of untreated scoliosis demonstrated that the mortality rate of these patients was twice that of the general population and respiratory failure or right-sided heart failure accounted for 60% of the deaths.

The increase in pulmonary vascular resistance is probably due to several factors. Hypoxemia produces pulmonary vasoconstriction, an increase in pulmonary vascular resistance, and hence an increase in pulmonary arterial pressure. Chronic hypoxemia will produce hypertensive vascular changes, and pulmonary hypertension may become irreversible. It has also been proposed that the chest wall deformity compresses some lung regions, increasing vascular resistance in those regions. Finally, if scoliosis develops in the first 6 years of life, the growth of the pulmonary vascular bed may be impaired by the chest wall deformity. Supporting this concept are reports of a decrease in the number of vascular units per lung volume in patients with scoliosis.

The most common cardiovascular abnormality in patients with scoliosis is mitral valve prolapse. Some conditions that are associated with scoliosis also affect the cardiovascular system. Patients with Duchenne muscular dystrophy develop a cardiomyopathy in the second decade of life that may not be appreciated on the basis of clinical symptoms because these patients are unable to exercise. The electrocardiogram (ECG)

may reveal tachycardia, prolonged PR and QRS intervals, ST abnormalities, bundle branch block, Q waves in the left precordial leads, and tall R waves in the right precordial leads. The ejection fraction may be decreased on echocardiogram.

Patients with Marfan syndrome may have mitral and aortic insufficiency, aneurysm of the proximal ascending aorta, and abnormalities of the conduction system.

The association of scoliosis and congenital heart disease has been well established. Although no specific cardiac lesion has been identified, some series have suggested that scoliosis is more common in patients with cyanotic heart disease.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:727–753.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2071–2101.

Kawakami N, Mimatsu K, Deguchi M, et al. Scoliosis and congenital heart disease. *Spine (Phila Pa 1976)*. 1995;20:1252–1255.

A.10. What is the relationship between scoliosis and malignant hyperthermia?

In the past 40 years, there has been no supportive evidence of a direct relationship. However, some scoliosis patients may have associated or underlying muscle disorders such as central core disease or multiminicore disease (also see Chapter 54, section A.3). These muscular dystrophies are associated with an increased risk of malignant hyperthermia.

Larach MG, Gronert GA, Allen GC, et al. Clinical presentation, treatment, and complications of malignant hyperthermia in North America from 1987 to 2006. *Anesth Analg*. 2010;110:498–507.

Rosenberg H, Davis M, James D, et al. Malignant hyperthermia. *Orphanet J Rare Dis*. 2007;2:21.

B. Preoperative Evaluation and Preparation

B.1. What should the anesthesiologist know about the nature of the spinal curve?

It is important to identify the location of the curve, the age of onset, its severity, the direction of the curve, and the etiology of the scoliosis. The location of the curve is important because thoracic scoliosis is associated with pulmonary function abnormalities. Cervical scoliosis may cause difficulties in airway management and may be associated with other congenital anomalies.

The age of onset of scoliosis is of critical importance because the lung continues to grow and develop from birth until 8 years of age. The number of alveoli increases from approximately 20 million at birth to 250 million at 4 years of age. The development of significant thoracic scoliosis during this phase of rapid growth impairs lung development. A significant reduction in alveolar number has been demonstrated in patients with early-onset thoracic scoliosis, predisposing these patients to impaired gas exchange and pulmonary hypertension.

The severity of the curve is important because thoracic curves greater than 60 degrees generally produce significant decreases in pulmonary function. Curves greater than 100 degrees may be associated with significant impairment in gas exchange. Most curves in adolescent idiopathic scoliosis are convex to the right, just as most people are right-handed. A left thoracic convexity should raise the index of suspicion to look for other underlying conditions and congenital anomalies. Finally, an understanding of the etiology of the scoliosis is important because underlying conditions such as muscular dystrophy or cerebral palsy will influence anesthetic management.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of*

Anesthesia for Infants and Children. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:727–753.

B.2. What aspects of the history are most important?

Initially, cardiopulmonary function should be assessed by inquiring about the patient's exercise tolerance. As a general rule, patients who can exercise normally and "keep up with friends" in vigorous activities will have good cardiopulmonary function. Pulmonary symptoms such as episodes of wheezing or cough may indicate parenchymal or reactive lung disease and alter perioperative management. Patients with muscular dystrophy, Marfan syndrome, and neurofibromatosis should be questioned about symptoms suggestive of cardiac conduction abnormalities such as palpitations or syncope.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:727–753.

B.3. What aspects of the physical examination are most important?

Particular emphasis in the physical examination should be directed toward the heart and lungs. Auscultation of the lungs may reveal wheezing or rales suggesting obstructive airway disease or parenchymal lung disease. On examination of the heart, in addition to auscultating for murmurs and gallops, signs of pulmonary hypertension and right ventricular hypertrophy should be sought. Pulmonary hypertension causes accentuation of the pulmonic component of the second heart sound, and a right ventricular lift indicates right ventricular enlargement. Signs of right ventricular failure include engorged neck veins, an enlarged liver resulting from passive liver congestion, and lower extremity edema. If neurofibromatosis is suspected, the skin should be examined for the presence of *café au lait spots* or cutaneous neurofibroma. The airway should be evaluated closely

for abnormalities such as cervical scoliosis, neurofibroma, or high-arched palate associated with Marfan syndrome that may make endotracheal intubation difficult.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:727–753.

B.4. Why is a preoperative neurologic assessment important?

A preoperative neurologic assessment is important because patients who have preexisting neurologic deficits are at increased risk for developing spinal cord injury during scoliosis surgery. Furthermore, it is important to document preoperative neurologic function in order to avoid confusion about postoperative neurologic complications.

If a patient has a ventriculoperitoneal shunt for hydrocephalus, it should be evaluated preoperatively by the patient's neurosurgeon. The shunt can malfunction during correction of the spinal deformity via disconnection, fracture, kinking, or inadequate length.

Abu-Sneineh K, Lipton GE, Gabos PG, et al. Dysfunction of a ventriculoperitoneal shunt after posterior spinal fusion in children with cerebral palsy: a report of two cases. *J Bone Joint Surg Am*. 2003;85:1119–1124.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:727–753.

B.5. What tests would you order preoperatively?

It is best to tailor diagnostic testing based on the severity of the scoliosis and underlying conditions. In the current climate emphasizing medical cost containment, each institution needs to critically reassess preoperative testing. Preoperatively, this healthy 14-year-old may only need a complete blood count and a

type and screen. If the history or physical examination suggests that pulmonary reserve is decreased, then standard pulmonary function testing should be considered. If vital capacity is significantly diminished, an arterial blood gas measurement is indicated. If routine pulmonary function testing reveals evidence of obstructive airway disease (a decrease in the ratio of FEV_1/FVC or a decrease in forced expiratory flow [25% to 75%]), a bronchodilator should be administered to determine if the airway obstruction is reversible.

Patients with onset of scoliosis in the first 8 years of life should have pulmonary function testing, arterial blood gas analysis, and an ECG. If the ECG reveals abnormalities such as right ventricular hypertrophy (large R wave in V_1 and V_2), right atrial enlargement (P_{wave} greater than 2.5 mm), or evidence of a cardiomyopathy, an echocardiogram or even cardiac catheterization may be indicated, particularly if pulmonary hypertension is suspected.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:727–753.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2071–2101.

McPhail GL, Ehsan Z, Howells SA, et al. Obstructive lung disease in children with idiopathic scoliosis. *J Pediatr*. 2015;166(4):1018–1021.

B.6. What is an enhanced recovery after surgery (ERAS) pathway? How has it been applied to the recovery for pediatric patients undergoing posterior spinal instrumentation and fusion?

The concept of ERAS was initially developed to examine and address the variability of surgical practices in concordance with evidence-based best practices. The first evidence-based consensus ERAS protocol was described in 2005 in adult

patients undergoing colorectal surgery. In 2010, the ERAS Society was founded with a mission to improve recovery through research, education, and implementation of evidence-based best practices. Recently, many centers have developed pathways for pediatric patients undergoing posterior spinal instrumentation and fusion. These protocols adapt components of ERAS with a standardized multidisciplinary perioperative approach for each patient during the preadmission, preoperative, intraoperative, and postoperative periods with an overarching goal of creating a best practice for these patients. However, a consensus best practice ERAS protocol encompassing the entire scope of perioperative care for pediatric patients undergoing spinal instrumentation and fusion has not been formulated.

Nevertheless, many centers have adapted components of ERAS protocols to their pathways while managing the perioperative care of patients with adolescent scoliosis. Prior to surgery, these patients will have the appropriate labs drawn and will be instructed to scrub with chlorhexidine the evening prior to surgery to reduce the incidence of infection. Patients may also be advised to drink a carbohydrate-rich beverage the morning of surgery, which has been shown to significantly reduce postoperative insulin resistance. Some will consider donating autologous blood in the weeks leading up to surgery to avoid an allogeneic transfusion. Patients will be educated how to use an incentive spirometer and how to potentially undergo a wake up test (see subsequent text). Intraoperatively, posterior spinal fusion pathways will focus on initiating multimodal analgesic therapies, preventing neurologic complications associated with the operation and positioning, and decreasing perioperative blood loss and the need for an allogeneic blood transfusion with antifibrinolytic therapy and the use of cell salvage. The postoperative course is structured to facilitate early recovery, rehabilitation, and the return to normal function. Several

multidisciplinary professionals, including orthopedic surgery, pain management, physical therapy, and nursing will work collectively to facilitate these goals. Implementation of posterior spinal fusion recovery pathways has demonstrated a decrease in length of hospital stay and a decrease in health care costs.

Borden TC, Bellaire LL, Fletcher ND. Improving perioperative care for adolescent idiopathic scoliosis patients: the impact of a multidisciplinary care approach. *J Multidiscip Healthc*. 2016;9:435–445.

Fearon KC, Ljungqvist O, Von Meyenfeldt M, et al. Enhanced recovery after surgery: a consensus review of clinical care for patients undergoing colonic resection. *Clin Nutr*. 2005;24(3):466–477.

Fletcher ND, Andras LM, Lazarus DE, et al. Use of a novel pathway for early discharge was associated with a 48% shorter length of stay after posterior spinal fusion for adolescent idiopathic scoliosis. *J Pediatr Orthop*. 2017;37(2):92–97.

Fletcher ND, Glotzbecker MP, Marks M, et al. Development of consensus-based best practice guidelines for postoperative care following posterior spinal fusion for adolescent idiopathic scoliosis. *Spine (Phila Pa 1976)*. 2017;42(9):E547–E554.

Muhly WT, Sankar WN, Ryan K, et al. Rapid recovery pathway after spinal fusion for idiopathic scoliosis. *Pediatrics*. 2016;137(4):e20151568.

Soop M, Nygren J, Myrenfors P, et al. Preoperative oral carbohydrate treatment attenuates immediate postoperative insulin resistance. *Am J Physiol Endocrinol Metab*. 2001;280(4):E576–E583.

B.7. How will the surgical procedure influence the anesthetic management?

A variety of surgical procedures are commonly performed for posterior spine fusion. The blood lost during these procedures may be considerable and varies according to the procedure, the operative time, the number of segments fused (>6), the degree of Cobb angle (>50 degrees), the need for osteotomies, whether deliberate hypotension is used, and other factors. Even when deliberate hypotension is employed, blood loss in the range of 15 to 25 mL per kg is not uncommon during uncomplicated spine fusion with segmental instrumentation. This represents a

blood loss of 1 to 2 L for a 70-kg patient.

Postoperative bleeding may equal or exceed this, emphasizing the need for continued monitoring of these patients in the postoperative period. More extensive procedures such as combined anteroposterior spine fusion, instrumentation into the pelvis, or especially osteotomy of the spine to correct rigid deformities may be associated with blood loss exceeding the patient's own blood volume (75 mL per kg). Patients who require these more extensive procedures are frequently those with neuromuscular scoliosis (Duchenne muscular dystrophy, cerebral palsy) who may already have diminished reserves. Before the patient is taken to the operating room, the anesthesiologist should confirm that the blood bank has the anticipated blood products readily available.

Moderate third-space losses of intravascular fluid occur during scoliosis surgery. These should be replaced with balanced salt solution at a rate of 5 to 7 mL/kg/hr. This is in addition to any deficit or maintenance requirements. Procedures that are more extensive may require higher infusion rates.

The anesthesiologist should speak with the surgeon about the surgical approach and technique. The surgical plan could affect the patient's position during the case. For example, patients undergoing an anterior approach or thoracotomy may need to be positioned laterally. Another consideration is whether the surgeon requires single-lung ventilation in which case the patient may need a double-lumen endotracheal tube.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:727–753.

Guay J, Haig M, Lortie L, et al. Predicting blood loss in surgery for idiopathic scoliosis. *Can J Anaesth*. 1994;41:775–781.

Oetgen ME, Litrenta J. Perioperative blood management in pediatric spine surgery. *J Am Acad Orthop Surg*. 2017;25(7):480–488.

C. Intraoperative Management

C.1. What monitoring would you use?

Basic monitoring for posterior spine fusion should include blood pressure, ECG, pulse oximetry, end-tidal carbon dioxide, esophageal stethoscope, core temperature, and spinal cord monitoring. A radial artery catheter is used for continuous monitoring of blood pressure, particularly if deliberate hypotension is planned to reduce blood loss. This will also facilitate obtaining blood samples for blood gas and hematocrit determination. All patients should have a urinary catheter placed to document urine output during and particularly after the surgical procedure. Monitoring of central filling pressures may be indicated if the expected blood loss is large, or cardiovascular disease is present or suspected. Although rarely placed in routine idiopathic scoliosis surgery, a pulmonary artery catheter may be useful in patients with cardiomyopathy from Duchenne muscular dystrophy, and patients with pulmonary hypertension or right ventricular failure, in order to optimize volume replacement therapy. When placing pulmonary artery catheters in patients with pulmonary hypertension, it must be considered that the risk of pulmonary artery rupture, a complication with a mortality rate of 50%, is increased in patients with pulmonary hypertension. An alternative technique is the transesophageal echocardiography (TEE), but this requires special expertise, and vigilance must be used when using the TEE probe for a lengthy operation in the prone position.

If neuromuscular block is used throughout the case, be certain to monitor continuously and discuss this with the neuromonitoring team in case there is any confusion interpreting the MEPs.

Anesthesia for Infants and Children. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:727–753.

C.2. What is the incidence of neurologic complications in scoliosis surgery, and which patients are at highest risk?

In a morbidity report of the Scoliosis Research Society (2006), the rate of complete or partial paraplegia was 0.26%. A study of 6,334 patients undergoing anterior, posterior, or combined anteroposterior spinal fusion reported an overall rate of spinal injury of 0.28%. Of note, combined anteroposterior procedures had a significantly higher rate of spinal cord injuries (1.12%) compared to anterior (0.0%) and posterior (0.21%) procedures.

It has been proposed that distraction of the cord and straightening of the deformity compresses the spinal cord and disrupts the arterial blood supply of the cord. The spinal cord and nerve roots may also be injured directly by hooks or instrumentation.

Prevention of neurologic complications begins with identification of the high-risk group. Patients are at increased risk for developing paraplegia if they have a severe rigid deformity (greater than 120 degrees), kyphosis, neurofibromatosis, congenital or postinfectious scoliosis, a preexisting neurologic deficit, or more invasive instrumentation. Congenital scoliosis is associated with intraspinal anomalies including lipomas, tethered cord, cysts, and teratomas that also increase the risk of postoperative neurologic complications. A preoperative myelogram or magnetic resonance imaging is indicated in these patients. Preoperative prophylaxis with high-dose corticosteroids should be considered for patients with a preexisting neurologic deficit.

Coe JD, Arlet V, Donaldson W, et al. Complications in spinal fusion for adolescent idiopathic scoliosis in the new millennium. A report of the

Scoliosis Research Society Morbidity and Mortality Committee. *Spine (Phila Pa 1976)*. 2006;31(3):345–349.

Kocher MS, Millis MB, eds. *Operative Techniques: Pediatric Orthopaedic Surgery*. Philadelphia, PA: Elsevier Saunders; 2011:719–730.

C.3. What monitoring techniques are used to minimize neurologic complication?

The two monitoring techniques most commonly used in the United States to monitor spinal cord function during scoliosis surgery are SSEPs and MEPs. Some centers continue to use the intraoperative wake-up test, although MEP monitoring has replaced the routine use of the wake-up test in many centers. The intraoperative wake-up test may still be required if SSEPs or MEPs become abnormal during the surgical procedure.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:727–753.

Schwartz D, Auerbach J, Dormans JP, et al. Neurophysiological detection of impending spinal cord injury during scoliosis surgery. *J Bone Joint Surg Am*. 2007;89(11):2440–2449.

C.4. What are somatosensory evoked potentials (SSEPs), and how are they used?

Sensory information from the periphery passes through the posterior columns of the spinal cord on its way to the cerebral cortex. The functional integrity of this pathway can be continually assessed by monitoring SSEPs. This technique involves applying repeated electrical stimuli to a peripheral nerve (e.g., posterior tibial nerve) and measuring the evoked response over the cerebral cortex and subcortical regions using standard electroencephalogram scalp electrodes (**Fig. 58.6**). These evoked potentials are of very low amplitude, so computer averaging or summation must be used to distinguish these potentials from background noise and the patient's electroencephalogram. A typical evoked potential waveform is

shown in **Figure 58.7**. The time interval between electrical stimulation of peripheral nerve to recording the evoked response over the cortex is defined as the latency. An increase in the latency (slower conduction), a decrease in the amplitude, or a complete loss of the evoked potential should be considered indicative of surgical injury or ischemia until proved otherwise. It is difficult to define standard values for latency and amplitude because of the differences in recording technique among laboratories, and therefore, it is important to be familiar with the normal limits for the system that is in use. In general, an increase in latency of 10% to 15% or more and a decrease in amplitude of greater than 50% should be cause for concern.

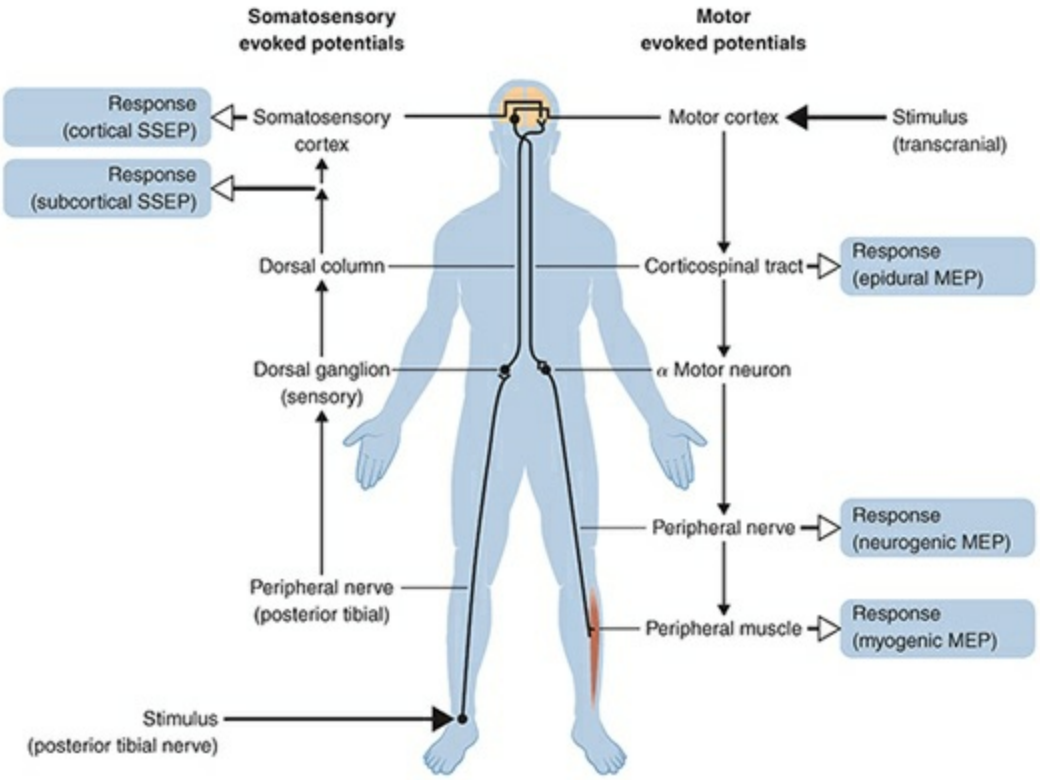

FIGURE 58.6. Outline of pathways involved in somatosensory evoked potential (SSEP) and motor evoked potential (MEP) monitoring. (*Modified from de Haan P, Kalkman CJ. Spinal cord monitoring: somatosensory- and motor-evoked potentials*. Anesthesiol Clin North Am. *2001;19[4]:923–945. Copyright © 2001 Elsevier. With permission.*)

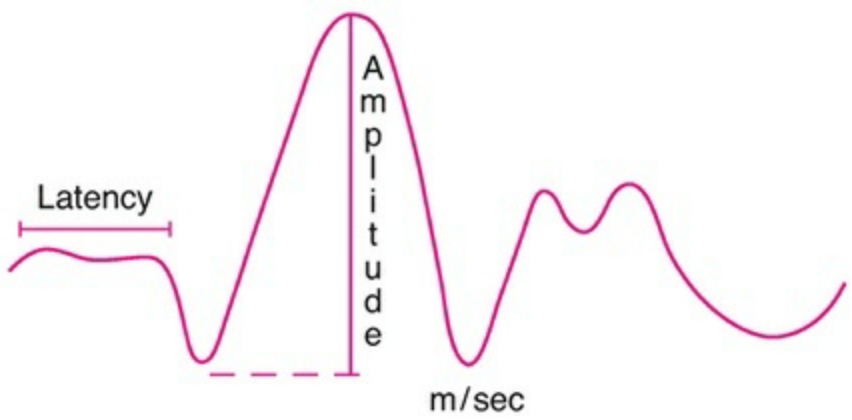

FIGURE 58.7. Typical SSEP trace. (*Reprinted with permission from Cunningham JN Jr, Laschinger JC, Merkin HA, et al. Measurement of spinal cord ischemia during operations upon the thoracic aorta: initial clinical experience*. Ann Surg. *1982;196[3]:285–296.*)

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:727–753.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1243–1278.

Koht A, Sloan TB, Toleikis JR, eds. *Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals*. New York: Springer; 2017:3–18.

C.5. How reliable are SSEPs for predicting spinal injury?

Normal intraoperative SSEPs are good predictors of normal postoperative sensory function. Although posterior (sensory) and anterior (motor) spinal injuries tend to occur together during spine surgery or spinal trauma, there have been reports of postoperative paraplegia with normal intraoperative SSEPs. This probably represents selective ischemia in the distribution of the anterior spinal artery. Sensory function and SSEPs are preserved because the posterior columns receive their blood supply from the posterior spinal arteries. For this reason, it is probably best not to rely exclusively on SSEPs to monitor spinal cord function during scoliosis surgery.

In a survey of 173 orthopedic spinal surgeons, it was found that experienced SSEP monitoring teams had fewer neurologic complications per 100 cases than teams with less experience.

Neurologic defects with normal SSEPs (false negative) occurred in only 0.063% of cases.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:727–753.

Kocher MS, Millis MB, eds. *Operative Techniques: Pediatric Orthopaedic Surgery*. Philadelphia, PA: Elsevier Saunders; 2011:719–730.

Koht A, Sloan TB, Toleikis JR, eds. *Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals*. New York: Springer; 2017:3–18.

Nuwer MR, Dawson EG, Carlson LG, et al. Somatosensory evoked potential spinal cord monitoring reduces neurologic deficits after scoliosis surgery: results of a large multicenter survey. *Electroencephalogr Clin Neurophysiol*. 1995;96:6–11.

C.6. What are motor evoked potentials (MEPs), and how are they used?

MEPs assess the integrity of the spinal motor pathways (anterior columns). MEPs are elicited by transosseous electrical stimulation of the motor cortex using scalp electrodes or by stimulation of the anterior columns using epidural electrodes. Conduction of these stimuli through the motor pathways is monitored as peripheral nerve impulses, electromyographic signals, or actual limb movements (**Fig. 58.6**).

In a study of 144 patients undergoing spinal deformity correction surgery, the authors report a sensitivity of 1 and a specificity of 0.97 using transcranial MEPs as the sole modality. No patient had any new neurologic deficits.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1243–1278.

Hsu B, Cree AK, Lagopoulos J, et al. Transcranial motor-evoked potentials combined with response recording through compound muscle action potential as the sole modality of spinal cord monitoring in spinal deformity surgery. *Spine (Phila Pa 1976)*. 2008;33:1100–1106.

Koht A, Sloan TB, Toleikis JR, eds. *Monitoring the Nervous System for*

Anesthesiologists and Other Health Care Professionals. New York: Springer; 2017:19–34.

C.7. How is spinal cord monitoring affected by anesthetic agents? What other factors affect spinal cord monitoring?

All anesthetic agents may affect spinal monitoring to a varying degree. This has been documented for potent inhalation agents, propofol, nitrous oxide, benzodiazepines, droperidol, etomidate, ketamine, barbiturates, and even opioids. Opioids probably have the least effect on SSEPs of all of these agents. Cortical SSEPs and MEPs are very sensitive to nitrous oxide and potent inhalational agents, whereas subcortical SSEPs are more resistant. The addition of nitrous oxide to isoflurane has been shown to have a profound effect on MEPs. MEPs are also profoundly affected by benzodiazepines and thiopental, whereas ketamine may enhance MEPs.

Nitrous oxide produces a decrease in amplitude in SSEPs without an increase in latency. Isoflurane, sevoflurane, halothane, and so on have similar effects on SSEPs; a dose-dependent increase in latency and decrease in amplitude. The addition of nitrous oxide appears to produce a larger decrease in amplitude than addition of 1% isoflurane or enflurane to a fentanyl-based anesthetic.

Muscle relaxants have no effect on SSEPs or MEP impulses monitored from peripheral nerves. They will affect the intensity of the motor response, which may lead to confusion in interpreting MEPs.

Although it is important to realize that anesthetic agents can affect spinal cord monitoring, excellent results can be obtained if anesthetic depth is stable. For example, it is preferable to administer opioids by continuous infusion rather than by intermittent doses. It is most important to maintain a stable

anesthetic before and during periods when monitoring is critical, that is, during spine distraction or instrumentation.

A decrease in arterial pressure below levels of cerebral autoregulation, hypothermia, hematocrits below 15%, and hypoxia will affect both SSEPs and MEPs.

Bernard JM, Péréon Y, Fayet G, et al. Effects of isoflurane and desflurane on neurogenic motor- and somatosensory-evoked potential monitoring for scoliosis surgery. *Anesthesiology*. 1996;85:1013–1019.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:1243–1278.

Koht A, Sloan TB, Toleikis JR, eds. *Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals*. New York: Springer; 2017:317–344.

C.8. What is the optimal anesthetic technique for scoliosis surgery?

There is no simple answer for the optimal anesthetic technique. Most patients with idiopathic scoliosis are healthy adolescents who tolerate anesthesia and surgery well, and a wide variety of techniques have been used successfully. Many healthy teenagers have a much higher tolerance for opioids and benzodiazepines and will have higher requirements for these agents intraoperatively, compared to adults. The primary concern is the ability to provide an anesthetic that is suitable for spinal cord monitoring while providing analgesia and amnesia. Prior to the use of MEP monitoring, anesthetic techniques were tailored to facilitate the wake-up test. Monitoring of MEPs has now replaced routine use of the wake-up test in many centers. Although cortical SSEPs and MEPs may be measurable in most healthy adults receiving 50% to 70% nitrous oxide and 0.5 minimal alveolar concentration isoflurane, this combination is not suitable in small children with immature corticospinal tracts or those with preexisting neurologic deficits. Furthermore, MEPs may be more sensitive to the combination of nitrous oxide

and potent inhalational agents than cortical SSEPs.

Therefore, a typical anesthetic is a combination of a low-dose potent agent (e.g., isoflurane 0.4%) in 50% oxygen per air mixture, with a low-dose propofol infusion and primarily opioid-based intravenous anesthetic. Intravenous midazolam should be given before induction for anxiolysis and amnesia. Small doses may be repeated later if necessary. An infusion of ketamine at a low dose (0.1 to 0.2 mg/kg/hr) may improve MEP monitoring. Many centers use total intravenous anesthesia. Dexmedetomidine has been used as an adjunct in total intravenous anesthesia with minimal effect on MEPs and SSEPs. Muscle relaxants, if used, should be administered by continuous infusion and titrated to a constant train-of-four because the neuromuscular blockade will affect the intensity of the motor response. A baseline set of SSEPs and MEPs should be performed by the neuromonitoring technician as early as possible, ideally before incision, so that changes to the anesthetic or monitoring technique can be made before the most critical part of the operation (i.e., spine distraction and instrumentation).

Succinylcholine should be avoided in patients with muscle disorders. Its administration in patients with Duchenne muscular dystrophy may produce hyperkalemia, cardiac arrhythmias, myoglobinuria, or precipitate malignant hyperthermia. Patients with myotonic muscular dystrophy may exhibit sustained skeletal muscle contractions in response to succinylcholine. This may produce difficulty in ventilation and intubation.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:727–753.

Gibson PR. Anaesthesia for correction of scoliosis in children. *Anaesth Intensive Care*. 2004;32:548–559.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed.

Philadelphia, PA: Elsevier; 2020:2096–2098.

Tobias JD, Goble TJ, Bates G, et al. Effects of dexmedetomidine on intraoperative motor and somatosensory evoked potential monitoring during spinal surgery in adolescents. *Paediatr Anaesth*. 2008;18:1082–1088.

C.9. What should be done if the SSEPs or MEPs become abnormal during surgery?

If spinal cord monitoring becomes abnormal, the anesthesiologist should ensure that oxygen delivery and spinal cord perfusion are adequate. Hypovolemia and anemia should be corrected. Arterial oxygen tension should be optimized, and arterial P_{CO_2} should be normalized if the patient is being hyperventilated. It has been reported that normalizing arterial pressure if deliberate hypotension is being used or raising arterial pressure above normal may improve spinal cord perfusion and restore SSEPs to normal. The surgeon should seek a surgical cause such as too much distraction or surgical trespass with instrumentation and correct the problem as quickly as possible. If the abnormality persists despite corrective action, a wake-up test should be considered to determine if the instrumentation should be adjusted or removed. Some surgeons may elect to abort the procedure if there is no improvement of neurophysiologic signals. Additionally, some centers advocate to administer high-dose steroids when evoked potential signals do not recover. There is evidence that the shorter the interval between detection of injury and removal of instrumentation, the better is the neurologic outcome.

Grundy BL, Nash CL Jr, Brown RH. Arterial pressure manipulation alters spinal cord function during correction of scoliosis. *Anesthesiology*. 1981;54:249–253.

Koht A, Sloan TB, Toleikis JR, eds. *Monitoring the Nervous System for Anesthesiologists and Other Health Care Professionals*. New York: Springer; 2017:317–344.

Lyon R, Lieberman JA, Grabovac MT, et al. Strategies for managing decreased motor evoked potential signals while distracting the spine during

correction of scoliosis. *J Neurosurg Anesthesiol*. 2004;16(2):167–170.

C.10. How is the "wake-up" test performed? What complications can occur during this test?

The wake-up test is used to assess the integrity of the spinal motor pathways and is performed by "lightening" the depth of anesthesia sufficiently to allow the patient to follow commands. This is usually done as soon as all instrumentation is in place or if an abnormality has been detected with spinal cord monitoring. The patient is first instructed to squeeze the anesthesiologist's hand, confirming that he or she is responsive, and then asked to move his or her feet and toes. Often, the patient wake-up is not a calm event, and the patient wakes up suddenly and moves his or her head and limbs simultaneously. If the patient is able to squeeze his or her hands but unable to move his or her feet, the amount of spine distraction must be reduced until a safe degree of correction is achieved, and in some cases, the hardware is removed. When the patient moves his or her feet, anesthesia is quickly deepened with small doses of propofol (0.5 mg per kg). Additional short-acting benzodiazepines may be given. Recall of intraoperative events is very unusual with this technique.

The anesthesiologist should have one or two assistants available in the event the patient moves excessively during the wake-up test. Although this occurs rarely when an adequate amount of opioid has been administered, it is best to be prepared. The authors do not recommend use of opioid antagonists because of the potential for the patient to experience pain and become agitated in the prone position. If naloxone is deemed necessary to arouse the patient, a small dose (0.3 to 0.5 μg per kg) should be administered and repeated every 2 to 3 minutes until the respiratory depression of the opioid is reversed. It is not typically necessary to reverse neuromuscular blockade if at least three twitches are present on train-of-four stimulation.

Complications of this technique include extubation in the prone position, recall of intraoperative events, myocardial ischemia, self-injury, and dislodgment of instrumentation or intravenous access. Air embolus from open venous sinuses may occur if the patient is breathing spontaneously and inhales vigorously.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:727–753.

Kocher MS, Millis MB, eds. *Operative Techniques: Pediatric Orthopaedic Surgery*. Philadelphia, PA: Elsevier Saunders; 2011:719–730.

C.11. Four hours into the surgical procedure, the surgeon reports some bubbling in the thoracic portion of the wound. Shortly thereafter, end-tidal carbon dioxide decreases abruptly from 35 to 18 mmHg, heart rate increases from 80 to 120 beats per minute, blood pressure begins to fall, and arterial saturation decreases to 90%. On auscultation through esophageal stethoscope, you hear a loud gurgling murmur. What is your diagnosis?

This constellation of symptoms strongly suggests venous air embolism. There are at least two reports indicating that air bubbling in the wound may be the first clinical sign of an air embolus before cardiovascular collapse. This is thought to occur as a result of retrograde flow of blood containing entrained air through the valveless venous system as a result of an increase in central venous pressure. Central venous pressure rises as a result of an air lock in the right heart. Positive pressure ventilation and pressure on the spine during placement of hardware may also produce bubbling of entrained air.

McCarthy RE, Lonstein JE, Mertz JD, et al. Air embolism in spinal surgery. *J*

Spinal Disord. 1990;3:1–5.

Wills J, Schwend RM, Paterson A, et al. Intraoperative visible bubbling of air may be the first sign of venous air embolism during posterior surgery for scoliosis. *Spine (Phila Pa 1976)*. 2005;30:E629–E635.

C.12. How common is significant air embolism during scoliosis surgery?

Fortunately, clinically significant air embolism is uncommon. Nevertheless, cases of fatal air embolism have been reported during scoliosis surgery in children. Most, but not all, cases involve extensive surgical dissection with excessive bleeding. The mortality rate in the reported cases may be 50%.

Wills J, Schwend RM, Paterson A, et al. Intraoperative visible bubbling of air may be the first sign of venous air embolism during posterior surgery for scoliosis. *Spine (Phila Pa 1976)*. 2005;30:E629–E635.

C.13. What should be done if an air embolus is suspected?

If an air embolus is suspected, the surgical field should be immediately flooded with saline, ventilation begun with 100% oxygen, and intravascular fluid administered to increase central venous pressure. Air is most likely entrained from open epidural and paravertebral veins and venous sinuses in decorticated bone. Flooding the field with saline prevents air entrainment. Ventilation with 100% oxygen reduces the volume of the air embolus, particularly if nitrous oxide was administered. Hypovolemia and low central venous pressure favor air entrainment by increasing the pressure gradient between open veins and the right atrium.

If the patient requires cardiopulmonary resuscitation, placing the patient in the left lateral decubitus position during external cardiac massage may improve blood flow by breaking the air lock of the pulmonary outflow tract. Removing air through either a central catheter or by direct intracardiac aspiration has also been advocated.

McCarthy RE, Lonstein JE, Mertz JD, et al. Air embolism in spinal surgery. *J Spinal Disord*. 1990;3:1–5.

Sutherland RW, Winter RJ. Two cases of fatal air embolism in children undergoing scoliosis surgery. *Acta Anaesthesiol Scand*. 1997;41:1073–1076.

C.14. What complications occur related to positioning the patient?

If the head is not positioned carefully, pressure on the eyes may cause thrombosis of the central retinal artery producing loss of vision or blindness. The horseshoe-type headrest (**Fig. 58.8**) has been implicated in a number of reports of unilateral eye blindness and should not be used for long procedures. The head should be positioned without excessive flexion or extension and in such a way that the face and eyes can be inspected easily. The position of the head and neck will move during surgical manipulation of the spine and should be inspected frequently during the procedure. It is extremely helpful to have a mirror under the patient's face that can be viewed throughout the case (**Fig. 58.9**). Patients with Marfan syndrome and neurofibromatosis may have abnormalities of the cervical spine and must be turned and positioned with great caution.

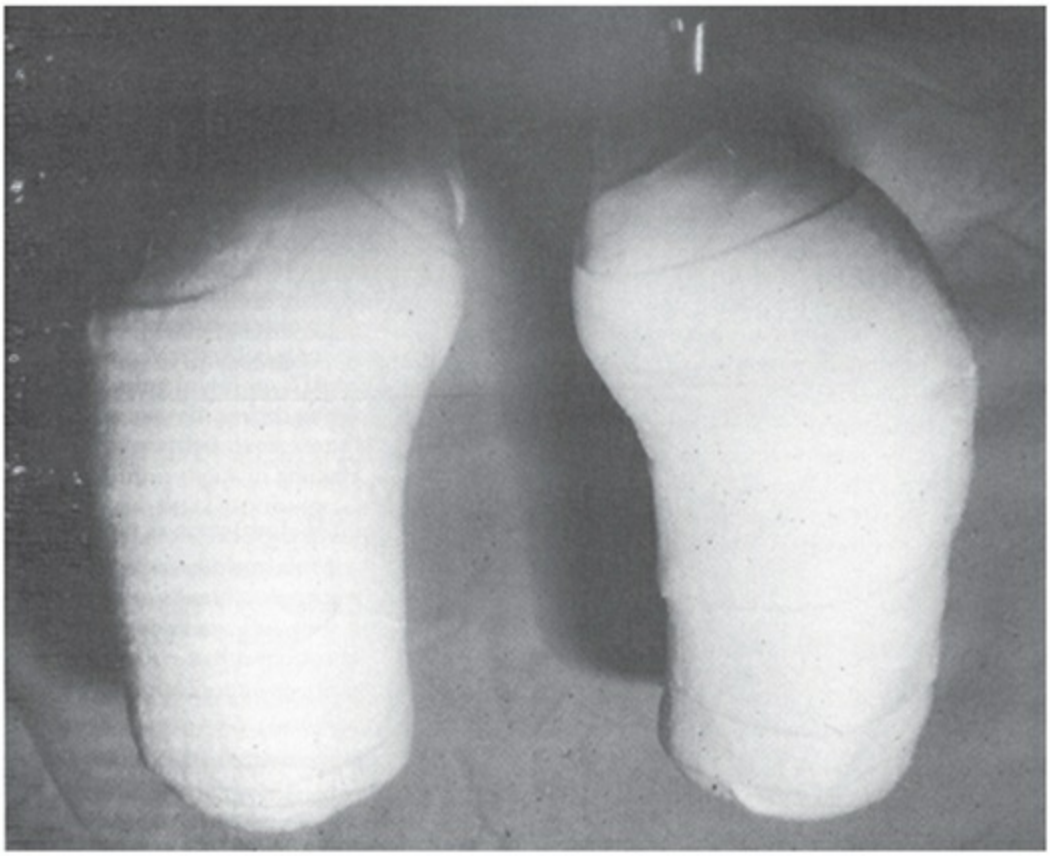

FIGURE 58.8. This horseshoe-type headrest has been associated with unilateral eye blindness resulting from pressure on the eye during surgery. The forehead rests on the upper portion, with the chin free in the wider, open portion.

FIGURE 58.9. Foam face rest with mirror.

The upper extremities should be positioned at no more than 90 degrees of abduction to the trunk, as illustrated in **Figure 58.10A**. **Figure 58.10B** demonstrates improper arm positioning because the arms are abducted above the head. This stretches the brachial plexus and may result in a brachial plexus palsy. Both axillae should be inspected to ensure that the frame does not compress the axillary sheath. Proper positioning is shown in **Figure 58.11A**. Note that there is ample space between the thoracic bolster of the frame and the axilla. **Figure 58.11B** demonstrates improper positioning on the frame resulting in pressure on the axilla. Care should be taken to pad the ulnar nerves at the elbow. Often, the surgeons will compress or unintentionally move the upper extremities, so the arms and shoulders must be continuously monitored. Impairment of ventilation and increased bleeding from increased venous

pressure may occur if the abdomen is compressed by the operating frame.

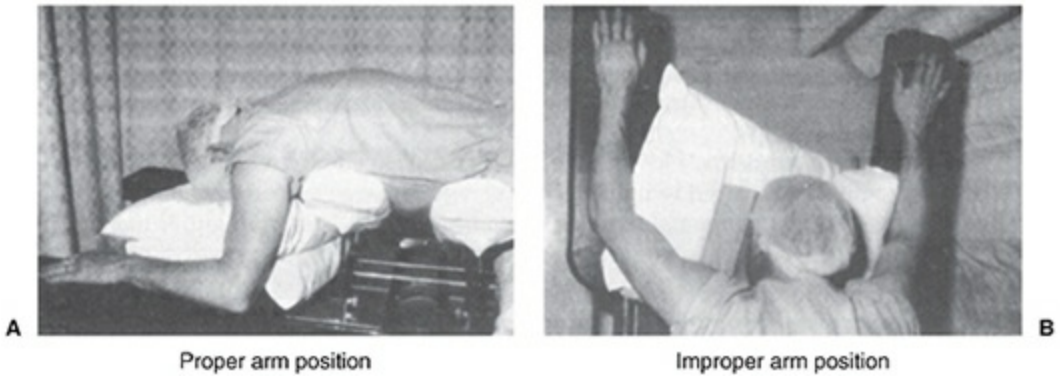

FIGURE 58.10. Proper arm position and improper arm position during scoliosis surgery. A. Degrees of abduction (relative to the trunk). **B.** Improper arm positioning with the arms abducted above the head. This results in stretching of the brachial plexus.

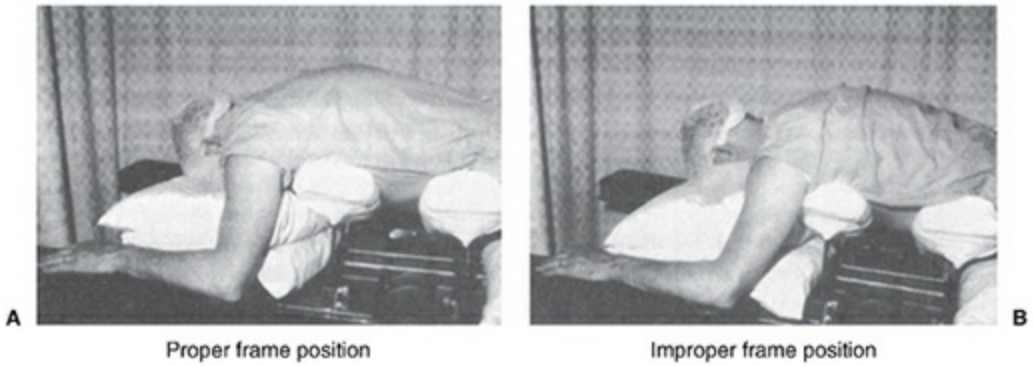

FIGURE 58.11. Proper and improper positioning on the four-poster frame during spine surgery. A. Proper positioning on the frame with ample space between the axilla and the thoracic bolster of the frame. **B.** Improper positioning on the frame resulting in compression of the axillary sheath by the thoracic bolster of the frame.

Life-threatening cardiovascular events have occurred due to right ventricular outflow tract obstruction and resultant decreased venous return due to positioning of bolsters.

Neira VM, Gardin L, Ryan G, et al. A transesophageal echocardiography examination clarifies the cause of cardiovascular collapse during scoliosis surgery in a child. *Can J Anaesth*. 2011;58:451–455.

C.15. What is transfusion-related acute lung injury (TRALI)? How do you distinguish it from

transfusion-associated circulatory overload (TACO)?

TRALI is noncardiogenic pulmonary edema occurring within 1 to 6 hours of transfusion of a plasma-containing blood product. In intubated patients, it presents as copious, pink, and frothy pulmonary edema fluid in the endotracheal tube. Although clinically indistinguishable from adult acute respiratory distress syndrome, TRALI is associated with a much lower mortality rate (5% to 10%). Typically, the chest radiograph and arterial oxygen saturation return to baseline within 72 hours. The exact mechanism of TRALI is unknown, but evidence points to pathologic leukocyte antibodies in donor plasma causing agglutination of white blood cells on pulmonary endothelial cells, resulting in increased permeability. Platelet transfusions have been most commonly implicated. Therapy is supportive, similar to that for acute respiratory distress syndrome.

TACO, on the other hand, is a result of increased hydrostatic pressure in the capillaries causing pulmonary edema. The clinical features and radiologic findings are similar, and the two are difficult to differentiate from each other. A thorough understanding of patient's fluid status, cardiovascular function, and amount and type of blood products transfused is helpful in identifying the cause.

Álvarez P, Carrasco R, Romero-Dapueto C, et al. Transfusion-related acute lung injured (TRALI): current concepts. *Open Respir Med J*. 2015;9:92–96.

Gajic O, Gropper MA, Hubmayr RD. Pulmonary edema after transfusion: how to differentiate transfusion-associated circulatory overload from transfusion-related acute lung injury. *Crit Care Med*. 2006;34(5 suppl):S109–S113.

Skeate RC, Eastlund T. Distinguishing between transfusion related acute lung injury and transfusion associated circulatory overload. *Curr Opin Hematol*. 2007;14(6):682–687.

C.16. What techniques can be used to minimize transfusion requirements?

Several techniques can be used to minimize homologous blood

transfusion requirements and subsequent risks, such as alloimmunization, infections, immunosuppression, and graft-versus-host disease in addition to TRALI and TACO. A simple and important way to minimize bleeding is to minimize intra-abdominal pressure because any increase in abdominal pressure is transmitted to the vertebral venous plexus, increasing venous bleeding. Careful positioning will avoid external pressure on the abdomen, and muscle relaxants or deeper levels of anesthesia have been used to prevent a rise in abdominal wall tension.

Isovolemic hemodilution may also be used to minimize red blood cell loss during surgery. Before incision, the hematocrit is lowered 20% to 25% by removing blood aseptically and storing it in anticoagulated bags. Intravascular volume is maintained by replacing the blood with 3 times the volume of a balanced saline solution or an equal volume of colloid. Intraoperatively, the previously collected blood is replaced as needed. Obviously, this technique requires careful monitoring of intravascular volume status and hemoglobin level. Most patients will require a central venous catheter to perform this technique. Some patients who are Jehovah's Witnesses and will not accept blood transfusions may accept this type of blood conservation method if the tubing is kept connected because the blood in the bag and the tubing is in continuity with the circulation.

Salvaging of blood during the surgical procedure can play an important role as an adjunct to an autologous blood program. Using standard salvaging techniques, 50% to 60% of the red blood cells lost can be recovered, concentrated, washed, and returned to the patient using commercially available autotransfusion devices. These red blood cells are obviously lacking in platelets and plasma. Some Jehovah's Witness patients may also accept this technique if the autotransfusion device is kept in continuity with the circulation.

The use of an antifibrinolytic drug such as aminocaproic acid

or tranexamic acid has been shown to decrease blood loss in pediatric patients undergoing scoliosis surgery. These drugs may be of particular benefit in patients with neuromuscular scoliosis. These patients have significantly greater intraoperative blood loss compared to patients with idiopathic scoliosis, as much as a twofold to eightfold increased risk. The antifibrinolytic agent is administered as a loading dose followed by a continuous infusion before the activation of the fibrinolytic system, which occurs with surgical incision. It is important to administer the full loading dose before surgical incision for maximum benefit. Some centers choose to use aminocaproic acid as their antifibrinolytic of choice because tranexamic acid has been associated with postoperative seizures, especially at elevated doses. This is of particular importance in patients with neuromuscular scoliosis who often have an underlying seizure disorder.

Deliberate (controlled) hypotension has been frequently used until recently to decrease blood loss and improve operating conditions during spine fusion surgery. Decrease in blood loss and transfusion requirement has been less significant in spine surgery when compared with oral-maxillofacial surgery employing controlled hypotension techniques. Safety of moderate controlled hypotension (mean arterial pressure [MAP] 50 to 65 mmHg) with close monitoring of invasive arterial and central venous pressures in conjunction with SSEPs and MEPs has been documented.

However, the major concern of using deliberate hypotension during scoliosis surgery is the potential for spinal cord blood flow to be compromised with resultant spinal cord injury. This is of particular concern when the spine is distracted because levels of hypotension that are considered safe under normal conditions may compromise spinal cord blood flow after spine distraction. In addition, the use of deliberate hypotension can interfere with

neuromonitoring signals, particularly the MEPs. For these reasons, the potential benefits of controlled hypotension should be carefully considered and discussed with the surgeon.

Florentino-Pineda I, Thompson GH, Poe-Kochert C, et al. The effect of Amicar on perioperative blood loss in idiopathic scoliosis: the results of a prospective, randomized double-blind study. *Spine (Phila Pa 1976)*. 2004;29:233–238.

Kako H, Gable A, Martin D, et al. A prospective, open-label trial of clevidipine for controlled hypotension during posterior spinal fusion. *J Pediatr Pharmacol Ther*. 2015;20(1):54–60.

Lecker I, Wang D-S, Romaschin AD, et al. Tranexamic acid concentrations associated with human seizures inhibit glycine receptors. *J Clin Invest*. 2012;122(12):4654–4666.

Paul JE, Ling E, Lalonde C, et al. Deliberate hypotension in orthopedic surgery reduces blood loss and transfusion requirements: a meta-analysis of randomized controlled trials. *Can J Anaesth*. 2007;54:799–810.

Schouten ES, van de Pol AC, Schouten AN, et al. The effect of aprotinin, tranexamic acid, and aminocaproic acid on blood loss and use of blood products in major pediatric surgery: a meta-analysis. *Pediatr Crit Care Med*. 2009;10:182–190.

Sethna NF, Zurakowski D, Brustowicz RM, et al. Tranexamic acid reduces intraoperative blood loss in pediatric patients undergoing scoliosis surgery. *Anesthesiology*. 2005;102:727–732.

Tobias JD, Hoernschemeyer DG. Clevidipine for controlled hypotension during spinal surgery in adolescents. *J Neurosurg Anesthesiol*. 2011;23(4):347–351.

D. Postoperative Management

D.1. When would you extubate the patient?

The decision to continue mechanical ventilation in the postoperative period is often made preoperatively. Most patients with adolescent idiopathic scoliosis have mild-to-moderate pulmonary function abnormalities and may be extubated in the operating room after they have moved all extremities to the surgeon's satisfaction. Mechanical ventilation should be

continued in patients with severe restrictive lung defects (vital capacity less than 30% of predicted) or severe gas exchange abnormalities such as carbon dioxide retention. Postoperative mechanical ventilation should be considered for patients with Duchenne muscular dystrophy, familial dysautonomia, or severe cerebral palsy. Patients who are mechanically ventilated postoperatively should be managed by nurses and physicians in an intensive care setting. Patients should be sedated to tolerate the endotracheal tube, yet arousable enough to be examined every hour for potential neurologic complications. Dexmedetomidine is a good choice for short-term sedation in this population. It offers potent synergy with opioids for analgesia, and it is titrated easily for frequent wake-ups.

The parameters for extubation given below are the same as for other respiratory disorders:

- Vital capacity greater than 10 mL per kg
- Tidal volume greater than 3 to 6 mL per kg
- Spontaneous respiratory rate less than 30 per minute
- Negative inspiratory force greater than 30 cm H_2O

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:727–753.

Yuen VM. Dexmedetomidine: perioperative applications in children. *Paediatr Anaesth*. 2010;20:256–264.

D.2. What should be done to optimize pulmonary status?

Incentive spirometry should be taught preoperatively and should be used aggressively in the postoperative period. Coughing and deep breathing should be encouraged. Patients with obstructive or reactive airway disease will benefit from bronchodilators. Opioids should be used on a patient-controlled basis with the goal of providing adequate analgesia to allow coughing and incentive spirometry without excessive respiratory depression.

Coté CJ, Lerman J, Anderson BJ, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier Saunders; 2018:727–753.

D.3. What laboratory tests should be ordered postoperatively?

Upon the patient's arrival in the postanesthesia care unit, blood should be sent for analysis of arterial blood gases, hematocrit, serum electrolytes, blood urea nitrogen, serum creatinine, and, if blood loss has been significant, platelet count, prothrombin, and partial thromboplastin time. Determination of arterial blood gases should be repeated if clinically indicated. Hyponatremia with high urinary sodium excretion has been reported following scoliosis surgery and has been attributed to the syndrome of inappropriate antidiuretic hormone secretion (SIADH). These patients produce small amounts of concentrated urine and excrete large amounts of urinary sodium. Efforts to increase urine output by administration of fluid are unsuccessful and worsen the hyponatremia. Therefore, serum electrolyte concentrations should be measured at least every 12 hours for the first 24 hours and then daily for the first 2 days. Rapid decreases in serum sodium concentration or sodium concentrations less than 125 mEq per L may produce cerebral edema and seizures.

Lieh-Lai MW, Stanitski DF, Sarnaik AP, et al. Syndrome of inappropriate antidiuretic hormone secretion in children following spinal fusion. *Crit Care Med*. 1999;27(3):622–627.

Taal MW, Chertow GM, Marsden PA, et al, eds. *Brenner & Rector's the Kidney*. 10th ed. Philadelphia, PA: Elsevier Saunders; 2016:460–510.

D.4. What fluid therapy would you use postoperatively?

Significant losses of intravascular fluid continue to occur in the postoperative period. These should be replaced with balanced salt solution such as lactated Ringer's solution to maintain urine output at a minimum of 0.5 to 1 mL/kg/hr. Hypotonic fluids

should be avoided in the first 24 to 36 hours postoperatively. The risk for postoperative hyponatremia is increased if fluid replacement is excessive or if hypotonic fluid is administered. Some authors recommend the use of colloid replacement solutions because serum albumin is often decreased following scoliosis surgery.

Lieh-Lai MW, Stanitski DF, Sarnaik AP, et al. Syndrome of inappropriate antidiuretic hormone secretion in children following spinal fusion. *Crit Care Med*. 1999;27(3):622–627.

Taal MW, Chertow GM, Marsden PA, et al, eds. *Brenner & Rector's the Kidney*. 10th ed. Philadelphia, PA: Elsevier Saunders; 2016:460–510.

D.5. What complications may occur following scoliosis surgery?

The most common postoperative complications in patients undergoing posterior spinal fusion for idiopathic scoliosis include wound infection (1.35%), pulmonary complications excluding pulmonary embolism (0.95%), and neurologic injury (0.32%). The pulmonary complications that have been reported in the postoperative period include pneumothorax, atelectasis, pleural effusion, hemothorax, and thoracic duct injury. Pneumothorax may occur as a result of anterior and posterior surgical dissections as well as secondary to central venous line placement. A chest radiograph should be obtained upon arrival in the postanesthesia care unit. Atelectasis may occur because of prolonged supine positioning and the use of opioids. Anterior spine fusion by thoracotomy poses the greatest risk of pulmonary complications. Almost 100% of patients undergoing these procedures will develop some degree of atelectasis. Incentive spirometry and deep breathing should be emphasized and may require specialized nursing care.

In addition to intraoperative neurologic complications during instrumentation or distraction of the spine, delayed paraplegia

has been also been reported shortly after arrival in the recovery room and during the initial postoperative days. This emphasizes the need for continued monitoring of neurologic status postoperatively.

In the first few postoperative days, an ileus can occur, particularly in conjunction with opioid use. Less commonly, superior mesenteric artery syndrome has been reported to occur in 0.5% of patients. This presents with nausea, vomiting, and abdominal pain after a mean time of 7.2 days. This is probably due to compression of the distal third of the duodenum by the superior mesenteric artery as a result of anatomic changes related to straightening of the spine.

Altiok H, Lubicky JP, DeWald CJ, et al. The superior mesenteric artery syndrome in patients with spinal deformity. *Spine (Phila Pa 1976)*. 2005;30:2164–2170.

Coe JD, Arlet V, Donaldson W, et al. Complications in spinal fusion for adolescent idiopathic scoliosis in the new millennium. A report of the Scoliosis Research Society Morbidity and Mortality Committee. *Spine (Phila Pa 1976)*. 2006;31(3):345–349.

Kocher MS, Millis MB, eds. *Operative Techniques: Pediatric Orthopaedic Surgery*. Philadelphia, PA: Elsevier Saunders; 2011:719–730.

Stöckl B, Wimmer C, Innerhofer P, et al. Delayed anterior spinal artery syndrome following posterior scoliosis correction. *Eur Spine J*. 2005;14:906–909.

D.6. Upon arrival to the recovery room, you notice that the urine appears to be tea colored. What is your diagnosis, and how should this be managed?

Tea-colored urine (**Fig. 58.12**) in the setting of a prolonged surgical procedure suggests rhabdomyolysis. Other possible diagnoses include a hemolytic transfusion reaction or a drug reaction. The pathogenic process of rhabdomyolysis results from an increase of intracellular calcium causing a complex series of intracellular processes ultimately leading to prolonged muscle cell contraction, mitochondrial damage, and the production of

reactive oxygen species. Skeletal tissue necrosis ensues with the subsequent release of toxic muscle cell contents, notably myoglobin, into the systemic circulation.

FIGURE 58.12. Example of tea-colored urine secondary to rhabdomyolysis.

Initial diagnostic workup should include serum creatine kinase (CK), a full electrolyte panel, and serum creatinine. The presence of blood in the urine on dipstick testing without red blood cells on urinalysis suggests rhabdomyolysis. Patients can have a CK value 5 times normal. The major concern of rhabdomyolysis is acute kidney injury (AKI). The pathophysiology of rhabdomyolysis of induced AKI is multifactorial and includes myoglobin cast formation in the distal convoluted tubules and the direct cytotoxic action of myoglobin on renal tubular cells. Acidity of the urine predisposes to deposition of myoglobin in the tubules; thus, the urine should be alkalinized by infusion of sodium bicarbonate in

the intravenous fluids. In order to prevent precipitation of myoglobin, urine output should be maintained above normal during the initial resuscitation period (>1 mL/kg/hr). Management should also include correction of electrolyte abnormalities. Hyperkalemic cardiac arrest is a perilous complication that can occur in cases of severe rhabdomyolysis.

Chatzizisis YS, Misirli G, Hatzitolios AI, et al. The syndrome of rhabdomyolysis: complications and treatment. *Eur J Intern Med*. 2008;19:568–574.

Giannoglou GD, Chatzizisis YS, Misirli G. The syndrome of rhabdomyolysis: pathophysiology and diagnosis. *Eur J Intern Med*. 2007;18:90–100.

Papadakis M, Sapkas G, Tzoutzopoulos A. A rare case of rhabdomyolysis and acute renal failure following spinal surgery. *J Neurosurg Spine*. 2008;9(4):387–389.

Prabhu M, Samra S. An unusual cause of rhabdomyolysis following surgery in the prone position. *J Neurosurg Anesthesiol*. 2000;12(4):359–363.

D.7. How would you manage this patient's pain, nausea, and vomiting postoperatively?

Most centers advocate for the use of multimodal analgesia to optimize postoperative pain control in pediatric patients undergoing posterior spinal fusion. Patients with idiopathic scoliosis are typically developmentally mature enough to use intravenous patient-controlled analgesia (PCA). The two commonly employed opioids for PCA are hydromorphone and morphine. Many practitioners will initiate oral opioid therapy (e.g., oxycodone) once the patient is tolerating a diet with a goal to wean the PCA by the end of the first postoperative day or the beginning of the second. Perioperative gabapentin has been shown to decrease the amount of morphine needed postoperatively in patients with idiopathic scoliosis undergoing spinal fusion. Acetaminophen is an effective analgesic that can be given intravenously intraoperatively and continued orally postoperatively. Intravenous acetaminophen has been shown in

this patient population to improve analgesia but not decrease opioid needs. Diazepam is typically administered on an as needed basis for muscle spasms.

Recently, ketorolac has become more accepted as a postoperative pain adjunct, even for spine surgery. A meta-analysis in 2011 showed no increased risk of nonunion in spine patients receiving nonsteroidal anti-inflammatory drugs (NSAIDs) postoperatively. Patients at several children's centers receive it for 48 to 72 hours after spine surgery.

Antiemetics should be given prophylactically, starting in the operating room. Serotonin receptor antagonists are the first-line treatment, but dexamethasone may also be used. Histamine-2 receptor blockers can also be helpful the first few days. A transdermal scopolamine patch may be placed preoperatively for patients with risk factors (female of childbearing age, history of motion sickness or postoperative nausea, nonsmokers). More children's centers are also encouraging chewing gum postoperatively to speed the return of normal bowel function after spine surgery.

Dodwell ER, Latorre JG, Parisini E, et al. Do non-steroidal anti-inflammatory drugs inhibit bone healing? A meta-analysis of cohort and case control studies. *J Bone Joint Surg Br*. 2011;93(suppl 4):585–586.

Gan TJ. Risk factors for postoperative nausea and vomiting. *Anesth Analg*. 2006;102:1884–1898.

Hiller A, Helenius I, Nurmi E, et al. Acetaminophen improves analgesia but does not reduce opioid requirement after major spine surgery in children and adolescents. *Spine (Phila Pa 1976)*. 2012;37(20):E1225–E1231.

Jennings J, Doyle J, Gilbert S, et al. The use of chewing gum postoperatively in pediatric scoliosis patients facilitates an earlier return to normal bowel function. *Spine Deform*. 2015;3(3):263–266.

Rusy LM, Hainsworth KR, Nelson TJ, et al. Gabapentin use in pediatric spinal fusion patients: a randomized, double-blind, controlled trial. *Anesth Analg*. 2010;110(5):1393–1398.

59 Hypoxia and Equipment Failure

James B. Eisenkraft and
Garrett W. Burnett

A 60-year-old woman with a past medical history of type II diabetes mellitus is to undergo robotic-assisted laparoscopic hysterectomy, bilateral salpingo-oophorectomy, and node dissection under general anesthesia and in steep Trendelenburg position. Breathing room air (fraction of inspired oxygen [F_{IO_2}] = 0.21), her pulse oximeter saturation reading (Spo_2) is 94%.

A. Medical Disease and Differential Diagnosis

1. What is hypoxia, and what is hypoxemia?
2. Is the partial pressure of oxygen in arterial blood (Pao_2) related to age?
3. Was this patient hypoxemic?
4. What is a pulse oximeter, and what is a hemoximeter?
5. How does a pulse oximeter work?
6. How is a two-wavelength pulse oximeter calibrated by the manufacturer?
7. What may affect the accuracy of a two-wavelength pulse oximeter?
8. How do the dyshemoglobins, methemoglobin (metHb), and

carboxyhemoglobin (HbCO) affect Spo_2 readings?

9. What is a capnometer, and what is capnography? Of what value are they in patient monitoring?
10. What is meant by the term *end-tidal carbon dioxide* ($EtCO_2$)?
11. What is the appearance of a normal capnogram, and what is its significance?
12. What are mainstream and sidestream capnometers?
13. Show some common capnograms and provide a differential diagnosis of each event.
14. What is the arterial–alveolar difference in carbon dioxide (CO_2)?
15. What are some of the important safety features of the contemporary anesthesia workstation?
16. What are the common sites for gas leakage?
17. How is the anesthesia machine checked for leaks?

B. Preoperative Evaluation and Preparation

1. What should be included in the equipment checkout in preparation for anesthesia?
2. What emergency equipment should be easily available to the anesthesiologist?
3. How should this patient be premedicated?

C. Intraoperative Management

1. How should this patient be monitored?
2. Following uncomplicated induction of anesthesia and endotracheal intubation, the procedure begins. Upon insufflation of the abdomen with CO_2, the Spo_2 decreases to 78%. What acute diagnostic and therapeutic interventions would you perform?
3. The endotracheal tube was withdrawn 2 cm. Squeezing the reservoir bag in the circle breathing system failed to generate positive pressure in the circuit. What are the common sites for

gas leaks in the circle breathing system?

4. The patient was taken out of Trendelenburg position. Direct laryngoscopy revealed the endotracheal tube to be supraglottic. Additionally, green secretions were noted to be pooled in the posterior pharynx. What should be done next?

D. Postoperative Management

1. What criteria would you use for tracheal extubation?
2. What are the causes of postoperative hypoxemia?
3. What is the difference between shunt, ventilation/perfusion mismatch, and dead space?
4. Postoperatively, the patient developed hypoxia and pulmonary edema. What is the differential diagnosis of pulmonary edema? What is the most likely cause of pulmonary edema in this patient?
5. How should the ventilator be set if mechanical ventilation is required postoperatively?
6. If this patient had acute respiratory distress syndrome (ARDS) secondary to aspiration, besides low-tidal volume ventilation, what other changes in routine therapy should be considered?
7. What therapies routinely administered by the anesthesiologist may cause acute lung injury?
8. What methods of oxygen administration may be used postoperatively?

A. Medical Disease and Differential Diagnosis

A.1. What is hypoxia, and what is hypoxemia?

Hypoxia is defined as reduction of oxygen supply to tissue below physiologic levels. Hypoxemia is defined as deficient oxygenation of the blood. From the anesthesiologist's perspective, hypoxia is usually considered to be decreased oxygen tension (Po_2) inside the body at the tissue level or

outside the body (e.g., hypoxic gas mixture), and hypoxemia is decreased oxygen tension in the arterial blood (PaO_2).

Dorland WAN. *Dorland's Illustrated Medical Dictionary*. 32nd ed. Philadelphia, PA: Saunders; 2012.

Longnecker DE, Newman MF, Zapol WM, et al, eds. *Anesthesiology*. 3rd ed. New York: McGraw-Hill; 2018:411–424.

A.2. Is the partial pressure of oxygen in arterial blood (PaO_2) related to age?

Yes. There is an age-dependent decrease in the PaO_2. Sorbini et al. suggested the following relationship in subjects breathing room air:

$$\text{Mean } PaO_2 \text{ in mmHg} = 109 - 0.43 \text{ (age in years) mmHg}$$

About this regression line, there are 95% confidence limits (2 standard deviations [SDs]) of 10 mmHg.

Cerveri et al. studied PaO_2 in normal nonsmoking subjects aged 40 to 90 years. They found that PaO_2 was related to age in subjects between 40 and 74 years and constructed the following reference equation:

$$PaO_2(\text{mmHg}) = 143.6 - (0.39 \times \text{age}) - (0.56 \times \text{body mass index [BMI]}) - (0.57 \times PaCO_2)$$

For subjects ≥75 years old, there was no correlation with age.

Cerveri I, Zoia MC, Fanfulla F, et al. Reference values of arterial oxygen tension in the middle-aged and elderly. *Am J Respir Crit Care Med*. 1995;152:934–941.

Sorbini CA, Grassi V, Solinas E, et al. Arterial oxygen tension in relation to age in healthy subjects. *Respiration*. 1968;25:3–13.

A.3. Was this patient hypoxemic?

No. An SpO_2 reading of 94% does not signify hypoxemia when the age of the patient is taken into consideration. Using Sorbini

et al.'s equation for expected Pa_{O_2}:

$$PaO_2 = 109 - (0.43 \times 60) = 83 \text{ mmHg}$$

Assuming normal adult hemoglobin, temperature, and pH, this Pa_{O_2} corresponds to a hemoglobin oxygen saturation of approximately 94% on the normal hemoglobin oxygen saturation versus P_{O_2} curve.

Although the definitions of hypoxemia given in sections A.1 and A.2 must take age into consideration, from a practical point of view, hypoxemia (in the absence of anemia) is generally considered to exist when the Pa_{O_2} is less than 60 mmHg, which is equivalent to a hemoglobin oxygen saturation of 90%.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:169–202.

A.4. What is a pulse oximeter, and what is a hemoximeter?

The pulse oximeter is a noninvasive device that provides a real-time estimate (designated the Spo_2%) of the arterial hemoglobin saturation with oxygen. It is a transmissive oximeter in which the patient's fingertip (or other probe site; e.g., earlobe) serves as an in vivo cuvette through which light at two different wavelengths is transmitted.

If one requires an accurate determination of the arterial hemoglobin saturation with oxygen, an arterial blood sample must be drawn and analyzed in a laboratory co-oximeter, sometimes called a *hemoximeter*. The laboratory co-oximeter is a transmissive oximeter that uses numerous wavelengths of light (e.g., radiometer's co-oximeter uses 128 wavelengths of light) to measure total hemoglobin (Hb_{TOT}), oxygenated hemoglobin (Hbo_2), deoxygenated ("reduced") hemoglobin (RHb), metHb, Hb_{CO}, and other dyshemoglobins, such as sulfhemoglobin.

Because each species of hemoglobin has a characteristic absorbance spectrum (i.e., absorbance vs. wavelength), examination of a sample of blood using these six or eight wavelengths permits identification and quantification of each hemoglobin species. Conventional pulse oximeters use only two wavelengths of light; therefore, they are unable to determine all of the different hemoglobin species and assume that only HbO_2 and RHb are present. *Fractional saturation* (*HbO_2%*) is defined as HbO_2 / (HbO_2 + RHb + HbCO + metHb)—that is, HbO_2 per total Hb. *Functional saturation (SaO_2)* is defined as HbO_2 / (HbO_2 + RHb). Note that dyshemoglobins are absent from the denominator in the definition of SaO_2.

Ehrenwerth J, Eisenkraft JB, Berry JM, eds. *Anesthesia Equipment: Principles and Applications*. 2nd ed. New York: Elsevier; 2013:256–270.

A.5. How does a pulse oximeter work?

The pulse oximeter combines the technologies of spectrophotometry and optical plethysmography. In the pulse oximeter probe, light-emitting diodes transmit red light at wavelength 660 nm and infrared light at wavelength 940 nm through the fingertip or other probe site. Light that passes through the probe site is sensed by a single photodetector and expressed as absorbance at each wavelength. It can be shown that the ratio of absorbances, 660/940 nm, is related to the hemoglobin saturation with oxygen. This is spectrophotometry. Detection of pulsatile flow is by optical plethysmography. With each pulse of arterial blood, the probe site (e.g., fingertip) increases in volume, the path length of the transmitted light increases, and the absorbance of light at 660 nm and 940 nm increases. This *pulse-added* absorbance is considered to be due to the pulsatile flow of arterial blood at the probe site, so that the ratio of pulse-added absorbances, 660/940 nm, can be used to

provide an estimate of hemoglobin oxygen saturation in arterial blood.

Ehrenwerth J, Eisenkraft JB, Berry JM, eds. *Anesthesia Equipment: Principles and Applications*. 2nd ed. New York: Elsevier; 2013:256–270.

Pologe JA. Pulse oximetry: technical aspects of machine design. *Int Anesthesiol Clin*. 1987;25:137–153.

A.6. How is a two-wavelength pulse oximeter calibrated by the manufacturer?

Each pulse oximeter manufacturer creates an empiric calibration algorithm, that is, one based on observations in human volunteers. The algorithm relates the average ratio of pulse-added absorbances, 660/990 nm, to the actual hemoglobin oxygen saturation in arterial blood samples drawn simultaneously and analyzed in a laboratory hemoximeter. Observations are made with the volunteers breathing varying F_{IO_2} values so that data for saturations as low as 70% are obtained. The calibration algorithm that is created relates the ratio (R) of pulse-added absorbances, 660/940 nm, to the laboratory hemoximeter readings of Hb_{O_2} or Sa_{O_2}% (depending on the pulse oximeter manufacturer). The calibration algorithm is then stored in the software of the pulse oximeter as a "lookup" table. Therefore, the pulse oximeter merely measures R, consults its lookup table, and displays the corresponding saturation reading as Sp_{O_2}. The pulse oximeter does not actually measure saturation; it infers it from R, and therefore, it predicts what the laboratory hemoximeter would read if an arterial sample drawn at that moment were analyzed.

A high value for R corresponds to a low Sp_{O_2} reading; R = 1 corresponds to an Sp_{O_2} reading of 85%, and a low value for R corresponds to a high Sp_{O_2} reading. Whenever the Sp_{O_2} reading is approximately 85%, one should consider the possibility of a

spurious reading as a result of the "R = 1" phenomenon. This is commonly due to malpositioning of the probe on the fingertip.

The pulse oximeter (Spo_2) reading is usually specified by the manufacturer to have an SD of ±2%. Therefore, assuming a normal distribution, if the Spo_2 reading is 96%, there is a 68% likelihood that the true saturation (as measured by a hemoximeter) is 96% ± 2% (i.e., ±1 SD) and a 95% likelihood that the true saturation is 96% ± 4% (i.e., ±2 SD).

Guan Z, Baker K, Sandberg WS. Misalignment of disposable pulse oximeter probes results in false saturation readings that influence anesthetic management. *Anesth Analg*. 2009;109:1530–1533.

Kelleher JF, Ruff RH. The penumbra effect: vasomotion-dependent pulse oximeter artifact due to probe malposition. *Anesthesiology*. 1989;71:787–791.

A.7. What may affect the accuracy of a two-wavelength pulse oximeter?

The two-wavelength pulse oximeter is most accurate when the conditions of its clinical use most closely resemble those of its calibration. Spurious readings or failure may occur during patient movement (e.g., shivering, peripheral nerve stimulation, "twitching"), presence of intense ambient light (low signal/noise ratio), electrocautery use, administration of intravenous dyes with absorbance peaks at 660 nm (e.g., methylene blue), presence of dyshemoglobins (e.g., metHb, HbCO, and sulfhemoglobin), certain colors of nail polish, poor pulsatile flow at the probe site (e.g., hypotension, vasoconstriction, Raynaud disease), and venous pulsations (e.g., tricuspid regurgitation or earlobe placement of the probe in a patient who is in a head-down position).

Recent improvements in pulse oximetry technology include paradigms to increase the signal/noise ratio, thereby permitting motion artifact reduction and increased sensitivity to pulsatile flow. Such pulse oximeters have significantly lower failure rates

during patient movement (such as in the postanesthesia care unit) and during conditions of low flow (e.g., hypothermia).

Barker SJ. "Motion-resistant" pulse oximetry: a comparison of new and old models. *Anesth Analg*. 2002;95:967–972.

Ehrenwerth J, Eisenkraft JB, Berry JM, eds. *Anesthesia Equipment: Principles and Applications*. 2nd ed. New York: Elsevier; 2013:256–270.

A.8. How do the dyshemoglobins, methemoglobin (metHb), and carboxyhemoglobin (HbCO) affect Spo_2 readings?

In metHb, iron in the heme moiety is oxidized (such as by dapsone, benzocaine, nitric oxide, prilocaine) to the Fe^{3+} state rather than being in the normal Fe^{2+} state. metHb cannot carry oxygen and creates a physiologic anemia. The absorbance spectrum for metHb shows it to have similar absorbances to light at 660 nm and 940 nm. Therefore, the more metHb that is present, the more R tends toward 1 and the Spo_2 reading toward 85%. In the presence of metHb, the Spo_2 reading overestimates the Hbo_2% and underestimates the Sao_2.

In carbon monoxide (CO) poisoning, CO combines with hemoglobin to create a physiologic hypoxemia. HbCO has a similar absorbance to Hbo_2 at 660 nm but a very low absorbance at 940 nm. In the presence of HbCO, the Spo_2 overestimates Hbo_2% and underestimates functional saturation. Although blood that is poisoned with CO appears "cherry red" to the naked eye, and therefore may look like it is fully saturated with oxygen, it is important to recognize that the ratio of absorbances 660/940 nm will suggest that the blood hemoglobin oxygen saturation is in the 90s. In a subject breathing an Fio_2 of 1 (when functional saturation is 100%), as the level of HbCO increases, Spo_2 decreases from close to 100% to approximately 91%.

If the presence of dyshemoglobins is suspected, arterial blood

must be drawn and analyzed in a laboratory hemoximeter to obtain accurate readings of saturation.

Pulse oximetry technology has evolved rapidly, and multiwavelength pulse oximeters, called pulse co-oximeters, are clinically available. They use more than seven wavelengths of light (Masimo Rainbow SET Pulse CO-Oximetry, Masimo Company, Irvine, CA), similar to a laboratory hemoximeter. This technology makes it possible to estimate carboxyhemoglobin (SpCO), methemoglobin (SpMet), and total hemoglobin (SpHbt), all noninvasively and in real time.

It should be noted that while continuous noninvasive total hemoglobin measurement provides information in real time, it may have a wide limits of agreement when compared to a traditional invasive laboratory value. Due to this, patients who have low SpHbTOT on a noninvasive monitor should have confirmation by sending a blood sample to the laboratory for analysis.

Barker SJ, Curry J, Redford D, et al. Measurement of carboxyhemoglobin and methemoglobin by pulse oximetry: a human volunteer study. *Anesthesiology*. 2006;105:892–897.

Kim SH, Lilot M, Murphy LS, et al. Accuracy of continuous noninvasive hemoglobin monitoring: a systematic review and meta-analysis. *Anesth Analg*. 2014;119:332–346.

Miller RD, Ward TA, Shiboski SC, et al. A comparison of three methods of hemoglobin monitoring in patients undergoing spine surgery. *Anesth Analg*. 2011;112:858–863.

Shamir MY, Avramovich A, Smaka T. The current status of continuous noninvasive measurement of total, carboxy, and methemoglobin concentration. *Anesth Analg*. 2012;114:972–978.

A.9. What is a capnometer, and what is capnography? Of what value are they in patient monitoring?

A capnometer is a device that measures the tension (in units of millimeters of mercury [mmHg] or kilopascals [kPa]) or

concentration (volumes %) of CO_2 in the gas near the patient's airway throughout the respiratory cycle. Capnography is the graphic display of the CO_2 concentration on the y-axis against time on the x-axis.

Capnometry may be achieved using different technologies that can monitor CO_2. Most capnometers now use infrared spectroscopy to measure the P_{CO_2} (i.e., CO_2 partial pressure in millimeters of mercury). A built-in barometer measures barometric pressure (P_B) so that CO_2 can also be displayed as a percentage ($P_{CO_2} \times 100/P_B = \%CO_2$).

Capnography is one of the American Society of Anesthesiologists' standards for basic anesthetic monitoring (i.e., "Continual monitoring for the presence of expired CO_2 shall be performed unless invalidated by the nature of the patient, procedure or equipment."). It is the "gold standard" for establishing the presence of ventilation.

American Society of Anesthesiologists. *Standards for Basic Anesthetic Monitoring*. Schaumburg, IL: American Society of Anesthesiologists; 2010. Last affirmed on October 28, 2015.

Ehrenwerth J, Eisenkraft JB, Berry JM, eds. *Anesthesia Equipment: Principles and Applications*. 2nd ed. New York: Elsevier; 2013:245–254.

A.10. What is meant by the term *end-tidal carbon dioxide ($EtCO_2$)*?

Et_{CO_2} is the tension of CO_2 in the exhaled gas at the end of an exhalation. Because this gas originates from the alveoli, it is considered to represent the CO_2 tension in the alveolar gas (P_{ACO_2}). The P_{ACO_2} results from the combination of gases coming from ideal alveoli, where ventilation and perfusion are perfectly matched and the CO_2 concentration is the same as arterial (Pa_{CO_2}), and alveolar dead space (alveoli that are ventilated but not perfused) where CO_2 concentration is the

same as inspired (P_{ICO_2}) and is normally zero.

The presence of a normal capnogram and Et_{CO_2} depends on (1) production of CO_2 by the tissues, (2) cardiac output and pulmonary blood flow to carry CO_2 to the lungs, and (3) ventilation. Monitoring of Et_{CO_2} can be used to adjust the setting of a mechanical ventilator and monitor ventilation as well as to detect ventilator malfunctions and breathing system problems, such as leaks, incompetent unidirectional valves, exhausted CO_2 absorbent, metabolic problems (e.g., malignant hyperthermia), and gas embolism.

Ehrenwerth J, Eisenkraft JB, Berry JM, eds. *Anesthesia Equipment: Principles and Applications*. 2nd ed. New York: Elsevier; 2013:245–254.

Lumb AB. Carbon dioxide. In: *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:151–167.

A.11. What is the appearance of a normal capnogram, and what is its significance?

A typical normal capnogram (P_{CO_2} vs. time) is shown in **Figure 59.1**. Four phases have been described.

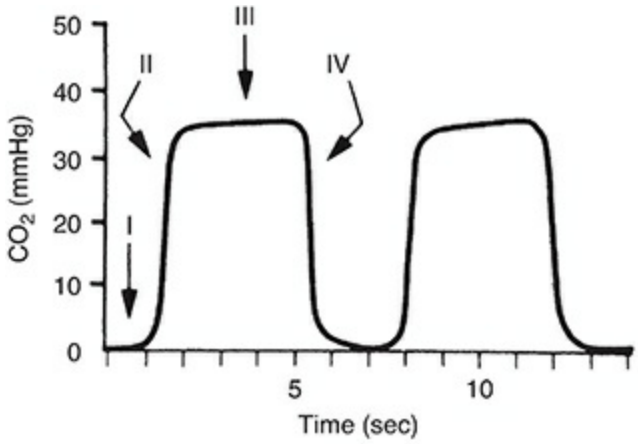

FIGURE 59.1. Phases of the normal capnogram. (*Phase I*) Inspiratory baseline. (*Phase II*) Expiratory upstroke. (*Phase III*) Expiratory plateau. (*Phase IV*) Inspiratory downstroke. (*Reprinted with permission from Good ML. Capnography. Uses, interpretation, and pitfalls. In*: ASA Refresher Courses in Anesthesiology. *1990;18:179.*)

Phase I. This is the expiratory baseline. During exhalation, CO_2-free gas from the mechanical (apparatus) dead space (e.g., flexible or "goose-neck" connector) and anatomic dead space (large conducting airways) flows past the CO_2 sampling port.

Phase II. This is the expiratory upstroke. It is due to CO_2 from alveoli mixed with anatomic dead space gas passing the gas sampling port and is usually a steep upslope.

Phase III. This is the expiratory or alveolar plateau and is due to alveolar CO_2.

In patients with healthy lungs, it is nearly horizontal, but in patients with obstructive airway disease, there is a more pronounced upward slope. The maximum expired CO_2 is usually considered as the Et_{CO_2}.

Phase IV. This is the inspiratory downstroke. During the commencement of inspiration, fresh (i.e., CO_2-free) gas is inhaled past the sensor, and the capnogram falls sharply to baseline.

The angle between the upstroke of phase II and the plateau of phase III is referred to as the *α angle*. The angle between phase III and IV is the *β angle*. An increase in the *α* angle and slope of phase III is seen commonly in acute bronchospasm. The angle usually decreases with treatment of the bronchospasm.

Ehrenwerth J, Eisenkraft JB, Berry JM, eds. *Anesthesia Equipment: Principles and Applications*. 2nd ed. New York: Elsevier; 2013:245–254.

Lumb AB. Carbon dioxide. In: *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:151–167.

A.12. What are mainstream and sidestream capnometers?

In a mainstream or nondiverting type of analyzer, the gas analyzer sensor is brought to the airway itself, and no gas is removed from the breathing system. A cuvette with a quartz

window is placed between the breathing system Y-piece and the tracheal tube connector. As respired gases flow past the window in the cuvette, a beam of infrared radiation (wavelength 4.3 μm) is directed through the window. Absorbance of infrared radiation at 4.3 μm is used to measure P_{CO_2}. Advantages of the nondiverting analyzer are rapid response time, accurate waveform, and no need to scavenge gases. Disadvantages are that this additional device in the airway can be a site for a disconnect and needs sterilization (or replacement of a disposable single-use cuvette) between cases, needs to be heated because water vapor condensing on the window causes error, and can be blocked by secretions or blood on its window.

A sidestream or diverting gas analyzer aspirates gas from the breathing circuit through a sampling adapter placed by the airway. The sampled gas passes through a sampling catheter (usually 6 to 10 ft in length) to reach the gas analyzer. Advantages of diverting analyzers are that the breathing circuit adapter is disposable. The analyzer, being remote from the airway, can be more versatile and incorporate several technologies in one "box" to analyze multiple gases (e.g., infrared analysis for CO_2, nitrous oxide, anesthetic agents; paramagnetic sensor or fuel cell for oxygen). Disadvantages of sidestream sampling analysis are slower response times, the possibility of sampling leaks, errors resulting from the length of the gas sampling tube, the need to scavenge gases from the analyzer after analysis, and susceptibility of the sampling tube to becoming clogged by water or secretions. Because of their versatility in regard to gas monitoring, most anesthetizing locations now use sidestream sampling analyzers.

Ehrenwerth J, Eisenkraft JB, Berry JM, eds. *Anesthesia Equipment: Principles and Applications*. 2nd ed. New York: Elsevier; 2013:191–222.

A.13. Show some common capnograms and provide a

differential diagnosis of each event.

Elevated baseline equals the amount of CO_2 present in inspired gas (**Fig. 59.2A**).

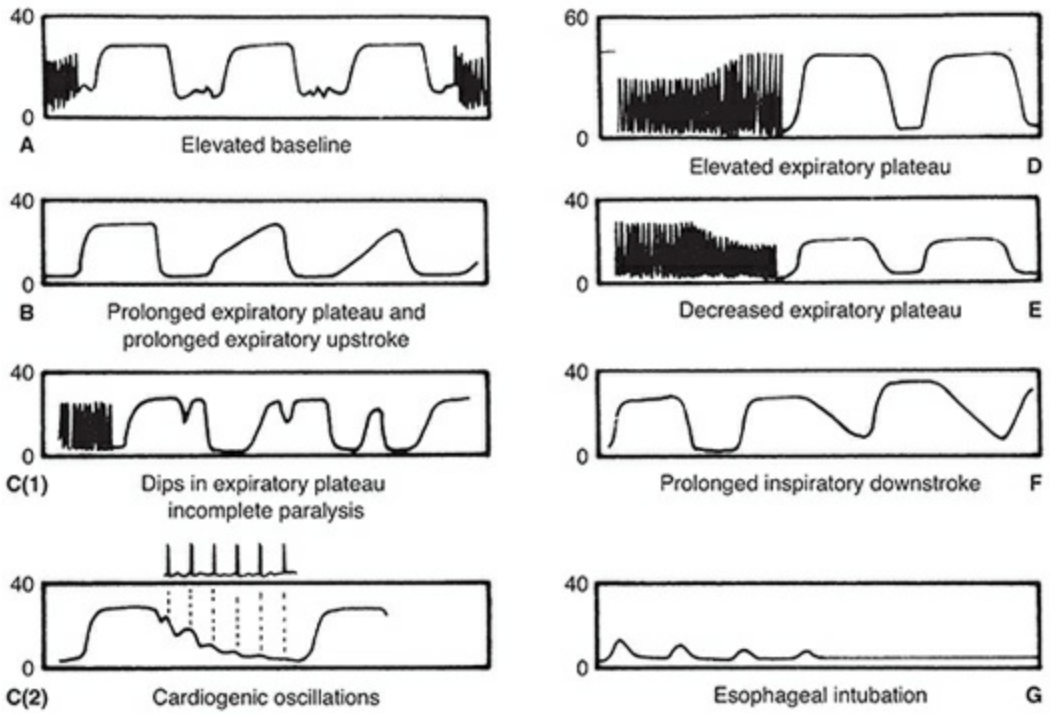

FIGURE 59.2. Abnormal capnograms.

- Capnometer not properly calibrated to zero
- Delivery of CO_2 to breathing system through fresh gas inflow
- Incompetent unidirectional valves
- Failure of CO_2 absorber (channeling, exhaustion, bypass)

Prolonged expiratory plateau and expiratory upstroke (**Fig. 59.2B**)

- Mechanical obstruction to exhalation
- Chronic obstructive pulmonary disease
- Bronchospasm

Dips in expiratory plateau (**Fig. 59.2C[1]**)

- Patient making spontaneous inspiratory effort
- "Curare cleft"

Cardiogenic oscillations if synchronized with

electrocardiogram (**Fig. 59.2C[2]**)

- Ventilator pressure relief valve perturbations

Elevated expiratory plateau (**Fig. 59.2D**)

- Incorrect calibration
- Increased CO_2 production/delivery versus laparoscopic CO_2 gas insufflation
- Decreased CO_2 removal
- Hypoventilation
- Leak

Decreased expiratory plateau (**Fig. 59.2E**)

- Incorrect calibration
- Air leak into gas sampling system
- Hyperventilation
- Decreased CO_2 production (hypothermia)
- Increased arterial–alveolar CO_2 gradient (ventilation/perfusion mismatch pulmonary embolus)

Prolonged inspiratory downstroke and raised baseline (**Fig. 59.2F**)

- Incompetent or missing inspiratory unidirectional valve
- Inspiratory obstruction to gas flow (e.g., kinked tracheal tube)

Esophageal intubation (**Fig. 59.2G**)

- As CO_2 that has been insufflated into the stomach during bag-mask ventilation or produced as a result of ingestion of a carbonated beverage is washed out during esophageal ventilation, the CO_2 waveform disappears within a few breaths.

Ehrenwerth J, Eisenkraft JB, Berry JM, eds. *Anesthesia Equipment: Principles and Applications*. 2nd ed. New York: Elsevier; 2013:245–254.

A.14. What is the arterial–alveolar difference in carbon dioxide (CO_2)?

The arterial–alveolar difference in CO_2 is usually expressed as

the difference between the arterial and Et_{CO_2} tensions. In an ideal alveolus, the Pa_{CO_2} equals P_{ACO_2} and the "Pa_{CO_2}–P_{ACO_2}" difference is zero. Ventilation of unperfused alveoli leads to alveolar dead space or wasted alveolar ventilation. Because the Et_{CO_2} comprises gas from both ideal and dead space alveoli, the Pa_{CO_2}–P_{ACO_2} difference is a measure of alveolar dead space ventilation. For example,

$$\begin{aligned}
&\text{Tidal volume} = 500\ \text{mL, anatomic dead space} = 150\ \text{mL}\\
&\text{PaCO}_2 = 40\ \text{mmHg; EtCO}_2 = 36\ \text{mmHg}\\
&\text{Alveolar tidal volume} = (500 - 150) = 350\ \text{mL}\\
&\text{Ratio of}\ \frac{\text{Alveolar dead space}}{\text{Alveolar tidal volume}} = \frac{(\text{PaCO}_2 - \text{EtCO}_2)}{\text{PaCO}_2} = \frac{(40 - 36)}{40} = 10\%
\end{aligned}$$

Therefore, 350 mL × 10% = 35 mL of wasted ventilation from each alveolar tidal volume.

$$\begin{aligned}
&\text{Ideal alveolar ventilation} = (350 - 35) = 315\ \text{mL per breath}\\
&\text{In this example, physiologic dead space} = \text{anatomic} + \text{alveolar}\\
&\qquad = 150 + 35 = 180\ \text{mL per breath}\\
&\frac{\text{Physiologic dead space}}{\text{Tidal volume}} = \frac{185}{500} = 37\%
\end{aligned}$$

Therefore, Pa_{CO_2}–Et_{CO_2} measures alveolar dead space ventilation as a percentage of total *alveolar* ventilation. The alveolar dead space is increased by ventilation in excess of perfusion or a decrease in perfusion, such as occurs with pulmonary embolism. Shunt has minimal effect on the Pa_{CO_2}–Et_{CO_2} difference.

The Pa_{CO_2}–Et_{CO_2} difference is normally 3 to 5 mmHg in the patient under general anesthesia, but it is not constant. Therefore, although one commonly uses Et_{CO_2} to noninvasively estimate Pa_{CO_2}, only analysis of an arterial blood sample in a blood gas analyzer can provide an accurate measure of Pa_{CO_2}, and this should be measured when critical, such as during

neurosurgical anesthesia.

Lumb AB. Carbon dioxide. In: *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:151–167.

A.15. What are some of the important safety features of the contemporary anesthesia workstation?

Because most problems with anesthesia machines are due to use error, safety design of the contemporary workstation is at four levels.

Features Intended to Prevent Human Error

The medical gas pin index and diameter index safety systems ensure that medical gas connections are made correctly. Therefore, one cannot hang a nitrous oxide cylinder in an oxygen hanger yoke or connect a nitrous oxide hose to the oxygen pipeline inlet of the machine.

The "fail-safe" valve is a pressure-sensitive device that interrupts flow of all hypoxic gases on the machine to their flow control valves if the supply pressure of oxygen in the intermediate-pressure system (i.e., components downstream of the first stage oxygen regulator that reduces the high pressure in the tank to 45 lb psi, and upstream of the oxygen flow control needle valve) falls below a threshold (approximately 20 psi in GE machines; 12 psig in Dräger machines).

When the pressure of oxygen in the intermediate-pressure system falls below 30 psig, an oxygen supply pressure failure alarm is annunciated. The oxygen flow control knob is "touch coded"; that is, it is fluted and larger in diameter than the other gas flow control knobs and is normally located on the right of all other gas flow control valves. In the Dräger Fabius GS workstation, the gas flow controls are arranged vertically, with the oxygen flow control knob as the lowest.

Key-fill systems for anesthesia vaporizers are safety features

that also decrease the likelihood of atmospheric contamination during vaporizer filling. The most important of such systems is the Safe-T-Fill system used on desflurane bottles and desflurane vaporizers because filling a vaporizer specific for another agent with desflurane could result in a lethal overdose of desflurane.

A pressure relief valve built into the machine common gas outlet, breathing system, or ventilator provides some protection against positive pressure barotrauma.

Features to Correct for Use Error

Gas flow proportioning systems ensure a minimum oxygen concentration of 25% when nitrous oxide and oxygen are being used. Therefore, if the anesthesiologist were to accidentally attempt to increase the flow of nitrous oxide, either the oxygen flow would be increased automatically or the flow of nitrous oxide would be limited according to the flow of oxygen that was set.

On older machines, during use of the anesthesia ventilator, changes in fresh gas flow, inspiratory–expiratory (I:E) ratio, or respiratory rate cause changes in delivered tidal volume that might result in over-ventilation, under-ventilation, or even barotrauma. On modern systems (e.g., GE workstations that incorporate a ventilator with the Smart Vent feature; Dräger Fabius GS, and Dräger Apollo workstations), once the ventilation parameters have been set; they are maintained because the ventilator or circuit automatically compensates for changes in fresh gas flow settings. In the GE workstations with Smart Vent, tidal volume is monitored continually by a computer. If measured tidal volume changes from that set to be delivered, the computer adjusts the volume delivered by the ventilator bellows. Dräger workstations use fresh gas decoupling to maintain a constant tidal volume. In this system, during the inspiratory phase, a decoupling valve closes so that fresh gas

entering the breathing system is directed into the reservoir bag and only gas from the ventilator is delivered to the patient. During exhalation, the ventilator chamber refills from the fresh gas flow and the fresh gas that was collected in the reservoir bag during the previous inspiration.

A vaporizer interlock system prevents the unintentional simultaneous use of more than one vaporizer.

Monitoring Systems

A monitor of oxygen in the gas delivered to the patient is mandatorily enabled, and the low oxygen concentration alarm is activated whenever the anesthesia workstation is capable of delivering an anesthetic gas mixture into the breathing system.

Other monitors in the anesthesia workstation include pressure, volume, flow, and gas composition. Some also incorporate airway gas flow monitoring. The breathing system low-pressure monitor alarm is automatically enabled when the ventilator is turned on.

Alarm Systems

Contemporary workstations incorporate an integrated prioritized alarm system with visible and audible alerts when set parameter limits are exceeded.

An important safety feature of all modern machines/workstations is the preuse checkout. In 1993, the U.S. Food and Drug Administration (FDA) published anesthesia apparatus checkout recommendations. The machine should be checked by an educated user. Item 1 on the FDA checklist is that an alternative means to ventilate the patient's lungs should be present and functioning. Therefore, if a problem arises with the machine, the patient's lungs can be ventilated using a self-inflating resuscitation bag (e.g., Ambu bag). If a machine problem arises and the cause/remedy is not immediately obvious, one should instinctively reach for the self-inflating

resuscitation bag and call for help. A recent analysis of the American Society of Anesthesiologists Closed Claims Project data found that 35% of adverse outcomes were likely preventable if a proper preuse checkout had been performed.

In 2008, recognizing that not all of the FDA 1993 checkout recommendations can be applied to many of the contemporary anesthesia workstations, the American Society of Anesthesiologists published guidelines applicable to all anesthesia delivery systems so that individual departments can develop their own workstation-specific preuse checkout that can be performed consistently and expeditiously. The 2008 guidelines are intended to provide a template for developing checkout procedures that are appropriate for each individual anesthesia machine design and practice setting. They discuss which systems and components should be checked, the checkout interval (e.g., before first case vs. before every case), and who may be responsible for performing each checkout procedure—the anesthesiologist or technician (**Table 59.1**). Examples of user-developed workstation-specific checkouts are available on the American Society of Anesthesiologists' website (http://www.asahq.org).

TABLE 59.1 Preanesthesia Equipment Checkout Procedures

To Be Completed Daily		Responsible Party
Item to Be Completed		
Item 1:	Verify auxiliary oxygen cylinder and self-inflating manual ventilation device are available and functioning.	Provider and Tech
Item 2:	Verify patient suction is adequate to clear the airway.	Provider and Tech
Item 3:	Turn on anesthesia delivery system and confirm that AC power is available.	Provider and Tech
Item 4:	Verify availability of required monitors, including alarms.	Provider and Tech
Item 5:	Verify that pressure is adequate on the spare oxygen cylinder mounted on the anesthesia machine.	Provider and Tech
Item 6:	Verify that the piped gas pressures are ≥50 psig.	Provider and Tech

Item 7:	Verify that vaporizers are adequately filled and, if applicable, that the filler ports are tightly closed.	Provider and Tech
Item 8:	Verify that there are no leaks in the gas supply lines between the flowmeters and the common gas outlet.	Provider and Tech
Item 9:	Test scavenging system function.	Provider and Tech
Item 10:	Calibrate, or verify calibration of, the oxygen. Monitor and check the low oxygen alarm.	Provider and Tech
Item 11:	Verify carbon dioxide absorbent is not exhausted.	Provider and Tech
Item 12:	Breathing system pressure and leak testing	Provider and Tech
Item 13:	Verify that gas flows properly through the breathing circuit during both inspiration and exhalation.	Provider and Tech
Item 14:	Document completion of checkout procedures.	Provider and Tech
Item 15:	Confirm ventilator settings and evaluate readiness to deliver anesthesia care. (ANESTHESIA TIME OUT)	Provider

To Be Completed Prior to Each Procedure		Responsible Party
Item to Be Completed		
Item 2:	Verify patient suction is adequate to clear the airway.	Provider and Tech
Item 4:	Verify availability of required monitors, including alarms.	Provider or Tech
Item 7:	Verify that vaporizers are adequately filled and, if applicable, that the filler ports are tightly closed.	Provider
Item 11:	Verify carbon dioxide absorbent is not exhausted.	Provider or Tech
Item 12:	Breathing system pressure and leak testing	Provider and Tech
Item 13:	Verify that gas flows properly through the breathing circuit during both inspiration and exhalation.	Provider and Tech
Item 14:	Document completion of checkout procedures.	Provider and Tech
Item 15:	Confirm ventilator settings and evaluate readiness to deliver anesthesia care. (ANESTHESIA TIME OUT)	Provider

American Society of Anesthesiologists. *Recommendations for Pre-Anesthesia Checkout Procedures*. Park Ridge, IL: American Society of Anesthesiologists; 2008. https://www.asahq.org/standards-and-guidelines/2008-asa - recommendations-for-pre-anesthesia-checkout. March 13, 2008. Accessed October 29, 2018.

Ehrenwerth J, Eisenkraft JB, Berry JM, eds. *Anesthesia Equipment: Principles and Applications*. 2nd ed. New York: Elsevier; 2013:591–620, 653–680.

Mehta SP, Eisenkraft JB, Posner KL, et al. Patient injuries from anesthesia gas delivery equipment: a closed claims update. *Anesthesiology*. 2013;119:788–795.

U.S. Food and Drug Administration. Anesthesia apparatus checkout recommendations, 1993. http://vam.anest.ufl.edu/FDApreusecheck.pdf.

Updated April 20, 2006. Accessed October 29, 2018.

A.16. What are the common sites for gas leakage?

Because gas can leak from numerous points in the anesthesia workstation and breathing system, the anesthesiologist must be educated and able to trace the flow of gases from the supply and storage sources through the system components. Most commonly, leaks occur in the breathing system and low-pressure parts of the machine (i.e., components downstream of the gas flow control valves). For the breathing system, trace the flow of gas from the common gas outlet (if accessible), through the anti-disconnect fitting and hose, to the breathing circuit fresh gas inlet. Trace the flow of gas past the inspiratory valve, inspiratory limb, gas sampling connector, elbow adaptor, to the tracheal tube or airway device. Common sites for leaks include a partially deflated tracheal tube cuff or a disconnection of the sidestream sampling gas analyzer sampling line. Check flow back down the expiratory limb, spirometer, expiratory valve, absorber, pressure gauge, pressure sampling lines, and any user-added components such as filters, humidifiers, condensers, and positive end-expiratory pressure (PEEP) valves. Check both the bag and the ventilator circuits for leaks.

Leaks in the machine low-pressure system can occur as a result of cracked rotameter flow tubes, incorrectly mounted vaporizers, vaporizer leak around agent filling device, or fracture in the gas piping. Leaks in the high-pressure and intermediate-pressure systems usually result from defective valves, connectors, and hanger yokes.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:582, 606–607, 629–630.

Raphael DT, Weller RS, Doran DJ. A response algorithm for the low-pressure alarm condition. *Anesth Analg*. 1988;67:876–883.

A.17. How is the anesthesia machine checked for leaks?

Leaks in the machine low-pressure system should be tested for according to the manufacturer's specific recommendations for that particular brand and model.

In general, older model Dräger machines (Narkomed 2, 3, 4) are tested using a positive pressure leak check. In principle, the inspiratory and expiratory connections on the absorber are connected by a short length of 22-mm diameter tubing (i.e., the circle breathing system tubing is removed). The reservoir bag (usually 3 L size) is removed, and a test terminal is connected to the bag mount. A short piece of plastic tubing and a sphygmomanometer bulb are connected to the test terminal. With no gases flowing and with the pop-off valve closed, the system is pressurized to 50 cm H_2O by squeezing the sphygmomanometer bulb. Pressure should not decrease by more than 20 cm H_2O in 30 seconds. In this test, the pressure is applied to all of the rigid components of the breathing system and through the fresh gas hose into the machine low-pressure system all the way back to the flow control valves. This test is then repeated with each vaporizer turned on in turn to test for leaks in each vaporizer.

Some anesthesia machines (e.g., GE Excel) have a one-way outlet check valve just upstream of the common gas outlet. Other models have no outlet check valve. The presence of an outlet check valve precludes the application of a positive pressure leak check. If such a valve is present, a negative pressure leak test can be used to check the low-pressure system. In this test, a suction bulb (negative pressure leak-check device) is connected to the common gas outlet. With all gas flows turned off and vaporizers off, the bulb is squeezed empty (to create a negative pressure of −65 mmHg) and then connected to the common gas outlet of the workstation. Reexpansion of the bulb should not occur in less than 30 seconds. The test is repeated with each vaporizer turned on in turn to check for leaks in the

vaporizers.

The FDA 1993 preuse checkout recommendations describe the use of the negative pressure (bulb) leak-check device and state that the bulb should not refill within 10 seconds. The anesthesiologist must understand how to perform a low-pressure system leak check and must have the means (i.e., appropriate leak-check device) to check his or her own particular machine.

The newer electronic anesthesia workstations incorporate a partially automated checkout to test for leaks. The user of the workstation must understand what the automated checkout is designed to check and, more importantly, what it does not check. Even with an automated preuse checkout, some steps must be performed manually as prompted and directed by the checkout screen.

Eng TS, Durieux MR. Automated machine checkout leaves an internal gas leak undetected: the need for complete checkout procedures. *Anesth Analg*. 2012;114:144–146.

Myers JA, Good ML, Andrews JJ. Comparison of tests for detecting leaks in the low pressure system of anesthesia gas machines. *Anesth Analg*. 1997;84:179–184.

U.S. Food and Drug Administration. Anesthesia apparatus checkout recommendations, 1993. http://vam.anest.ufl.edu/FDApreusecheck.pdf. Updated April 20, 2006. Accessed October 29, 2018.

B. Preoperative Evaluation and Preparation

B.1. What should be included in the equipment checkout in preparation for anesthesia?

In 1993, the FDA published its *14-Step Anesthesia Apparatus Checkout Recommendations* (accessible at http://vam.anest.ufl.edu/fdacheckout.html). It is worthwhile to review in principle the steps in this checkout, recognizing that in contemporary computerized workstations many of the steps have been automated.

The preamble to the FDA 1993 recommendations states that:

This checkout, or a reasonable equivalent, should be conducted before administration of anesthesia. These recommendations are valid only for an anesthesia system that conforms to the then current (1993) and relevant standards and includes an ascending bellows ventilator and at least the following monitors: capnograph, pulse oximeter, oxygen analyzer, respiratory volume monitor (spirometer), and breathing system pressure monitor with high- and low-pressure alarms. This is a guideline that users are encouraged to modify to accommodate differences in equipment design and variations in local clinical practice. Such local modifications should have appropriate peer review. Users should refer to the operator's manual for the manufacturer's specific procedures and precautions, especially the manufacturer's low-pressure leak test (step 5).

Emergency ventilation equipment

Step 1. Verify backup ventilation equipment is available and functioning.

High-pressure system

Step 2. Check oxygen cylinder supply.

- Open oxygen cylinder and verify at least half full (approximately 1,000 psi).
- Close cylinder.

Step 3. Check central pipeline supplies.

- Check that hoses are connected and pipeline gauges read approximately 50 psi.

Low-pressure systems

Step 4. Check initial status of low-pressure system.

- Close flow control valves and turn vaporizers off.
- Check fill level and tighten vaporizer filler caps.

Step 5. Perform leak check of machine low-pressure system.

- Verify that the machine master switch and flow control valves are off.
- Attach "suction bulb" to common fresh gas outlet.
- Squeeze the bulb repeatedly until it is fully collapsed.
- Verify that the bulb stays fully collapsed for at least 10 seconds.
- Open one vaporizer at a time and repeat the tests as discussed earlier.
- Remove suction bulb, and reconnect fresh gas hose.

Step 6. Turn on machine master switch and all other necessary electrical equipment.

Step 7. Test flowmeters.

- Adjust flow of all gases through their full range, checking for smooth operation of floats and undamaged flow tubes.
- Attempt to create a hypoxic oxygen/nitrous oxide mixture and verify correct changes in flow and/or alarm.

Scavenging system

Step 8. Adjust and check scavenging system.

- Ensure proper connections between the scavenging system and both the adjustable-pressure limit (APL, or "pop-off") valve and ventilator relief valve.
- Adjust waste gas vacuum (if possible).
- Fully open APL valve and occlude Y-piece.
- With minimum oxygen flush activated, allow the scavenger reservoir bag to distend fully and then verify that the absorber pressure gauge reads less than 10 cm H_2O.

Breathing system

Step 9. Calibrate oxygen monitor.

- Ensure monitor reads 21% in room air.
- Verify low oxygen alarm is enabled and functioning.
- Reinstall sensor in circuit and flush breathing system with

oxygen.
- Verify that monitor now reads more than 90%.

Step 10. Check initial status of breathing system.
- Set selector switch to "bag" mode.
- Check that breathing circuit is complete, undamaged, and unobstructed.
- Verify that CO_2 absorbent is adequate.[1]
- Install breathing circuit accessory equipment (e.g., humidifier, PEEP valve) to be used during the case.

Step 11. Perform leak check of the breathing system.
- Set all gas flows to zero (or minimum).
- Close APL (pop-off) valve and occlude Y-piece.

[1] Note that in step 10, checking adequacy of the CO_2 absorbent should include changing or hydrating it if there is any possibility that it may have become desiccated. This is because desiccated soda lime can react with desflurane, enflurane, and isoflurane, and sevoflurane to produce high levels of CO in the breathing system. Also be aware that the color of the new absorbent, Amsorb, changes to violet when it is desiccated and when it is exhausted.

- Pressurize breathing system to approximately 30 cm H_2O with oxygen flush.
- Ensure that pressure remains fixed for at least 10 seconds.
- Open APL (pop-off) valve and ensure that pressure decreases to zero.

Manual and automatic ventilation systems

Step 12. Test ventilation systems and unidirectional valves.
- Place a second breathing bag on the Y-piece.
- Set appropriate ventilator parameters for the next patient.
- Switch to automatic ventilation ("ventilator") mode.
- Fill bellows and breathing bag with oxygen flush and then turn the ventilator on.
- Set oxygen flow to minimum, and other gas flows to zero.
- Verify that during inspiration, bellows deliver appropriate

tidal volume, and that during expiration, bellows fill completely.

- Set fresh gas flow to approximately 5 L per minute.
- Verify that the ventilator bellows and simulated lungs fill and empty appropriately without sustained pressure at end expiration.
- Check for proper action of unidirectional valves.
- Exercise breathing circuit accessories to ensure proper function.
- Turn ventilator off and switch to manual ventilation ("bag/APL") mode.
- Ventilate manually and ensure inflation and deflation of artificial lungs and appropriate feel of system resistance and compliance.
- Remove second breathing bag from the Y-piece.

Monitors

Step 13. Check, calibrate, and/or set alarm limits of all monitors.

- Capnometer
- Pulse oximeter
- Oxygen analyzer
- Respiratory volume monitor (spirometer)
- Pressure monitor
- High- and low-airway alarms

Final position

Step 14. Check final status of machine.

- Vaporizers off
- APL valve open
- Selector switch to "bag"
- All flowmeters to zero
- Patient suction level adequate
- Breathing system ready to use

The preanesthesia equipment checkout procedures are shown

in **Table 59.1**.

Although many modern anesthesia machines have automated many of the steps described earlier, it is important to understand the principles of each step of a pre-anesthesia checkout procedure.

American Society of Anesthesiologists. *Summary of American Society of Anesthesiologists 2008 Checkout Recommendations by Frequency and Responsible Party. Recommendations for Pre-Anesthesia Checkout Procedures*. Schaumburg, IL: American Society of Anesthesiologists; 2008.

Loeb RG, Gravenstein N. Simultaneous color change at opposite ends of carbon dioxide absorbent canisters. *Anesthesiology*. 2018;129:1170.

B.2. What emergency equipment should be easily available to the anesthesiologist?

In checking the anesthesia machine, step 1 on the FDA 1993 checklist and the 2008 American Society of Anesthesiologists' guidelines is to verify that backup ventilation equipment is available and functioning. This means a self-inflating resuscitation bag appropriate for patient size (adult vs. pediatric) is present and tested. Emergency airway management equipment must be available.

One method for having emergency airway management equipment available and accessible is to have a "difficult airway cart" for the "cannot intubate, cannot ventilate" scenario. This cart should include supraglottic airways such as a laryngeal mask airway, nasal trumpets, or oral airways as well as supplies for a needle cricothyrotomy and jet ventilation.

Other emergency equipment includes a working flashlight, a backup battery for any electricity-dependent workstation, an oxygen tank and regulator, a malignant hyperthermia cart, a "code" cart and defibrillator, a difficult airway cart, a fire extinguisher, knowledge of appropriate response to a fire, and an evacuation plan.

Apfelbaum JL, Caplan RA, Barker SJ, et al. Practice advisory for the prevention and management of operating room fires: an updated report by the American Society of Anesthesiologists Task Force on Operating Room Fires. *Anesthesiology*. 2013;118:271–290.

ECRI Institute. New clinical guide to surgical fire prevention. Patients can catch fire—here's how to keep them safer. *Health Devices*. 2009;38:314–330.

B.3. How should this patient be premedicated?

The goal of premedication must be established preoperatively. Commonly considered objectives listed in order of most to least common are as follows:

- Anxiolysis
- Minimization of gastric volume and acidity when "full stomach" is of concern
- Antibiotic prophylaxis administered within 1 hour of incision per Surgical Care Improvement Project (SCIP) guideline
- Antisialagogue effect

This patient may require anxiolysis. Premedication for anxiolysis in an ambulatory patient must consider the patient's need to arrive from home and ambulate as well as the desire for rapid return of clear mental status postoperatively. Most commonly, therefore, no agent is administered preoperatively. Alternatively, for the highly anxious patient, a small dose of a short-acting agent (e.g., midazolam 1 to 2 mg intravenously) may be administered.

Longnecker DE, Newman MF, Zapol WM, et al. *Anesthesiology*. 3rd ed. New York: McGraw-Hill; 2018:56–69.

Munday GS, Deveaux P, Roberts H, et al. Impact of implementation of the Surgical Care Improvement Project and future strategies for improving quality in surgery. *Am J Surg*. 2014;208:835–840.

C. Intraoperative Management

C.1. How should this patient be monitored?

The "Standards for Basic Anesthetic Monitoring" are

established by the American Society of Anesthesiologists and were last amended in October 2010 and affirmed in October 2015. In summary, they are as follows:

- *Standard I*: Qualified anesthesia personnel shall be present in the room throughout the conduct of all general anesthetics, regional anesthetics, and monitored anesthesia care.
- *Standard II*: During all anesthetics, the patient's oxygenation, ventilation, circulation, and temperature shall be continually evaluated.

Oxygenation

- *Inspired gas*: During every administration of general anesthesia using an anesthesia machine, the concentration of oxygen in the patient breathing system shall be measured by an oxygen analyzer with a low oxygen concentration limit alarm in use.*
- *Blood oxygenation*: During all anesthetics, a quantitative method of assessing oxygenation such as pulse oximetry shall be employed.* When the pulse oximeter is utilized, the variable pitch pulse tone and the low threshold alarm shall be audible to the anesthesiologist or the anesthesia care team personnel.* Adequate illumination and exposure of the patient are necessary to assess color.*

Ventilation

- Every patient receiving general anesthesia shall have the adequacy of ventilation continually evaluated. Qualitative clinical signs such as chest excursion, observation of the reservoir breathing bag, and auscultation of breath sounds are useful. Continual monitoring for the presence of expired CO_2 shall be performed unless invalidated by the nature of the patient, procedure, or equipment. Quantitative monitoring of the volume of expired gas is strongly encouraged.*
- When an endotracheal tube or laryngeal mask is inserted, its

correct positioning must be verified by clinical assessment and by identification of CO_2 in the expired gas. Continual $Etco_2$ analysis, in use from the time of endotracheal tube/laryngeal mask placement, until extubation/removal or initiating transfer to a postoperative care location, shall be performed using a quantitative method such as capnography, capnometry, or mass spectroscopy.* When capnography or capnometry is utilized, the $Etco_2$ alarm shall be audible to the anesthesiologist or the anesthesia care team personnel.*

- When ventilation is controlled by a mechanical ventilator, there shall be in continuous use a device that is capable of detecting disconnection of components of the breathing system. The device must give an audible signal when its alarm threshold is exceeded.
- During regional anesthesia and monitored anesthesia care, the adequacy of ventilation shall be evaluated by continual observation of qualitative clinical signs and/or monitoring for the presence of exhaled CO_2.

Circulation

- Every patient receiving anesthesia shall have the electrocardiogram continuously displayed from the beginning of anesthesia until preparing to leave the anesthetizing location.*
- Every patient receiving anesthesia shall have arterial blood pressure and heart rate determined and evaluated at least every 5 minutes.*
- Every patient receiving general anesthesia shall have, in addition to earlier, circulatory function continually evaluated by at least one of the following: palpation of a pulse, auscultation of heart sounds, monitoring of a tracing of intra-arterial pressure, ultrasound peripheral pulse monitoring, or pulse plethysmography or oximetry.

Body temperature

- Every patient receiving anesthesia shall have temperature monitored when clinically significant changes in body temperature are intended, anticipated, or suspected.

Under extenuating circumstances, the responsible anesthesiologist may waive the requirements marked with an asterisk (*); it is recommended that when this is done, it should be so stated (including the reasons) in a note in the patient's medical record.

The reader should visit the American Society of Anesthesiologists' website for the most recent version of the standards: https://www.asahq.org/standards-and-guidelines/standards-for-basic-anesthetic-monitoring.

C.2. Following uncomplicated induction of anesthesia and endotracheal intubation, the procedure begins. Upon insufflation of the abdomen with CO_2, the SpO_2 decreases to 78%. What acute diagnostic and therapeutic interventions would you perform?

Immediately, it should be determined if the tracheal tube is in the trachea. Visualization of the tube passing between the vocal cords, visualization of bilateral chest rise, equal breath sounds bilaterally with auscultation, and sustained end-tidal CO_2 are rapid methods for confirming endotracheal placement of the tube.

The differential diagnosis for a desaturation is shown in **Table 59.2**.

TABLE 59.2 Differential Diagnosis of Low SpO_2 Reading

Cause	Examples
Hypoxic gas mixture	Low FIO_2, altitude
Hypoventilation	Airway obstruction, splinting associated with chest or abdominal surgery, bronchospasm

Right-to-left shunt	Atelectasis, main-stem intubation, mucus plug, intracardiac shunt, pulmonary edema
$\dot{V}/\dot{Q}$ mismatch	Chronic obstructive pulmonary disease, pulmonary embolism, pneumonia, pulmonary edema
Diffusion impairment	Interstitial lung disease
Spurious reading	Sensor not properly applied to extremity causing penumbra effect; methemoglobinemia

FIO_2, fraction of inspired oxygen; $\dot{V}/\dot{Q}$, ventilation/perfusion.

In this patient, the presence of bilateral breath sounds and the quality of those breath sounds must be ascertained. The FIO_2, $EtCO_2$, heart rate, and blood pressure also need to be checked.

Therapeutically, the FIO_2 should be increased immediately to 1 (i.e., 100%) and a change to manual ventilation should be initiated. The surgeon should desufflate the abdomen until the patient has stabilized. If unilateral breath sounds are heard, potential sources include endobronchial intubation, mucus plug, bronchospasm, or pneumothorax.

Given the steep Trendelenburg positioning and insufflation of the abdomen required for this procedure, main-stem intubation is most likely, in which case the endotracheal tube should be gradually withdrawn until breath sounds become bilateral; the tube should then secured.

Maerz DA, Beck LN, Sim AJ, et al. Complications of robotic-assisted laparoscopic surgery distant from the surgical site. *Br J Anaesth*. 2017;118:492–503.

C.3. The endotracheal tube was withdrawn 2 cm. Squeezing the reservoir bag in the circle breathing system failed to generate positive pressure in the circuit. What are the common sites for gas leaks in the circle breathing system?

A leak can occur anywhere in the breathing circuit. One might logically check for a leak in the circuit starting from the tip of

the tracheal tube and working backward toward the anesthesia workstation, checking the following common potential leak sites:

- Incomplete seal between the endotracheal tube cuff and the trachea (e.g., deflated cuff, supraglottic position, incompetent valve on pilot balloon)
- Connection between the endotracheal tube and the breathing circuit (e.g., disconnected elbow adapter)
- Spirometric and end-tidal monitoring connections at both the patient end (near the connection between the breathing circuit and endotracheal tube) and the monitor end
- Connection between inspiratory and expiratory gas hoses and the anesthesia machine
- Within the low-pressure system, including the unidirectional valves, APL valve, reservoir bag or bellows housing, absorber, vaporizers, flowmeters, and scavenging system

One method for rapidly determining if a leak is proximal or distal to the connection of the circuit to the endotracheal tube involves disconnecting the endotracheal tube from the circuit and attaching a manual self-inflating resuscitator bag. If positive pressure ventilation is possible without a leak using the manual self-inflating resuscitator bag, the leak is within the circuit or anesthesia machine. If positive pressure ventilation is not possible, the leak is within the endotracheal tube or patient.

In the case of a leak following withdrawal of the tube from an endobronchial position, two likely sources of the leak can be identified. Withdrawal of a tube requires deflation of the cuff and reinflation after repositioning to seal the system; the cuff pilot balloon should be palpated to confirm inflation of the cuff and air should be added if necessary. Secondly, the tube may have been withdrawn too far and the tip may have become supraglottic. Correct endotracheal placement must be confirmed. Fiberoptic bronchoscopy may be utilized to visualize the

endotracheal tube in position proximal to the carina.

Ehrenwerth J, Eisenkraft JB, Berry JM, eds. *Anesthesia Equipment: Principles and Applications*. 2nd ed. New York: Elsevier; 2013:591–620.

C.4. The patient was taken out of Trendelenburg position. Direct laryngoscopy revealed the endotracheal tube to be supraglottic. Additionally, green secretions were noted to be pooled in the posterior pharynx. What should be done next?

The endotracheal tube should be replaced in order to protect the airway from possible aspiration. The posterior oropharynx should be suctioned thoroughly. Once the endotracheal tube is secured, the trachea should be suctioned to determine if gastric contents were aspirated. If aspiration is confirmed, the trachea should be suctioned prior to initiation of positive pressure ventilation to prevent distal spread of the aspirate. If the airway cannot be secured, the patient should be placed in the lateral and head down position to prevent further aspiration.

Bronchoscopy and pulmonary lavage are only necessary if particulate aspiration has occurred. Antibiotics are warranted postoperatively only if aspiration pneumonitis develops. There is currently no evidence that administration of steroids reduces mortality or improves outcomes.

In a patient with a history of poorly controlled diabetes, delayed gastric emptying may result in retained gastric contents despite appropriate fasting times. Rapid sequence intubation followed by orogastric tube placement to empty any remaining contents should take place in such patients as this.

Robinson M, Davidson A. Aspiration under anaesthesia: risk assessment and decision-making. *Contin Educ Anaesth Crit Care Pain*. 2014;14:171–175.

D. Postoperative Management

D.1. What criteria would you use for tracheal extubation?

In the operating room, traditional extubation criteria fall into two categories: global and respiratory. Global criteria include return of consciousness, demonstration of ability to protect the airway, adequate reversal of residual neuromuscular blockade, absence of hypothermia, and presence of a normal metabolic milieu (e.g., no significant anemia, acidosis, and electrolyte abnormality). Commonly applied respiratory criteria are a vital capacity greater than 15 mL per kg, a tidal volume of ≥6 mL per kg, and a predicted Spo_2 >90% while breathing an Fio_2 <0.40.

Patients with a respiratory insult and the need for postoperative mechanical ventilation in the postanesthesia care unit or intensive care unit will be assessed using additional and more stringent criteria. The ratio of respiratory rate to tidal volume is widely used and commonly referred to as the *rapid shallow breathing index* (RSBI). Slow, deep breathing during minimal respiratory support predicts successful extubation and rapid, shallow breathing predicts probable failure. To determine this ratio, the patient is observed breathing from a T-bar, or a low level of pressure support (PS) (e.g., usually approximately 5 cm H_2O); this is referred to as a spontaneous breathing trial (SBT). The following is then calculated:

RSBI = respiratory rate (breaths per minute) / tidal volume (liters)

An RSBI greater than 100 is rapid, shallow breathing, and predictably the patient will fail an extubation attempt. When the RSBI is less than 100, it is predicted that the patient will breathe at a rate and tidal volume that can be easily maintained after extubation and will be able to adequately maintain a normal Pao_2 and $Paco_2$. It does not, however, rule out the possibility of an upper airway obstruction complicating that effort. If during the period of observation while breathing from a T-bar or on PS,

the patient develops signs of distress such as diaphoresis, agitation, tachycardia, bradycardia, hypertension, hypotension, hypoxemia, or hypercarbia, the trial is abandoned and the patient is said to have had a "weaning" or "SBT" failure.

Although more sophisticated measurements might be helpful, including measurement of the maximum negative inspiratory force, vital capacity, elastance index, etc., the routine application of this basic and easy-to-reproduce measurement has stood the test of time and certainly for most patients who are intubated and mechanically ventilated for less than 7 to 10 days should be a daily routine.

Frutos-Vivar F, Ferguson ND, Esteban A, et al. Risk factors for extubation failure in patients following a successful spontaneous breathing trial. *Chest*. 2006;130:1664–1671.

Yang KL, Tobin MJ. A prospective study of indexes predicting the outcome of trials of weaning from mechanical ventilation. *N Engl J Med*. 1991;324:1445–1450.

D.2. What are the causes of postoperative hypoxemia?

The etiology of hypoxemia can be classified physiologically or pathologically.

Physiologically, all instances of hypoxemia have only four basic potential causes:

- Low F_{IO_2}
- Hypoventilation (which will also be associated with an increased P_{aCO_2})
- Ventilation/perfusion mismatch
- Shunt

Pathologically, common etiologies likely to present postoperatively include airway obstruction, atelectasis (especially with upper abdominal retraction and Trendelenburg positioning), right main-stem intubation, aspiration, pulmonary edema, and pulmonary embolus.

Gropper MA, Cohen NH, Eriksson LI, et al, eds. *Miller's Anesthesia*. 9th ed. Philadelphia, PA: Elsevier; 2020:2592–2593.

D.3. What is the difference between shunt, ventilation/perfusion mismatch, and dead space?

The relative quantity of perfusion and ventilation defines these terms. A normal lung has a small portion in which perfusion and ventilation are perfectly matched. Two extreme conditions may exist at either end of the spectrum of perfectly matched perfusion and ventilation; those extremes are shunt and dead space ventilation.

In a shunt, the alveolus is perfused, but it is not ventilated. The physiologic result is hypoxemia. This is characterized by a failure of the Pa_{O_2} to rise despite an increase in the F_{IO_2}. Hypoxemia caused by small amounts of shunted blood (i.e., less than 20% of cardiac output) is easily overcome by increasing the F_{IO_2}. This is because the blood that is not shunted will contain enough "extra" dissolved oxygen to make up for the deficit that the shunted blood contributes to the combined total blood oxygen content. Once the shunt fraction approaches 0.3 (30%), increasing the F_{IO_2} even to 1 will not be effective in preventing hypoxemia. The term *venous admixture* is often used synonymously for shunt.

In dead space, the alveolus is ventilated, but it is not perfused; hence, the alveolar space is essentially "dead." The physiologic result is hypercarbia. This is characterized by a failure to maintain a normal Pa_{CO_2} despite an increase in minute ventilation (i.e., tidal volume × respiratory rate).

Ventilation/perfusion mismatch is the term applied to any condition that is not a perfect match, completely shunt, or completely dead space. The physiologic result is a variable combination of hypoxemia and hypercarbia. The resultant degree of hypoxemia and hypercarbia depends on the relative

contribution of partial shunt and dead space.

Lumb AB. *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:109–135.

D.4. Postoperatively, the patient developed hypoxia and pulmonary edema. What is the differential diagnosis of pulmonary edema? What is the most likely cause of pulmonary edema in this patient?

Pulmonary edema is categorized into cardiac or noncardiac in etiology. The differential diagnosis of pulmonary edema is shown in **Table 59.3**.

TABLE 59.3 Differential Diagnosis of Pulmonary Edema

Condition	Pathophysiology	Sample Cause
Congestive heart failure	↑ Filling pressure, ↓ cardiac output	Myocardial infarction
Negative pressure pulmonary edema	↑ Outside–inside pressure gradient	Laryngospasm
Acute respiratory distress syndrome	↑ Permeability	Sepsis, aspiration, fat embolus, TRALI

↓, decrease; ↑, increase; TRALI, transfusion-related acute lung injury.

Conditions that physiologically result from an increase in the pressure within the vessel that cause transudation of fluid from inside the vessel to outside the vessel are traditionally termed congestive heart failure (CHF). CHF will be associated with a diminution of cardiac function (e.g., ejection fraction) and an increase in the left ventricular end-diastolic pressure.

A decrease in the pressure outside of the vessel may also result in the net movement of fluid from inside to outside. A classic example is negative pressure pulmonary edema—a condition seen in patients who inspire against a closed glottis and generate a large net negative force, which acutely draws fluid into the alveolus, leading to pink frothy sputum and

hypoxemia almost instantaneously.

A change in the permeability of the vessel wall is the major cause of pulmonary edema seen in ARDS. These conditions require a history of exposure to a risk factor within 1 week, the development of bilateral infiltrates on chest radiography, decreased oxygenation, and respiratory failure not explained by cardiac failure or volume overload. Previously, a pulmonary artery catheter was required for diagnosis of ARDS, but this was removed in 2012 when the Berlin definition for ARDS was determined. The requirement for pulmonary artery catheter was removed due to declining use of pulmonary artery catheters and because hydrostatic edema may coexist with ARDS. The diagnostic criteria for ARDS are listed in **Table 59.4**.

TABLE 59.4 Diagnostic Criteria for Acute Respiratory Distress Syndrome

Timing	Within 1 week of clinical insult or new or worsening respiratory symptoms
Imaging	Bilateral infiltrates on chest radiography
Origin of edema	Respiratory failure not explained by cardiac failure or volume overload
Decreased oxygenation	*Mild:* PaO_2/FIO_2 ≤300 mmHg with PEEP or CPAP ≥5 cm H_2O
	Moderate: PaO_2/FIO_2 ≤200 mmHg with PEEP ≥5 cm H_2O
	Severe: PaO_2/FIO_2 ≤100 mmHg with PEEP ≥5 cm H_2O

CPAP, continuous positive airway pressure; FIO_2, fraction of inspired oxygen; PaO_2, partial pressure of oxygen in arterial blood; PEEP, positive end-expiratory pressure.

Risk factors for ARDS include aspiration, long bone fracture, transfusion-related acute lung injury (TRALI), pancreatitis, inhalational injury, and sepsis.

Aspiration pneumonitis leading to ARDS is most likely to develop in this patient who had gastric secretions in the posterior pharynx and an unprotected airway.

ARDS Definition Task Force. Acute respiratory distress syndrome: the Berlin definition. *JAMA*. 2012;307: 2526–2533.

Longnecker DE, Newman MF, Zapol WM, et al, eds. *Anesthesiology*. 3rd ed.

New York: McGraw-Hill; 2018: 1251–1268.

D.5. How should the ventilator be set if mechanical ventilation is required postoperatively?

Parameters that must be set include the mode, respiratory rate, tidal volume, PEEP, and F_{IO_2}.

Patients with an acute need for mechanical ventilation should be given full support with the mode set as volume control (sometimes also known as *assist control*) or pressure control, so that all the breaths are delivered by the ventilator, even those initiated by the patient. Other modes to be considered as the patient improves include synchronized intermittent mandatory ventilation (SIMV), PS, and combinations of SIMV and PS.

Tidal volume was traditionally set at 10 mL per kg. Normally, during spontaneous ventilation, the respiratory rate is 12 to 16 breaths per minute, and the tidal volume is 6 mL per kg. However, during spontaneous ventilation, there are yawns and sighs that prevent atelectasis. Yawns and sighs are not administered during routine mechanical ventilation. Therefore, standard mechanical ventilation settings developed more than 50 years ago use a lower respiratory rate and higher tidal volume than spontaneous values, resulting in the same minute ventilation and no need for sigh (150% of tidal volume) breaths.

More recently, traditional mechanical ventilation utilizing a tidal volume of 10 mL per kg has been recognized as a potential cause of morbidity and mortality when applied to injured lungs and may even have adverse consequences when applied routinely in the operating room. The excessive tidal volume is associated with alveolar injury and worsened pulmonary function (i.e., volutrauma). This should be distinguished from the more easily recognized concern of pneumothorax, resulting from ventilation of stiff lungs with high inflation pressures, commonly referred to as barotrauma. Hence, the current

recommendation in ARDS is that the tidal volume be set at 6 mL per kg of premorbid weight. Additionally, the peak inspiratory pressure should ideally be less than 35 cm H_2O. This may result in CO_2 retention, but if the pH is more than 7.25, no intervention is necessary. If CO_2 retention is severe and the pH is less than 7.25 after increasing the respiratory rate to as high as 20 breaths per minute, administration of sodium bicarbonate should be considered. To maximize oxygenation and limit exposure to potentially toxic concentrations of oxygen (i.e., $FIO_2 = 1$), usually an end-expiratory pressure of 10 cm H_2O is set.

In addition to standard monitoring, prolonged mechanical ventilation in ARDS will require arterial line placement to facilitate frequent arterial blood gas determinations. Further, a daily chest radiograph will be required.

The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med*. 2000;342: 1301–1308.

D.6. If this patient had acute respiratory distress syndrome (ARDS) secondary to aspiration, besides low-tidal volume ventilation, what other changes in routine therapy should be considered?

Other management strategies include efforts at minimizing lung water and usual standard intensive care unit measures aimed at deep venous thrombosis (DVT) prophylaxis, gastrointestinal (GI) aspiration prophylaxis, daily sedations breaks, and early mobility. Conservative administration of intravenous fluids originated in a National Institutes of Health-sponsored study; the excessive administration of fluid is harmful, whereas minimizing intravenous fluids appears to be safe and not associated with other organ insufficiency or failure.

Wiedemann HP, Wheeler AP, Bernard GR, et al. National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Comparison of two fluid-management strategies in acute lung injury. *N Engl J Med*. 2006;354:2564–2575.

D.7. What therapies routinely administered by the anesthesiologist may cause acute lung injury?

TRALI has become the leading cause of transfusion-related morbidity and mortality in the United States. This injury is almost always recognized during or shortly after transfusion and is diagnosed by the absence of cardiac failure and fluid overload. Although any blood product can cause this injury, the transfusion of fresh frozen plasma and platelets, especially those donated by women who were previously pregnant, is most often responsible. This injury can be seen even after the transfusion of a single blood product unit and "massive" transfusion is not, as previously thought, a prerequisite.

Alam A, Huang M, Yi QL, et al. Perioperative transfusion-associated lung injury: the Canadian Blood Service experience. *Transfus Apher Sci*. 2014;50:392–398.

D.8. What methods of oxygen administration may be used postoperatively?

Most postoperative patients who are prone to develop hypoxemia may be managed with a nasal cannula or face mask. Nasal cannulas are inexpensive and comfortable, but regardless of flow rates, they cannot achieve an F_{IO_2} of more than 0.30 unless special high-flow devices are used. Face masks have the capability of delivering a wide range of precise F_{IO_2} levels of up to 1.

Occasionally, a patient may require more aggressive oxygen therapy than can be provided by nasal cannula or face mask but less invasive than tracheal intubation and mechanical ventilation. Noninvasive positive pressure ventilation should be

considered. Continuous positive airway pressure, bilevel positive airway pressure, or high-flow nasal cannula may be applied. Additionally, a single-use nasal positive airway pressure device called SuperNO_2VA can be used intraoperatively or postoperatively. These modes may be used in patients who either have previously used these devices at home or who are on the verge of requiring tracheal intubation and mechanical ventilation but have conditions thought to be rapidly resolving (e.g., CHF and chronic obstructive pulmonary disease exacerbation). These patients usually do not require an arterial catheter for blood sampling but do need frequent assessment of their respiratory effort, particularly their respiratory rate and use of accessory muscles, as well as continuous Spo_2 monitoring. A respiratory therapist should be involved to individually achieve the best mask fit and patient comfort possible. In case noninvasive ventilation fails, preparation to emergently tracheally intubate must always be maintained.

Jaber S, Chanques JS, Jung B. Postoperative noninvasive ventilation. *Anesthesiology*. 2010;112:453–461.

60 Electroconvulsive Therapy

Patricia Fogarty Mack

A 72-year-old man with major depressive disorder who has failed medication therapy and psychotherapy is scheduled for electroconvulsive therapy (ECT). His past medical history reveals significant coronary artery disease status after three-vessel coronary bypass surgery 5 years ago. He also has chronic atrial fibrillation. He had a transient ischemic attack (TIA) 2 years previously after which he underwent left carotid endarterectomy. In addition, he has sleep apnea and gastroesophageal reflux disease (GERD). The patient weighs 115 kg and is 5 ft 3 in. tall and had a Mallampati class 2 airway. Medications include venlafaxine, rivaroxaban, atenolol, and esomeprazole.

A. Medical Disease and Differential Diagnosis

1. What are the indications for ECT?
2. Are there any contraindications to ECT?
3. What is the mechanism of action of ECT?

B. Preoperative Evaluation and Preparation

1. How would you assess the cardiac status of this patient?
2. How should his anticoagulation be managed during ECT?
3. What implications do his history of sleep apnea have on

management of ECT?
4. How does his history of TIA and carotid endarterectomy impact your preoperative evaluation?
5. Is ECT contraindicated in a patient with a permanent pacemaker or implantable cardioverter-defibrillator?
6. Are there any psychiatric medications he is taking that would impact your anesthetic care?

C. Intraoperative Management

1. Describe the hemodynamic and cardiac response to ECT in a typical patient.
2. Is an arterial line warranted in this patient?
3. By what means would you attempt to maximize hemodynamic stability?
4. Describe the cerebral hemodynamic effects of ECT.
5. How would you proceed with an anesthetic induction for this procedure?
6. How do you intend to manage his airway during each treatment?

D. Postoperative Management

1. The patient is extremely agitated upon emergence. Discuss the risk factors for postictal agitation (PIA) as well as the therapeutic options.
2. After three consecutive uneventful inpatient treatments, the psychiatrist asks if the patient may undergo ECT as an outpatient. Would you agree to this plan?

A. Medical Disease and Differential Diagnosis

A.1. What are the indications for ECT?

For centuries, it had been noted that psychosis did not tend to occur in those people with epilepsy. Since the 16th century, patients with severe mental illness were treated with various

agents, such as camphor, to induce seizures (pharmacoconvulsive therapy). ECT was first instituted in the late 1930s and gained acceptance in providing a better controlled seizure. The addition of curare followed in 1951 by succinylcholine greatly diminished incidence of fracture due to the convulsions. Finally, the advent of methohexital, which ensured unconsciousness without significantly diminishing the seizure, led to the acceptance of ECT as an efficacious and safe treatment.

From the mid-1970s to the 1980s, many new drug treatments for psychiatric illness were developed and found to be efficacious. ECT fell into disfavor as a barbaric treatment when compared to pharmacotherapy.

In the past three decades, the pendulum has again swung back in favor of ECT as a safe and effective treatment for drug-resistant major depressive disorder and bipolar disorder.

Specific indications for ECT include, but are not limited to, major depressive disorder and bipolar disorder, acute schizophrenia (especially with affective or catatonic symptoms), and schizoaffective disorder. Although usually reserved as a second-line therapy for those who are resistant to pharmacologic treatment, ECT has, in some circumstances, been recommended as a first-line therapy, especially if a rapid response is urgently required as in patients with severe suicidal potential, malnutrition/dehydration, and catatonia. Finally, ECT has been recommended in patients who are unable to tolerate pharmacotherapeutic agents for any reason, including during pregnancy.

American Psychiatric Association. *The Practice of Electroconvulsive Therapy: A Task Force Report of American Psychiatric Association*. 2nd ed. Washington, DC: American Psychiatric Association; 2001:5–26.

Kellner CH. *Handbook of ECT: A Guide to Electroconvulsive Therapy for Practitioners*. Cambridge, United Kingdom: Cambridge University Press;

2019:19–20.

A.2. Are there any contraindications to ECT?

There is no absolute contraindication to ECT. There is considered to be significantly increased risk in patients with intracranial space occupying lesions, any condition associated with intracranial hypertension, recent myocardial infarction with diminished ventricular function, severe hypertension especially associated with pheochromocytoma, evolving stroke, retinal detachment, and any American Society of Anesthesiologists physical status 4 or 5 patient.

American Psychiatric Association. *The Practice of Electroconvulsive Therapy: A Task Force Report of American Psychiatric Association*. 2nd ed. Washington, DC: American Psychiatric Association; 2001:27–30.

Kellner CH. *Handbook of ECT: A Guide to Electroconvulsive Therapy for Practitioners*. Cambridge, United Kingdom: Cambridge University Press; 2019: 19–20.

A.3. What is the mechanism of action of ECT?

The mechanism of ECT is unknown. There are many neurochemical, neuroendocrine, electrophysiologic, and neuropsychological theories regarding the mechanism of ECT (**Table 60.1**).

TABLE 60.1 Mechanism of Action of Electroconvulsive Therapy—Physiologic Theories

Neurophysiologic
Anticonvulsant (changes in seizure threshold)
Cerebral blood flow and metabolic rate change
Increased slow-wave EEG activity
Antidelirium/sleep theories
Neuroendocrinologic
Prolactin release
Neuropeptide release
Melatonin
Neurochemical

Stimulation of β-receptors
Monoamine release
Modulation of serotonin
Neuropeptide/Neurotrophic
Brain-derived neurotrophic factor
Increased endorphins
Increased gray matter volume and cortical thickness amygdala, hippocampus, and other brain areas

EEG, electroencephalography.

In addition, although it was long assumed that a generalized seizure of adequate duration is sufficient for effective treatment, research has shown that barely suprathreshold stimulation, especially with unilateral ECT, is also efficacious. The cognitive impairment associated with ECT may be reduced by utilizing "ultrabrief" stimulus, marked by a shorter pulse width of electrical stimulation, apparently without sacrificing efficacy.

Cognitive impairment after ECT has been extensively investigated. In addition, the major depressive state is associated with a decline in cognition. Although acute confusion and amnesia, both anterograde and retrograde, may occur as a result of ECT, studies have shown that verbal memory showed greater improvement in depressed patients treated with ECT as compared to controls.

In addition, there is no increased risk of dementia for patients with major depression who are treated with ECT versus patients who did not receive ECT.

Biedermann SV, Bumb JM, Demiracka T, et al. Improvement in verbal memory performance in depressed in-patients after treatment with electroconvulsive therapy. *Acta Psychiatr Scand*. 2016;134:461–468.

Kellner CH. *Handbook of ECT: A Guide to Electroconvulsive Therapy for Practitioners*. Cambridge, United Kingdom: Cambridge University Press; 2019:3–6.

Loo CK, Katalinic K, Smith DJ, et al. A randomized controlled trial of brief and ultrabrief pulse right unilateral electroconvulsive therapy. *Int J Neuropsychopharmacol*. 2014;18(1):pyu145.

Osler M, Rozing MP, Christensen GT, et al. Electroconvulsive therapy and risk of dementia in patients with affective disorders: a cohort study. *Lancet Psychiatry*. 2018;5:348–356.

B. Preoperative Evaluation and Preparation

B.1. How would you assess the cardiac status of this patient?

The cardiac status of the patient needs to be assessed as it would for any other general anesthetic. Because there can be periods of significant tachycardia and hypertension following seizure induction, it would be useful to ensure that there is no longer significant myocardium at risk for ischemia and that systolic function is not compromised. If this information cannot be obtained from patient history and assessment of his functional status, it may be useful to obtain a stress test and echocardiogram. Bear in mind that it may be difficult to get an accurate history of functional status from patients who are psychotic or severely depressed.

American Psychiatric Association. *The Practice of Electroconvulsive Therapy: A Task Force Report of American Psychiatric Association*. 2nd ed. Washington, DC: American Psychiatric Association; 2001:77–80.

De Hert S, Staender S, Fritsch G, et al. Pre-operative evaluation of adults undergoing elective noncardiac surgery: updated guideline from the European Society of Anaesthesiology. *Eur J Anaesthesiol*. 2018;35:407–465.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130:2215–2245.

B.2. How should his anticoagulation be managed during ECT?

The anticoagulation for his atrial fibrillation should be continued throughout his course of therapy, maintaining an international

normalized ratio (INR) between 2.0 and 3.0. Although intracerebral hemorrhage is a theoretic concern, a retrospective study from the Mayo Clinic suggests that ECT can be safely performed in patients on warfarin therapy. Although the safety of newer anticoagulants has not been formally investigated in ECT, case series do not report any hemorrhagic complication in patients receiving either dabigatran or rivaroxaban. Finally, if a patient has drug-eluting arterial stents, aspirin and clopidogrel or any alternative antiplatelet maintenance medication should be continued.

American Psychiatric Association. *The Practice of Electroconvulsive Therapy: A Task Force Report of American Psychiatric Association*. 2nd ed. Washington, DC: American Psychiatric Association; 2001:40–41.

January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *Heart Rhythm*. 2019;16(8):e66–e93. doi:10.1016/j.hrthm.2019.01.024.

Mehta V, Mueller PS, Gonzalez-Arriaza HL, et al. Safety of electroconvulsive therapy in patients receiving long-term warfarin therapy. *Mayo Clin Proc*. 2004;79:1396–1401.

Schmidt ST, Lapid MI, Sundsted KK, et al. Safety of electroconvulsive therapy in patients receiving dabigatran therapy. *Psychosomatics*. 2014;55:400–403.

Shuman M, Hieber R, Moss L, et al. Rivaroxaban for thromboprophylaxis in a patient receiving electroconvulsive therapy. *J ECT*. 2015;31:e19–e20.

B.3. What implications do his history of sleep apnea have on management of ECT?

His history of sleep apnea is important because suboptimal management of respiratory function may reduce efficacy of treatment and increase complications. Hypocarbia is sometimes required to ensure adequate seizure duration. Additionally, after onset of seizure activity, oxygen consumption is increased dramatically as is carbon dioxide (CO_2) production. Hypercarbia

can exacerbate the tachycardia and hypertensive responses to seizure. Therefore, adequate mask ventilation is required to ensure optimal respiratory status. The use of a supraglottic airway device may be required to ensure adequate ventilation in this patient.

Finally, if the patient uses continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BIPAP) at home, it may be useful to have that machine available to the patient in the postprocedure period when postanesthetic and postictal somnolence may compromise his ability to maintain a patent airway.

Saito S. Anesthesia management for electroconvulsive therapy: hemodynamic and respiratory management. *J Anesth*. 2005;19:142–149.

Trakada G, Velentza L, Konsta A, et al. Complications of anesthesia during electroconvulsive therapy due to undiagnosed obstructive sleep apnea: a case study. *Respir Med Case Rep*. 2017;20:145–149.

B.4. How does his history of TIA and carotid endarterectomy impact your preoperative evaluation?

A history of TIA or stroke is an indication for magnetic resonance imaging (MRI) of the head before their first course of ECT. Additionally, this study may be utilized to rule out an organic cause for depression. Although a comprehensive neurologic examination before ECT is routinely recommended by the American Psychiatric Association, it may be that in this patient, more sophisticated neuropsychological testing would be useful in documenting subtle deficits and establishing a true baseline. Finally, if the patient has not had follow-up carotid Doppler examination, it may be useful to ensure that there has not been restenosis or that no new plaques have formed. This is particularly important in view of the fact that the rate pressure product may be increased by as much as 400% in the

sympathetic phase of the cardiac response.

American Psychiatric Association. *The Practice of Electroconvulsive Therapy: A Task Force Report of American Psychiatric Association*. 2nd ed. Washington, DC: American Psychiatric Association; 2001:77–80.

B.5. Is ECT contraindicated in a patient with a permanent pacemaker or implantable cardioverter-defibrillator?

See Chapter 8, section C.11.

B.6. Are there any psychiatric medications he is taking that would impact your anesthetic care?

Medications for depression can have many serious side effects. In fact, one of the indications for ECT is that the patient cannot tolerate pharmacologic therapy. Furthermore, there are many possible drug interactions between antidepressant medications and anesthetic agents as well as other medications that might be administered in the course of an anesthetic. The most common of these side effects and interactions are shown in **Table 60.2**.

TABLE 60.2 The Most Common Side Effects and Anesthetic Interactions of Psychiatric Medications

Drug Group	Examples of Drug	Mechanism	Side Effects/Toxicities	Perioperative Concerns
SSRI/SNRI	Venlafaxine, fluoxetine	Presynaptic inhibition of SER/NE	Nausea, vomiting Sexual dysfunction Headache Agitation SIADH (rare) Cytochrome P450 inhibition	Prolonged/increased action of β-blockers, benzodiazepines, barbiturates, anticholinergics
Bupropion		SNRI/dopamine reuptake antagonist	Dry mouth, nausea, tremor	Theoretically reduced seizure threshold, prolonged seizure
Lithium	Lithium	Unclear	Sinus node dysfunction	Prolongation of

			AV block Bradycardia Nephrogenic diabetes insipidus	nondepolarizing muscle relaxants Reducing MAC
TCAs	Amitriptyline, imipramine	Presynaptic inhibition of SER uptake	Conduction deficits (wide QRS, prolonged QT Postural hypotension Anticholinergic symptoms Sedation	Muscarinic, histaminergic, and α_1-adrenergic blocking effects
MAOIs	Phenelzine, tranylcypromine	Inhibit breakdown of NE and SER by MAO enzyme	Hypertension Nausea Dizziness Headache Sleep disturbance Severe hypertension with tyramine-containing foods Thrombocytopenia and anemia	Avoid indirect acting sympathomimetics. Avoid serotonin crisis precipitants.
Antipsychotics	Prochlorperazine, chlorpromazine	Block D2 dopamine receptors Atypical antipsychotics also block some serotonin receptors. Also block histamine and α_1-adrenergic receptors	Hypotension Tachycardia, prolonged QT interval Extrapyramidal symptoms Tremor Tardive dyskinesia Neuroleptic malignant syndrome Muscle rigidity, hyperthermia, autonomic dysfunction	

Serotonin syndrome: hyperreflexia, agitation, hyperthermia. AV, atrioventricular; ECT, electroconvulsive therapy; MAC, minimal alveolar concentration; MAO, monoamine oxidase; MAOI, monoamine oxidase inhibitor; NE, norepinephrine; NSAIDs, nonsteroidal anti-inflammatory drugs;

SER, serotonin; SIADH, syndrome of inappropriate antidiuretic hormone secretion; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCAs, tricyclic antidepressants; TIVA, total intravenous anesthesia.

C. Intraoperative Management

C.1. Describe the hemodynamic and cardiac response to ECT in a typical patient.

First, a parasympathetic discharge occurs within a few seconds of application of the electrical stimulus. This may result in bradycardia, which may be profound and even progress to asystole. Because many patients are volume-depleted due to poor oral intake or mildly hypotensive secondary to their psychotropic medications, they can be susceptible to further hypotension due to anesthetic induction. Within 1 minute, sympathetic activation due to the seizure results in a tachycardia and at times dysrhythmias as well as hypertension to up to 150% of baseline values. This hypertension usually lasts for between 2 and 5 minutes. If the patient is not adequately ventilated, hypercarbia may add to the hypertension. During the first ECT treatment, the electrical stimulus may often be titrated upward in succession until a generalized seizure occurs. When a generalized seizure does not follow the electrical stimulation, the parasympathetic response predominates and the patient may experience a sustained bradycardia.

With such a dramatic increase in heart rate and blood pressure, the rate pressure product, an indicator of myocardial oxygen demand, is significantly elevated. This can lead to electrocardiographic ischemia as well as regional wall motion abnormalities on echocardiography.

Messina AG, Paranicas M, Katz B, et al. Effect of electroconvulsive therapy on the electrocardiogram and echocardiogram. *Anesth Analg*. 1992;75:511–514.

Saito S. Anesthesia management for electroconvulsive therapy: hemodynamic and respiratory management. *J Anesth*. 2005;19:142–149.

C.2. Is an arterial line warranted in this patient?

No, in spite of the potential dramatic perturbations in heart rate and blood pressure, these responses are fairly predictable and can be attenuated by judicious use of anticholinergics and antihypertensives. Atropine (0.4 mg) or glycopyrrolate (0.2 mg) are used to prevent the bradycardia associated with the parasympathetic discharge. The tachycardia and hypertension seen as part of the sympathetic response may be prevented with short-acting β-blockade, nitroglycerin, or even remifentanil, administered just at the beginning of the sympathetic stimulation. Pretreatment with dexmedetomidine may also ameliorate the tachycardia and hypertension that occurs immediately post seizure.

Patients may have transient ECG changes around the time of the procedure. There is also evidence that patients may experience a transient decrease in left ventricular function. Rarely, Takotsubo cardiomyopathy occurs. Although severe cardiac complications during ECT have been thought to be very rare, even in patients with underlying coronary disease, a recent meta-analysis identified indicates a rate of cardiac event as frequent as 1 out of 50 patients or 1 in 200 ECT treatments. Another meta-analysis indicated a mortality of 1 in 200,000 treatments.

Cristancho MA, Sattherwaite TD, O'Reardon JP. Cardiac complications of ECT: myocardial stunning syndrome and Takotsubo cardiomyopathy after ECT: different names for the same phenomenon. *J ECT*. 2010;26:146–147.

Duma A, Maleczek M, Panjikaran B, et al. Major adverse cardiac events and mortality associated with electroconvulsive therapy: a systematic review and metaanalysis. *Anesthesiology*. 2019;130:83–91.

Fuenmayor AJ, el Fakih Y, Moreno J, et al. Effects of electroconvulsive therapy on cardiac function in patients without heart disease. *Cardiology*. 1997;88:254–257.

McCully RB, Karon BL, Rummans TA, et al. Frequency of left ventricular dysfunction after electroconvulsive therapy. *Am J Cardiol*. 2003;91:1147–1150.

Messina AG, Paranicas M, Katz B, et al. Effect of electroconvulsive therapy on the electrocardiogram and echocardiogram. *Anesth Analg*. 1992;75:511–514.

Saito S. Anesthesia management for electroconvulsive therapy: hemodynamic and respiratory management. *J Anesth*. 2005;19:142–149.

Tørring N, Sanghani SN, Petrided G, et al. The mortality rate of electroconvulsive therapy: a systematic review and pooled analysis. *Acta Psychiatr Scand*. 2017;135:388–397.

C.3. By what means would you attempt to maximize hemodynamic stability?

First, one should continue antihypertensive medication on the evening before and the morning of the procedure. Second, a small dose of atropine (0.4 mg) or glycopyrrolate (0.2 mg) may be given several minutes before the electrical stimulation in order to prevent the subsequent bradycardia. At Weill Cornell Medical Center, we are more likely to use glycopyrrolate as it is a quaternary compound, which will not cross an intact blood–brain barrier. In addition, the tachycardic response from the seizure is not as pronounced when glycopyrrolate is used as compared with atropine. Anticholinergic pretreatment is most important during the first treatment when the electrical stimulation is being titrated, and it is likely not to progress into a generalized seizure on the first or second stimulus. If the pretreatment with an anticholinergic leaves a fragile patient with an undesirable tachycardia, we may omit it during subsequent treatments as long as the bradycardia is not too severe or prolonged.

Similarly, medications to attenuate the sympathetic response are typically not administered until it is certain that the seizure will generalize. This results in a requirement for very fast-acting drugs to control heart rate and blood pressure. The drug of

choice at Weill Cornell Medicine is esmolol (0.5 to 1.0 mg per kg) or labetalol (5 to 20 mg). If there is a contraindication to β-blockers, diltiazem, or nicardipine may be substituted. Nitroglycerin may be particularly useful in patients with ischemic cardiac disease. Remifentanil has also been found to be effective in attenuating the sympathetic response.

A study of American Society of Anesthesiologists Physical Status I and II patients assessed echocardiographic and hemodynamic parameters when the sympathetic response was pretreated with intravenous β-blocker, calcium channel blocker, or nitroglycerin prior to the electrical stimulus. No new regional wall motion abnormalities were found, but β-blocker seemed to be the most effective medication at attenuating fractional shortening and the entire sympathetic response.

Kadoi Y, Takahashi K, Saito S, et al. Effects of antihypertensive medication on left ventricular function during electroconvulsive therapy: study with transthoracic echocardiography. *J Clin Anesth*. 2006;18:441–445.

Saito S. Anesthesia management for electroconvulsive therapy: hemodynamic and respiratory management. *J Anesth*. 2005;19:142–149.

van Zijl DH, Gordon PC, James MF. The comparative effects of remifentanil or magnesium sulfate versus placebo on attenuating the hemodynamic responses after electroconvulsive therapy. *Anesth Analg*. 2005;101:1651–1655.

C.4. Describe the cerebral hemodynamic effects of ECT.

Electrically induced seizures lead to cerebral hyperemia (increase in cerebral blood flow) as documented by transcranial Doppler and near-infrared spectroscopy. This response occurs even if the seizure does not generalize, suggesting that they are a result of the electric stimulation itself. The increase in cerebral blood flow has been shown to be related to the degree of systemic hypertension and occurs whether bilateral or unilateral stimulus is applied. Although there is a correlation with systemic hypertension, the systemic antihypertensives do not fully

ameliorate the increase in cerebral blood flow. This is due to the fact that these drugs have differing effects on the cerebral and systemic circulations.

Saito S. Anesthesia management for electroconvulsive therapy: hemodynamic and respiratory management. *J Anesth*. 2005;19:142–149.

C.5. How would you proceed with an anesthetic induction for this procedure?

Anesthetic induction may be accomplished with any one of a number of medications. Traditionally, methohexital (0.5 to 1.0 mg per kg) has been the induction agent of choice because it has very little effect on seizure duration and has a rapid onset and recovery profile. Other medication includes etomidate (0.2 to 0.3 mg per kg) or propofol (0.5 to 1.0 mg per kg). In research studies, etomidate provides for longer seizure duration when compared to methohexital and propofol; however, postictal hypertension is more severe and myoclonic contractions may be undesirable. In addition, there is a greater incidence of nausea, increased confusion, and prolonged recovery time. Although adrenal suppression has been reported in patients on continuous infusions of etomidate, there are no reports of adrenal suppression in patients receiving multiple bolus doses of etomidate as part of a course of ECT. In patients in whom etomidate is not well tolerated, propofol or thiopental may be used. Studies concur that propofol and thiopental reduce seizure duration; however, there is controversy as to how this reduction in seizure duration impacts the efficacy of therapy.

Ketamine has been noted to have antidepressant effects and potentiate the early reduction of depressive symptoms when given in conjunction with ECT. It appears that ketamine may be useful in some patients in whom a rapid decrease in depressive symptoms is essential, such as those with extreme suicidal ideation or catatonia. A randomized controlled trial of “ketofol,”

a combination of ketamine and propofol, determines that ketofol was associated with a longer seizure time than propofol, faster recovery than ketamine, with good hemodynamic stability. Current investigations are focused on the optimal dosing of the optimal anesthetic agent to improve ECT efficacy.

Muscle relaxation is usually achieved with succinylcholine (0.5 to 1.0 mg per kg) unless there is a contraindication. In that case, a short-acting nondepolarizing muscle relaxant may be substituted.

Okamoto N, Nakai T, Sakamoto K, et al. Rapid antidepressant effect of ketamine anesthesia during electroconvulsive therapy of treatment-resistant depression: comparing ketamine and propofol anesthesia. *J ECT*. 2010;26:223–227.

C.6. How do you intend to manage his airway during each treatment?

The diagnosis of sleep apnea and the patient's body habitus raise concerns regarding the ease and effectiveness of mask ventilation. In spite of these concerns, a plan to proceed with mask ventilation as well as a backup plan of supraglottic airway or intubation is reasonable. As ECT is usually administered three times a week, repeated intubations may lead to airway trauma and edema. GERD may also be of concern; however, patients for ECT are not intubated solely because of GERD. Continuation of medication to reduce stomach acid and promote gastric emptying as well as a dose of preinduction sodium bicitrate may be used to reduce gastric acidity.

Effective mask ventilation is important for several reasons. First, hypocapnia may lower seizure threshold and promote more effective therapy. Second, avoidance of postseizure hypercapnia is necessary as hypercapnia will exacerbate hypertension and tachycardia.

In anticipation of potential difficult ventilation during ECT,

the patient is preoxygenated for 3 to 5 minutes prior to induction. As soon as induction is accomplished, both an oral and a well-lubricated nasal airway may be placed. A second person ideally is available in case two-person ventilation is required. Jackson-Rees circuits are advantageous for ventilation during ECT. First, it allows adjustment of the amount of positive pressure administered; second, the weight of a tradition bag-valve–mask ventilator may make maintenance of ideal mask placement difficult; finally, as the patient regains spontaneous ventilation, he or she may breathe comfortably and effectively through the Jackson-Rees circuit. If mask ventilation were not effective, an appropriately sized supraglottic airway may be placed.

If necessary for adequate ventilation, intubation may be considered. Unfortunately, repeated intubations over several days and weeks may lead to glottic edema and trauma.

Saito S. Anesthesia management for electroconvulsive therapy: hemodynamic and respiratory management. *J Anesth*. 2005;19:142–149.

D. Postoperative Management

D.1. The patient is extremely agitated upon emergence. Discuss the risk factors for postictal agitation (PIA) as well as the therapeutic options.

PIA manifests as disorientation, inability to consistently follow commands, and motor agitation. Risk factors for PIA include prolonged seizure duration, bilateral versus unilateral ECT, and concomitant lithium therapy. In addition, low doses of induction agent as well as very low doses of succinylcholine are considered risk factors. The use of low-dose succinylcholine may be related to excess lactate production in those patients who have greater manifestation of clinical seizure activity. Increased

lactate levels were noted in patients who experienced PIA versus those who did not.

It is of critical importance to rule out nonconvulsive status epilepticus as an etiology for the PIA. Nonconvulsive status may present as agitation or conversely as mutism.

Treatment of PIA usually consists of benzodiazepine, such as midazolam 1 to 2 mg. If this is not effective, haloperidol may be added. In some circumstances, propofol as a bolus or an infusion have been effective. Current management of PIA may include the use of dexmedetomidine, either as a pretreatment or postseizure therapy.

Other potential adverse effects of ECT include aspiration, headache, nausea, and dental or tongue injuries.

Aksay SS, Bumb JM, Remennick D, et al. Dexmedetomidine for the management of postictal agitation after electroconvulsive therapy after S-ketamine anesthesia. *Neuropsychiatr Dis Treat*. 2017;13:1389–1394.

Cohen MB, Stewart JT. Treatment of post-electroconvulsive therapy agitation with dexmedetomidine. *J ECT*. 2013;29:e23–e24.

Tzabazis A, Schmitt HJ, Ihmsen H, et al. Postictal agitation after electroconvulsive therapy: incidence, severity, and propofol as a treatment option. *J ECT*. 2013;29:189–195.

D.2. After three consecutive uneventful inpatient treatments, the psychiatrist asks if the patient may undergo ECT as an outpatient. Would you agree to this plan?

Outpatient ECT has become an acceptable therapeutic option for many patients. Primarily, it is used for maintenance therapy. It may also be used to complete an initial course of ECT provided that the first several treatments are uneventful medically (i.e., no respiratory or cardiovascular problems) and that the patient is demonstrating improvement in psychiatric status. In addition, because psychiatric patients may be unreliable in following preoperative instructions, such as nothing by mouth status, they

must have another adult who assumes responsibility for ensuring that those instructions are followed. Of course, they must also have an escort to bring them home.

Finally, there needs to be close communication between the treating psychiatrist and the ECT psychiatrist to keep abreast of any change in psychiatric status or in any medical condition.

Ambulatory Surgery

Melinda Randall, Hugh C. Hemmings Jr.

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A 71-year-old female with mild discomfort and an outward bulge in the abdominal area is scheduled for open ventral hernia repair in the ambulatory surgery center. The surgeon's history and physical indicate that it is a small hernia. The patient has a significant family history of hernias. Her preoperative outpatient questionnaire indicates that she has hypertension that is well controlled by medication. She walks and exercises >4 metabolic equivalent of task (METS) physical activity four to five times per week without symptoms of chest pain or shortness of breath. She is 165 cm in height with a weight of 82 kg. The only medication she takes is lisinopril for hypertension. There is a history of postoperative nausea and vomiting (PONV) with prior anesthetics, even with monitored anesthesia care (MAC) for a bunionectomy. This patient is concerned about memory loss after anesthesia; she had some issues after colonoscopy with midazolam, fentanyl, and propofol.

A. Medical Disease and Differential Diagnosis

1. Is this patient morbidly obese?
2. What medical conditions may be associated with obesity and morbid obesity?
3. Is there a link to a decline in memory and thinking with

anesthesia and surgery?

B. Preoperative Evaluation and Preparation

1. What advantages does outpatient surgery offer?
2. What are the goals of the preoperative evaluation of the surgical outpatient?
3. In order to thoroughly screen for disease, should one put all outpatients through a full battery of laboratory testing?
4. What preoperative laboratory testing is necessary for surgical outpatients?
5. Which outpatients should receive a preoperative chest roentgenogram?
6. In which patients is an electrocardiogram (ECG) necessary before outpatient anesthesia and surgery?
7. Would age or physical status influence the decision to perform outpatient surgery?
8. What patients are considered inappropriate for ambulatory surgery?
9. What questions are critically important to ask this patient when obtaining her history?
10. What instructions should the patient be given with regard to continuing or discontinuing lisinopril in the perioperative period?
11. What is an enhanced recovery after surgery (ERAS) protocol, and how would you apply it in the outpatient setting?
12. How would you premedicate this patient?
13. Should every outpatient receive prophylaxis against aspiration pneumonitis?
14. Is an overnight fast justified for all outpatients?

C. Intraoperative Management

1. What are the important considerations in choosing an anesthetic technique for outpatient surgery?
2. How would you monitor this patient?

3. What is the bispectral index (BIS) monitor, and what information does it convey?
4. What benefits might be derived from using a BIS monitor?
5. Is BIS monitoring applicable to children?
6. What are the major limitations of BIS monitoring?
7. What does a BIS reading of 56 mean?
8. What anesthetic agents would you use to induce and maintain general anesthesia in this patient?
9. Under what circumstances might spinal anesthesia be appropriate for outpatient surgery?

D. Postoperative Management

1. What are the common causes of nausea and vomiting in outpatients?
2. How would you pharmacologically prevent PONV in the susceptible ambulatory patient?
3. How is postoperative pain treated?
4. What criteria would you use to establish that a patient can be safely discharged after ambulatory surgery?
5. How would you decide when to discharge a patient after regional anesthesia?
6. What instructions should be given to an ambulatory surgical patients upon discharge?

A. Medical Disease and Differential Diagnosis

A.1. Is this patient morbidly obese?

Morbid obesity is defined by a body mass index greater than 40 kg per m^2. This patient has a body mass index of 30.2 and would, therefore, be considered obese (>30 kg per m^2) but not morbidly obese.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1278–1297.

A.2. What medical conditions may be associated with obesity and morbid obesity?

An abundance of medical conditions may be associated with obesity and morbid obesity. Obstructive sleep apnea (OSA) is the most prevalent sleep-related breathing disorder in *severely obese patients*. Screening tools such as the *STOP-BANG questionnaire* (also see Chapter 63, section B.1) help to identify patients at high risk for OSA, and it is prudent to observe these patients for a minimum of 3 hours postoperatively in an ambulatory setting.

Obesity hypoventilation syndrome is defined as hypoventilation in an obese individual that cannot be attributed to other conditions associated with alveolar hypoventilation. These patients may exhibit hypoxemia and serum electrolyte abnormalities. Transesophageal echocardiography to assess global cardiac function, pulmonary hypertension, and specifically right heart function is recommended in these patients.

Other conditions associate with obesity include the following:

- Hypertension
- Cardiovascular disease
- Diabetes mellitus, type 2 is strongly associated with obesity
- Metabolic syndrome, or the co-occurrence of metabolic risk factors in both type 2 diabetes mellitus and cardiovascular disease (abdominal obesity, insulin resistance, dyslipidemia, and hypertension).
- Kidney disease

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1278–1297.

A.3. Is there a link to a decline in memory and thinking with anesthesia and surgery?

Postoperative cognitive dysfunction (POCD) or neurocognitive

decline is an objectively measured decline in cognition postoperatively compared with preoperative function. Cognitive change after anesthesia was described over 100 years ago, initially as delirium and dementia. The term POCD was applied in the 1980s to refer to cognitive decline assessed purely on the basis of a change in neuropsychological test results. Increasing age, baseline cognitive impairment, and fewer years of education are consistently associated with POCD. According to the Mayo Clinic Study of Aging, 2,000 participants showed that anesthetic exposure after the age of 70 years was positively associated with long-term changes in brain physiology. The decline in cognitive function was small but significant for those who were already suffering from low cognitive function or preexisting mild impairment when exposed to general anesthesia for surgery. Elderly people whose clinical symptoms of cognitive dysfunction are not yet clinically symptomatic can manifest if exposed to anesthesia. It is not possible to determine whether anesthesia, surgery, or the underlying conditions necessitating surgery cause the decline.

There are two anesthesia-related risks that are more common in older people: **Postoperative delirium** is a temporary condition that causes the patient to be confused, disoriented, unaware of her surroundings and to have problems with memory and attention. It may not start until a few days after surgery, may come and go, and usually disappears after about a week. Both hyperactive and hypoactive forms exist, the latter being particularly difficult to diagnose. Many older elective orthopedic surgical patients have probable cognitive impairment preoperatively. Such impairment is associated with development of delirium postoperatively, a longer hospital stay, and lower likelihood of going home upon hospital discharge. *POCD* is a more serious condition that can lead to long-term memory loss with difficulties in learning, concentration, and thinking.

Because some of these problems are already common in elderly people, the only way to determine if a patient actually has POCD (more recently termed postoperative neurocognitive dysfunction [NCD]) is to conduct cognitive testing before and after surgery/anesthesia. Certain conditions including heart disease (especially congestive heart failure), lung disease, Alzheimer disease, Parkinson disease, and previous stroke increase the risk for POCD. Also see Chapter 24, sections D.4 and D.5.

The American College of Surgeons and the American Geriatric Society have suggested that preoperative cognitive screening should be performed in older surgical patients. Recently, the clock drawing task has been promoted as a cognitive screening tool—either by asking a patient to draw a clock free hand with a specific time or handing a patient a piece of paper with a circle on it and asking them to fill it in with the numbers and time on a clock.

Culley DJ, Flaherty D, Fahey MC, et al. Poor performance on a preoperative cognitive screening test predicts postoperative complications in older orthopedic surgical patients. *Anesthesiology*. 2017;127:765–774.

Schulte PJ, Roberts RO, Knopman DS, et al. Association between exposure to anesthesia and surgery and long-term cognitive trajectories in older adults: report from the Mayo Clinic Study of Aging. *Br J Anaesth*. 2018;121(2):398–405.

B. Preoperative Evaluation and Preparation

B.1. What advantages does outpatient surgery offer?

Outpatient surgery typically offers greater convenience to the patient (less time away from home, family, and work), a more pleasant environment with less stress and emotional disturbance, and a reduced risk of infection, particularly for immunocompromised or pediatric patients. Outpatient surgery is

more economical and enables more efficient use of operating rooms with greater flexibility in scheduling surgery, and does not depend on hospital bed availability.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:847–861.

B.2. What are the goals of the preoperative evaluation of the surgical outpatient?

The objectives of the preoperative evaluation are:

- To perform necessary medical assessments, obtain data, arrange for laboratory tests and consultations as indicated, and prescreen for relevant conditions in order to optimize perioperative outcome
- To obtain informed consent
- To provide information and instructions to reduce patient anxiety and improve perioperative management

Organization of preoperative screening varies among ambulatory surgical facilities. The screening process may be organized with an office or facility visit before the day of surgery, by a telephone interview or review of health questionnaire without a visit, or by preoperative screening and visit on the morning of surgery. Each of these systems has its advantages and disadvantages. Nevertheless, the system for preoperative evaluation of ambulatory surgical patients should ensure that screening is performed far enough in advance so that preexisting diseases can be evaluated, treatment optimized, and laboratory data recorded before the patient presents for anesthesia. Written instructions should be supplied to the patient in advance describing the preoperative workup, medications to be taken or held preoperatively, admission, and recovery periods.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:586–611, 847–861.

B.3. In order to thoroughly screen for disease, should one put all outpatients through a full battery of laboratory testing?

Extensive preoperative laboratory testing is rarely required for ambulatory surgery. The practice of preoperative "shotgun" laboratory screening for outpatient surgery has received much criticism. In addition to unnecessarily adding billions of dollars annually to the cost of health care, laboratory screening tests in asymptomatic patients have are of dubious value and can actually increase complications from unnecessary follow-up procedures. History and physical examination are a better means of screening for disease and bleeding risks and should serve to reduce expensive, potentially harmful, and inappropriate tests.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:586–611.

Chung F, Yuan H, Yin L, et al. Elimination of preoperative testing in ambulatory surgery. *Anesth Analg*. 2009;108:467–475.

Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 3rd ed. Philadelphia, PA: Elsevier Saunders; 2013:8–13.

B.4. What preoperative laboratory testing is necessary for surgical outpatients?

Most outpatient surgical facilities consider the operative procedure and patient's age, medical condition, medication history, and state and local regulations in determining which preoperative tests are "required." For the healthy ambulatory patient between the ages of 1 and 40 years having a minor surgical procedure, no laboratory testing may be required. Pregnancy testing is a controversial issue. Many believe that pregnancy testing should be offered to all consenting females of childbearing potential. This approach, however, does not substitute for an appropriate pregnancy history and physical examination. Hemoglobin or hematocrit determination is

appropriate for surgical procedures associated with potential blood loss (unlikely in the ambulatory venue) and for patients at risk for anemia or polycythemia, such as children younger than 1 year or with suspected sickle cell disease, patients with a history of anemia, blood dyscrasia or malignancy, congenital heart disease or chronic disease, or women with heavy menstrual flow, or patients older than 60 years old. Additional testing depends on preexisting conditions. For example, serum electrolyte testing is indicated for a patient with a history of hypertension, diabetes mellitus, renal disease, or taking diuretics, digoxin, steroids, or angiotensin-converting enzyme inhibitors (ACEIs). Likewise, measurement of the partial thromboplastin time (PTT) and the prothrombin time (PT) would be indicated in the presence of a bleeding disorder, anticoagulant use, liver disease, or poor nutritional status. Preoperative urinalysis has been shown to be not useful as a screening test and is no longer required in a routine anesthetic evaluation.

Finegan BA, Rashiq S, McAlister FA, et al. Selective ordering of preoperative investigations by anesthesiologists reduces the number and cost of tests. *Can J Anaesth*. 2005;52:575–580.

Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 3rd ed. Philadelphia, PA: Elsevier Saunders; 2013:8–13, 26–30.

B.5. Which outpatients should receive a preoperative chest roentgenogram?

Abnormalities in the chest radiograph in asymptomatic patients are rare, and the risks to the patient probably exceed the benefits. A preoperative chest radiograph is indicated only for patients with a history or clinical findings of active pulmonary disease. Extremes of age, smoking, stable chronic obstructive pulmonary disease, stable cardiac disease, or resolved recent upper respiratory infection should not be considered absolute

indications.

American Society of Anesthesiologists Task Force on Preanesthesia Evaluation. Practice advisory for preanesthesia evaluation: a report by the American Society of Anesthesiologists Task Force on Preanesthesia Evaluation. *Anesthesiology*. 2002;96:485–496.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:586–611.

Joo HS, Wong J, Naik VN, et al. The value of screening preoperative chest x-rays: a systematic review. *Can J Anaesth*. 2005;52:568–574.

B.6. In which patients is an electrocardiogram (ECG) necessary before outpatient anesthesia and surgery?

It has not been established that information obtained from the preoperative ECG affects clinical care. The American College of Cardiology/American Heart Association (ACC/AHA) guidelines published in 2007 were silent on the need for a preoperative ECG based on age alone. According to the updated 2014 ACC/AHA guideline, a preoperative ECG is "reasonable for patients with known coronary artery disease, significant arrhythmia, peripheral arterial disease, cerebrovascular disease, or other significant structural heart disease, except for those undergoing low-risk surgery." The 2014 guideline specifically states that a preoperative ECG is "not useful for asymptomatic patients undergoing low-risk surgical procedures." The 2007 ACC/AHA guidelines considered ambulatory surgery as one entity, classifying *all* ambulatory procedures as low-risk, with reported cardiac mortality <1%. The 2014 version, however, defines a *low-risk* procedure as one in which the combined surgical and patient characteristics predict a risk of a major adverse cardiac event (MACE) of death or myocardial infarction to be <1%, such as cataract or plastic surgery. A further refinement in the 2014 guideline was to eliminate the separate categories of *intermediate risk* and *high risk*, substituting the category of *elevated risk*, reflecting procedures with a risk of

MACE of ≥1%. These guidelines reflect the belief that in the absence of active cardiac conditions (defined as unstable coronary syndromes, decompensated heart failure, and significant arrhythmias [e.g., high-degree atrioventricular block, symptomatic ventricular arrhythmias, and supraventricular tachycardia with uncontrolled ventricular rate]), cardiovascular testing in stable patients would rarely result in a change in management and it would be appropriate to proceed with surgery without further testing.

Nonetheless, Correll and colleagues found that age older than 65 years is an independent predictor of preoperative ECG abnormalities. In general, a preoperative ECG should be considered in ambulatory patients in whom there is a reasonably high likelihood of cardiac dysfunction and the results of the ECG would have the potential to influence perioperative management. The patient's history, including a thorough exploration of activity level and exercise tolerance, the physical examination, and the proposed surgical procedure are vital elements in the assessment of whether an ECG is indicated.

Correll DJ, Hepner DL, Chang C, et al. Preoperative electrocardiograms: patient factors predictive of abnormalities. *Anesthesiology*. 2009;110:1217–1222.

Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 3rd ed. Philadelphia, PA: Elsevier Saunders; 2013:20–25.

Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to revise the 2002 guidelines on perioperative cardiovascular evaluation for noncardiac surgery): developed in collaboration with the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, and Society for Vascular Surgery. *Circulation*. 2007;116:1971–1996.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline

on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary. *J Am Coll Cardiol*. 2014;64:2373–3405.

B.7. Would age or physical status influence the decision to perform outpatient surgery?

Patients at the extremes of age (e.g., younger than 6 months and older than 80 years) can be managed successfully at ambulatory centers. With the exception of the former preterm infant and newborns in the first few weeks of life, age alone should not be considered a deterrent in the selection of patients for outpatient surgery. Premature infants (gestational age at birth <37 weeks) who undergo general anesthesia during the first months of life are at increased risk for postoperative apnea for up to 12 hours. This risk is greatest for infants younger than 46 weeks postconceptional age, but some investigators have reported apnea in infants as old as 60 weeks postconceptional age. Unfortunately, the postconceptional age at which the former premature infant no longer has an increased risk for postoperative apnea, and therefore would be considered an acceptable candidate for an ambulatory surgical procedure, is not known. It is safest to admit to a hospital or to a 24-hour recovery unit all former premature infants less than 46 weeks postconceptional age so that they can be monitored for apnea. Many anesthesiologists are more conservative and adhere to cut-offs ranging from 52 to 60 weeks postconceptional age. If anemia, bronchopulmonary dysplasia, or other neonatal problems are present, this period may need to be extended. Postoperative apneic episodes have been described in otherwise healthy full-term infants who are anesthetized in the first few weeks of life. For this reason, many anesthesiologists are reluctant to proceed with outpatient anesthesia and surgery on a healthy full-term infant of younger than 2 to 4 weeks of age.

For geriatric patients, recent clinical experience has not

shown an age-related effect on the duration of recovery or the incidence of postoperative complications after outpatient surgery. However, in determining the acceptability of a geriatric patient for an ambulatory surgical procedure, one must consider physiologic age and physical status, the surgical procedure, the anesthetic technique, and the quality of care that will be provided at home. Chronologic age is not a determinant of suitability for ambulatory surgery.

No longer is outpatient surgery restricted to patients of American Society of Anesthesiologists (ASA) physical status I and II. ASA physical status III and IV patients whose diseases are well controlled preoperatively may be considered acceptable candidates for outpatient surgery.

Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 3rd ed. Philadelphia, PA: Elsevier Saunders; 2013:523–528.

Lerman J. Pediatric anesthesia. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1220–1259.

Reeves JC, Barnett SR, McSwain J, et al, eds. *Geriatric Anesthesiology*. 3rd ed. New York: Springer; 2018:353–371.

B.8. What patients are considered inappropriate for ambulatory surgery?

An individual may be considered inappropriate for ambulatory surgery for the following reasons:

- Existence of a condition that places an infant at risk
- History of prematurity in an infant less than 46 to 60 weeks postconceptional age
- Apneic episodes, feeding difficulty, or failure to thrive
- Respiratory distress syndrome that has required intubation and ventilatory support (may take up to a year for symptoms to resolve)
- Bronchopulmonary dysplasia with any significant decrease in pulmonary function or requirement for supplemental oxygen

- Acute concurrent illness
- ASA physical status III or IV with poorly controlled disease
- Active cardiac conditions, as defined by ACC/AHA guidelines
- Acute substance abuse
- Morbid obesity with other serious systemic diseases, such as severe OSA and ventricular dysfunction
- Placement of a bare metal stent within 4 to 6 weeks of the proposed surgery
- Placement of a drug-eluting stent less than at least 1 year before the date of proposed surgery
- No available adult at home
- Refusal to have surgical procedure done as an outpatient
- Unwilling to follow instructions

The appropriateness of each patient must be evaluated on an individual basis, taking into account a combination of several factors, such as the patient's circumstances, the nature of the surgical procedure, anesthetic technique, anticipated severity of postoperative pain, and comfort level of the anesthesiologist.

American Society of Anesthesiologists Committee on Standards and Practice Parameters. Practice alert for the perioperative management of patients with coronary artery stents: a report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. *Anesthesiology*. 2009;110:22–23.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:847–861.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary. *J Am Coll Cardiol*. 2014;64:2373–3405.

Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI guidelines for percutaneous coronary intervention: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. *Circulation*. 2011;124:2574–2609.

Motovska Z. Management of antiplatelet therapy inpatients at risk for coronary stent thrombosis undergoing non-cardiac surgery. *Drugs*. 2011;71:1797–1806.

Reeves JC, Barnett SR, McSwain J, et al, eds. *Geriatric Anesthesiology*. 3rd ed. New York: Springer; 2018:353–371.

B.9. What questions are critically important to ask this patient when obtaining her history?

It is important to rule out OSA in view of the patient's obesity, hypertension, and complaints of fatigue. Does she snore, have frequent awakenings during the night, and daytime somnolence? Not all patients with OSA are appropriate candidates for ambulatory surgery. It is, therefore, important to probe this possibility further with an assessment instrument such as the STOP-BANG questionnaire. A high STOP-BANG score indicates a high probability of OSA. Moreover, obese patients with severe sleep apnea and certain associated conditions (pulmonary hypertension, ventricular dysfunction, etc.) having painful surgery under general anesthesia that may require significant amounts of opioids postoperatively for pain control are typically considered poor candidates for planned outpatient surgery.

American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Obstructive Sleep Apnea. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: an updated report by the American Society of Anesthesiologists Task Force on the Management of Patients with Obstructive Sleep Apnea. *Anesthesiology*. 2014;120:268–286.

Chung F, Subramanyam R, Liao P, et al. High STOP-Bang score indicates a high probability of obstructive sleep apnoea. *Br J Anaesth*. 2012;108:768–775.

Joshi GP, Ankichetty SP, Gan TJ, et al. Society for Ambulatory Anesthesia consensus statement on preoperative selection of adult patients with obstructive sleep apnea scheduled for ambulatory surgery. *Anesth Analg*. 2012;115:1060–1068.

B.10. What instructions should the patient be given with

regard to continuing or discontinuing lisinopril in the perioperative period?

This is a controversial issue, perhaps especially for ambulatory surgery patients. Notable hypotension has been reported after induction of general anesthesia in patients continuing to take ACEIs and angiotensin II subtype 1 receptor antagonists (angiotensin II receptor blockers [ARBs]) on the morning of surgery. A recent study, however, compared two groups of ambulatory and same-day admission patients who were taking either ACEIs or ARBs; one group took the ACEI or ARB on the day before surgery but not on the day of surgery, whereas the other group took the drug on the day of surgery at least 2 hours preoperatively along with other prescribed medications. Discontinuing ACEIs and ARBs on the morning of surgery did not place patients at risk for preoperative hypertension, increased cancellations, unplanned admissions, or notable hypertension in the postoperative care unit. Moreover, patients who continued treatment on the day of surgery did not have more stable hemodynamics perioperatively than did those who discontinued these drugs. Although current opinion generally favors continuation of antihypertensive medications, especially *β*-blockers, up to the time of surgery, it would appear that discontinuing ACEIs and ARBs on the day of surgery is safe and does not increase the incidence of adverse hemodynamic outcomes. Specifically, the 2014 ACC/AHA guidelines state that continuation of ACEIs or ARBs perioperatively is "reasonable" and that if these drugs are held before surgery, it is "reasonable to restart as soon as clinically feasible postoperatively."

Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 3rd ed. Philadelphia, PA: Elsevier Saunders; 2013:48–54.

Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline

on perioperative cardiovascular and management of patients undergoing noncardiac surgery: executive summary. *J Am Coll Cardiol*. 2014;64:2373–3405.

Twersky RS, Goel V, Narayan P, et al. The risk of hypertension after preoperative discontinuation of angiotensin-converting enzyme inhibitors or angiotensin receptor antagonists in ambulatory and same-day admission patients. *Anesth Analg*. 2014;118:938–944.

Wolf A, McGoldrick KE. Cardiovascular pharmacotherapeutic considerations in patients undergoing anesthesia. *Cardiol Rev*. 2011;19(1):12–16.

B.11. What is an enhanced recovery after surgery (ERAS) protocol, and how would you apply it in the outpatient setting?

ERAS programs are perioperative protocols of evidence-based interventions that have been grouped together with the goals of speeding functional recovery and improving postoperative outcomes. Also known as "enhanced recovery protocols" (ERPs) or "fast-track surgery," ERAS programs typically include multidisciplinary and multimodal interventions aimed at minimizing the physiologic changes associated with surgery. Patient benefits associated with ERAS include reduction in postoperative opioid use and length of stay. An enhanced recovery program includes education and engagement through the preoperative, intraoperative, and postoperative period.

Preoperative:

- Preoperative medical optimization, preoperative nutrition, avoidance of prolonged fasting including a carbohydrate drink and clear liquids up to 2 hours prior to surgery. Multimodal anesthesia given preoperative, which can be divided into pharmacologic and nonpharmacologic techniques. Systemic pharmacologic modalities involve opioids and nonopioids, such as acetaminophen, nonsteroidal anti-inflammatory drugs, *N*-methyl-D-aspartate receptor antagonist, anticonvulsants (e.g., γ-aminobutyric acid analogues), β-blockers, α_2-agonists, transient receptor

potential vanilloid receptor agonists (capsaicin), and glucocorticoids.

Intraoperative:

- Central neuraxial techniques, surgical site infiltration with local anesthetics and regional anesthesia.
- Adjunctive techniques include acupuncture, music therapy, transcutaneous electrical nerve stimulation, and hypnosis.

Tan M, Law LS, Gan TJ. Optimizing pain management to facilitate enhanced recovery after surgery pathways. *Can J Anaesth*. 2015;62:203–218.

B.12. How would you premedicate this patient?

Whether the ambulatory surgical patient should receive premedication has been the subject of much interest and debate. Keeping in mind that a prompt recovery is an important consideration in outpatient anesthesia, many authors recommend that little or no premedication (especially centrally active depressant premedicants) be given to surgical outpatients so that recovery is not prolonged. Interestingly, most prospective clinical studies have failed to demonstrate a prolonged recovery following premedication with sedative-anxiolytic and analgesic drugs. However, opioid premedicants have been shown to increase the incidence of postoperative nausea, which could prolong recovery time, and are not recommended unless the patient is in pain preoperatively.

In view of the goals one might want to achieve with outpatient preoperative medication, including anxiety relief, sedation, amnesia, analgesia, vagolysis, prophylaxis against aspiration pneumonia, and prevention of PONV, premedicant drugs may be safely used if needed, provided the drug and dosage are carefully chosen. Drugs commonly used as premedicants for outpatients include sedative-hypnotics, opioids, anticholinergics, antacids, gastro-prokinetics, H_2-receptor antagonists, and antiemetics. Most prospective studies

have not found recovery to be prolonged after the use of appropriate doses of sedative premedication (e.g., midazolam 1 to 2 mg intravenous [IV]). Appropriate use of premedication may actually expedite discharge by reducing postoperative side effects. Grant et al. found that administration of preoperative or intraoperative midazolam is associated with a significant decrease in overall PONV, nausea, vomiting, and rescue antiemetic use. Providers may consider administration of IV midazolam as part of a multimodal approach in preventing PONV. Lorazepam very long duration of action makes it unsuitable for use in the ambulatory surgical patient.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:586–611.

Grant MC, Kim J, Page AJ, et al. The effect of intravenous midazolam on postoperative nausea and vomiting: a meta-analysis. *Anesth Analg*. 2016; 122(3):656–663.

B.13. Should every outpatient receive prophylaxis against aspiration pneumonitis?

Despite early studies demonstrating that a large percentage of outpatients are potentially at risk for gastric aspiration, the actual incidence of pulmonary aspiration is very low (<1 per 35,000) in surgical patients with no specific risk factors. The possibility that outpatients have a greater potential for acid aspiration than inpatients prompted several authors to recommend some form of aspiration prophylaxis for all patients scheduled for outpatient surgery. This is costly and may result in undesired side effects. Although individual ambulatory surgery centers must determine their own policies, pharmacologic prevention of acid aspiration should not be routine but rather reserved for outpatients with predisposing factors (e.g., pregnancy, symptomatic hiatal hernia, diabetes mellitus with autonomic neuropathy). When antacids are used, they should be restricted to nonparticulate antacids.

American Society of Anesthesiologists Committee. Practice guidelines for perioperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. *Anesthesiology*. 2011;114:495–511.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:586–611.

B.14. Is an overnight fast justified for all outpatients?

Several investigators have questioned the value of the traditional overnight fast for surgical outpatients, particularly pediatric outpatients. Prolonged fasting does not guarantee an empty stomach at the time of induction. It does, however, cause patient discomfort and may produce significant physiologic disturbances in infants and young children. Studies in children and adults found no increase in volume or decrease in pH of gastric fluid when clear liquids were administered as late as 2 hours before induction of anesthesia. Therefore, arbitrary restrictions on the preoperative fast for surgical outpatients without risk factors for pulmonary aspiration, such as “nothing by mouth (NPO) after midnight,” appear unwarranted. Clear fluids in reasonable amounts (3 mL per kg) may be safely ingested until 2 hours before surgery. Although coffee is not transparent, it is devoid of particulate matter and is accepted as a clear liquid. There is some evidence that briefer periods of preoperative fasting (2 hours) are accompanied by less PONV as well as a reduced incidence of dizziness, drowsiness, and thirst. Breast milk should be withheld for at least 4 hours in neonates and infants who are being breastfed. Intake of nonclear liquids, nonhuman milk, and solid food should be discontinued at least 6 hours before induction of anesthesia.

American Society of Anesthesiologists Committee. Practice guidelines for perioperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective

procedures: an updated report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. *Anesthesiology*. 2011;114:495–511.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:847–861.

C. Intraoperative Management

C.1. What are the important considerations in choosing an anesthetic technique for outpatient surgery?

Important goals in ambulatory anesthesia include the following:

- Smooth and rapid onset of action
- Intraoperative amnesia and analgesia
- Hemodynamic stability
- Good operating conditions
- Rapid recovery period without side effects
- Cost-effectiveness

No ideal anesthetic drug or technique has been identified for outpatient anesthesia. No single agent or combination of agents, either inhaled or IV, has been clearly shown to reduce recovery time and allow faster discharge of the ambulatory surgical patient. However, with its smooth induction profile and short elimination half-life, propofol may prove to be the induction, if not the maintenance, agent of choice for most outpatient anesthesia. The newer halogenated ether compounds, sevoflurane and desflurane, have become increasingly popular in ambulatory anesthesia owing to their rapid onset and quick termination of clinical effects. Currently, desirable anesthetic conditions with an acceptable recovery profile may be produced by a large array of pharmacologically active drugs administered in conjunction with either general, regional, or local anesthesia techniques. It is essential, however, to combine these agents in a rational manner with carefully titration to optimal effect.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:847–861.

C.2. How would you monitor this patient?

The effects of anesthesia during ambulatory procedures should be monitored using the same standards applicable to inpatient procedures. Standard monitoring in this patient would include a blood pressure cuff, ECG, pulse oximeter, precordial or esophageal stethoscope, temperature probe, and measurement of inspired oxygen and end-tidal carbon dioxide.

Standards for Basic Anesthetic Monitoring. Committee of Origin: standards and practice parameters (approved by the ASA House of Delegates on October 21, 1986, last amended on October 20, 2010, and last affirmed on October 28, 2015.

C.3. What is the bispectral index (BIS) monitor, and what information does it convey?

The BIS monitor is a noninvasive monitoring system that is derived from a two-electrode electroencephalogram (EEG). Using a proprietary bispectral analysis of the EEG waveform and other features within the EEG, the BIS monitor is used to detect changes in purported depth of anesthesia or hypnosis. The proprietary algorithm translates complex data generated from the analysis of the EEG over a 30-second period into a single dimensionless number between 0 (i.e., no brain activity) and 100 (i.e., the patient is fully awake) that is displayed on the BIS monitor. The BIS is one of many brain function monitors that record or process brain electrical activity and convert these signals mathematically into a continuous measure, typically scaled from 0 to 100. It is important to appreciate that intraoperative awareness cannot be measured during the intraoperative phase of general anesthesia because the recall component of awareness can only be determined postoperatively by obtaining information directly from the patient. Although

clinically important, intraoperative awareness under general anesthesia is a rare occurrence, with a reported incidence of 0.1% to 0.2% in adults.

American Society of Anesthesiologists Task Force on Intraoperative Awareness. Practice advisory for intraoperative awareness and brain function monitoring: a report by the American Society of Anesthesiologists Task Force on Intraoperative Awareness. *Anesthesiology*. 2006;104:847–864.

Avidan MS, Zhang L, Burnside BA, et al. Anesthesia awareness and the bispectral index. *N Engl J Med*. 2008;358:1097–1108.

Kent CD, Domino KB. Depth of anesthesia. *Curr Opin Anaesthesiol*. 2009;22:782–787.

Sebel PS, Bowdle TA, Ghoneim MM, et al. The incidence of awareness during anaesthesia: a multicenter United States study. *Anesth Analg*. 2004;99:833–839.

C.4. What benefits might be derived from using a BIS monitor?

Information about the patient's hypnotic state obtained from the BIS, in combination with other monitored parameters and clinical signs, may allow better balancing of hypnotic and analgesic administration. Titration of hypnotic agents based on individual requirements arguably is improved, potentially reducing the incidence of relative under- and overdosing. Furthermore, selection of anesthetic interventions (e.g., administration of hypnotics, analgesics, and vasoactive drugs) may be more rational. Reduced drug usage, earlier awakening, and faster recovery have all been associated with using the BIS monitor to help guide anesthesia maintenance. This translates into a higher potential for bypassing the stage 1 postanesthesia care unit (PACU) and earlier discharge eligibility from the PACU. It is not known whether these benefits ultimately reduce medical costs significantly. A recent meta-analysis based on 1,380 subjects from 11 trials found that BIS monitoring reduced anesthetic consumption by 19%, reduced the incidence of

nausea/vomiting, and reduced time in the PACU by 4 minutes. However, these benefits did not lead to a significant reduction in time until patient discharge from the ambulatory surgery unit. Additionally, BIS monitoring actually increased the cost per patient by $5.55 owing to the cost of the BIS electrodes.

There has been considerable recent interest in depth of anesthesia and 1-year mortality. The investigators in the B-Aware trial reported a secondary analysis of long-term mortality and found that the absence of low BIS values (BIS <40 for >5 minutes) was associated with improved long-term survival and reduced morbidity (myocardial infarction, stroke). However, this association does not imply causation. Preoperative comorbidity is an important independent risk factor for postoperative mortality.

Not surprisingly, that patients with a history of intraoperative awareness are at increased risk to develop the complication again. These patients, and others at high risk of intraoperative awareness (e.g., use of total intravenous anesthesia [TIVA], patients having trauma surgery or cesarean delivery, patients with refractory hypotension), may well benefit from BIS monitoring. Other modalities can also be used to monitor purported anesthetic depth. These include, but are not limited to, end-tidal anesthetic concentration monitoring, auditory evoked potentials, and EEG entropy.

Aranake A, Gradwohl S, Ben-Abdallah A, et al. Increased risk of intraoperative awareness in patients with a history of awareness. *Anesthesiology*. 2013;119:1275–1283.

Leslie K, Myles PS, Forbes A, et al. The effect of bispectral index monitoring on long-term survival in the B-aware trial. *Anesth Analg*. 2010;110:816–822.

Liu S. Effects of bispectral index monitoring on ambulatory anesthesia: a meta-analysis of randomized controlled trials and a cost analysis. *Anesthesiology*. 2004;101:311–315.

Mashour GA, Kent C, Picton P, et al. Assessment of intraoperative awareness with explicit recall: a comparison of 2 methods. *Anesth Analg*. 2013;116:889–

891.

Pavlin JD, Souter KJ, Hong JY. Effects of bispectral index monitoring on recovery from surgical anesthesia in 1,580 inpatients from an academic medical center. *Anesthesiology*. 2005;102:566–573.

C.5. Is BIS monitoring applicable to children?

The BIS was developed and tested on adults. Because the EEG in infants and young children is different from that of an adult and changes as the brain matures, the BIS value may not necessarily apply directly to children. Validating the BIS monitor in infants and young children poses significant problems. End points used to confirm BIS in adults, such as assessment of sedation, sleep, or purposeful movement in response to voice commands, cannot be reliably obtained in young children. Furthermore, there are serious ethical problems in recruiting healthy children as volunteers in studies of general anesthesia. Nevertheless, recent data comparing BIS values between adults and children at various clinical end points during general anesthesia, such as before anesthesia, during maintenance, at emergence, and with increasing concentrations of volatile anesthetic, suggest that BIS generally performs similarly in adults and children with respect to dose response to anesthetic agents. However, in children aged 6 months to 12 years, the BIS increased paradoxically as end-tidal sevoflurane concentration increased from 3% to 4%. BIS values showed a wide variation at the same end-tidal sevoflurane concentration, and the age was considered to be a factor affecting BIS values. A consensus seems to be forming that BIS monitoring should be used with caution in infants younger than 1 year of age, and further work in this area is needed. Definitive studies correlating level of sedation, awareness, and anesthetic outcome with BIS in children have not been published. Nonetheless, consensus is emerging that the incidence of intraoperative awareness is greater in children than adults. Children, however, seem to be

less disturbed by the experience than adults who appear to be more vulnerable to the development of posttraumatic stress.

Bannister CF, Brosius KF, Sigl JC, et al. The effect of bispectral index monitoring on anesthetic use and recovery in children anesthetized with sevoflurane in nitrous oxide. *Anesth Analg*. 2001;92:877–881.

Blussé van Oud-Alblas HJ, van Dijk M, Liu C, et al. Intraoperative awareness during paediatric anaesthesia. *Br J Anaesth*. 2009;102:104–110.

Davidson AJ, Huang GH, Czarnecki C, et al. Awareness during anesthesia in children: a prospective cohort study. *Anesth Analg*. 2005;100:653–661.

Davidson AJ, Huang GH, Rebmann CS, et al. Performance of entropy and bispectral index as measures of anaesthesia effect in children of different ages. *Br J Anaesth*. 2005;95:674–679.

Davidson AJ, Smith KR, Blussé van Oud-Alblas HJ, et al. Awareness in children: a secondary analysis of five cohort studies. *Anaesthesia*. 2011;66(6):446–454.

Kim HS, Oh AY, Kim CS, et al. Correlation of bispectral index with end-tidal sevoflurane concentration and age in infants and children. *Br J Anaesth*. 2005;95:362–366.

C.6. What are the major limitations of BIS monitoring?

The BIS monitor is not a measure of global anesthetic depth but a measure of level of sedation and hypnotic state. As such, it helps the anesthesiologist assess the potential for patient awareness, but it cannot prevent it. In fact, use of the BIS has not been proven to reduce or eliminate the risk of intraoperative awareness. The BIS will not predict patient movement or hemodynamic response to noxious stimulation nor will it predict the exact moment when consciousness will return. Sedation produced by ketamine or nitrous oxide does not produce the expected decrease in BIS. The utility of BIS in patients with neurologic disease has not been adequately studied to validate its use in these patients. Finally, more work is necessary to establish whether BIS is an accurate measure of hypnosis in pediatric patients.

It is important to appreciate that a specific numerical value

may not correlate with a specific depth of anesthesia. Moreover, the measured values do not have uniform sensitivity across different anesthetic drugs or types of patients. Artifacts can be introduced by electrocautery, lasers, warming devices, and other devices and circumstances. The BIS cannot be relied on in all situations, including hypothermia, circulatory arrest, and brain death. Moreover, a small study recently reported that patient position may affect BIS readings, with the head-down position producing an increase in BIS value, and the head-up position being associated with a reduction in BIS value. Intraoperative monitoring of depth of anesthesia to minimize the risk of awareness should rely on multiple modalities, including clinical observations of purposeful or reflex movement, blood pressure, heart rate, end-tidal anesthetic analyzer, and capnography.

The consensus of the ASA Task Force on Intraoperative Awareness is that brain function monitoring is not routinely indicated for patients undergoing general anesthesia and that the decision to use a brain function monitor should be made on a case-by-case basis by the individual practitioner for selected patients at increased risk.

American Society of Anesthesiologists Task Force on Intraoperative Awareness. Practice advisory for intraoperative awareness and brain function monitoring: a report by the American Society of Anesthesiologists Task Force on Intraoperative Awareness. *Anesthesiology*. 2006;104:847–864.

Avidan MS, Zhang L, Burnside BA, et al. Anesthesia awareness and the bispectral index. *N Engl J Med*. 2008;358:1097–1108.

Barr G, Jakobsson JG, Owall A, et al. Nitrous oxide does not alter bispectral index: study with nitrous oxide as sole agent and as adjunct to I.V. anaesthesia. *Br J Anaesth*. 1999;82:827–830.

Chan MT, Gin T. What does the bispectral EEG index monitor? *Eur J Anaesthesiol*. 2000;17:146–148.

Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 3rd ed. Philadelphia, PA: Elsevier Saunders; 2013:332–337.

Kaki AM, Almarakbi WA. Does patient position influence the reading of the bispectral index monitor? *Anesth Analg*. 2009;109:1843–1846.

Wennervirta J, Salmi T, Hynynen M, et al. Entropy is more resistant to artifacts than bispectral index in brain-dead organ donors. *Intensive Care Med*. 2007;33:133–136.

C.7. What does a BIS reading of 56 mean?

The BIS scale is a dimensionless scale from 0 to 100. Typically, BIS values between 40 and 60 correspond with a moderate hypnotic state of general anesthesia and are associated with a low probability of patient consciousness. Deep sedation with a low probability of explicit recall occurs in the 60 to 70 BIS range, with higher values up to 85 associated with light to moderate sedation. A BIS number below 40 indicates a deep hypnotic state, with probability of EEG isoelectricity increasing as BIS approaches 0. However, there are multiple exceptions to these generalities, and the BIS is perhaps best thought of as a trend monitor rather than an "absolute" monitor of hypnotic depth.

Hemmerling TM, Migneault B. Falsely increased bispectral index during endoscopic shoulder surgery attributed to interferences with the endoscopic shaver device. *Anesth Analg*. 2002;95:1678–1679.

Johansen JW, Sebel PS. Development and clinical application of electroencephalographic bispectrum monitoring. *Anesthesiology*. 2000;93:1336–1344.

C.8. What anesthetic agents would you use to induce and maintain general anesthesia in this patient?

A number of anesthetic agents in a variety of combinations can be used successfully to provide general anesthesia in this patient. A reasonable approach would be to induce anesthesia with propofol after a preinduction dose of a short-acting benzodiazepine. After intubation, anesthesia is maintained with a volatile anesthetic, such as sevoflurane or desflurane in an air–oxygen mixture, supplemented with a short-acting opioid as needed and a muscle relaxant. Alternatively, a total IV technique with propofol as the primary agent could be used.

Although nitrous oxide has been thought to contribute to PONV, conclusive evidence is lacking to demonstrate an important effect of nitrous oxide on the incidence of postoperative emesis after laparoscopic cholecystectomy or pelvic laparoscopy. A recent review and meta-regression analysis reported that the increase in PONV sometimes seen with administration of nitrous oxide depends on the duration of exposure and is clinically unimportant up to at least 1 hour of exposure. Therefore, any potential benefit from its elimination for surgical cases of limited duration must be balanced against the potential increased risk of intraoperative awareness.

The Beers Criteria for Potentially Inappropriate Medication Use in Older Adults, commonly called the Beers List, are guidelines for health care professionals to help improve the safety of prescribing medications for older adults.

- *Dementia or cognitive drugs impairment in the geriatric population: drugs to avoid*
  - Anticholinergics, benzodiazepines, H_2-receptor antagonists, nonbenzodiazepine benzodiazepine receptor agonist hypnotics (eszopiclone, zolpidem, zaleplon), antipsychotics
- *Delirium: drugs to avoid*
  - Anticholinergics, antipsychotics, benzodiazepines, chlorpromazine, corticosteroids, H_2-receptor antagonists (cimetidine, famotidine, nizatidine, ranitidine), meperidine, sedative-hypnotics

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American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. *J Am Geriatr Soc*. 2019;67(4):674–694.

Clegg A, Young JB. Which medications to avoid in people at risk of delirium: a systemic review. *Age Ageing*. 2011;40(1):23–29.

Diemunsch PA, Torp KD, Van Dorsselaer T, et al. Nitrous oxide fraction in

the carbon dioxide pneumoperitoneum during laparoscopy under general inhaled anesthesia in pigs. *Anesth Analg*. 2000;90:951–953.

Peyton PJ, Wu CY. Nitrous oxide-related postoperative nausea and vomiting depends on the duration of exposure. *Anesthesiology*. 2014;120:1137–1145.

Rodriguez G, Joseph SE. Anesthesia for laparoscopic and robotic surgeries. In: Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:1262–1275.

C.9. Under what circumstances might spinal anesthesia be appropriate for outpatient surgery?

Spinal anesthesia is a quick and reliable technique. The limitations of using spinal anesthesia in the ambulatory setting include delayed ambulation, risk of urinary retention, and pain after block regression. In contrast, general anesthesia with fast-acting drugs provides a fast recovery that facilitates an early discharge. Reducing the dose of the commonly used long-acting local anesthetics can reduce recovery time, but discharge times are still prolonged compared with general anesthesia. 2-Chloroprocaine is an amino-ester local anesthetic with a very short half-life that can be used as a local anesthetic for ultra-short outpatient procedures; it has also shown to have a very low risk of urinary retention and transient neurologic symptoms when compared with bupivacaine or lidocaine.

Ben-David B, Maryanovsky M, Gurevitch A, et al. A comparison of minidose lidocaine-fentanyl and conventional-dose lidocaine spinal anesthesia. *Anesth Analg*. 2000;91:865–870.

Fanelli A, Ghisi D, Allegri M. Is spinal anaesthesia a suitable technique for ultra-short outpatient procedures? *Acta Biomed*. 2013;84(1):76–80.

D. Postoperative Management

D.1. What are the common causes of nausea and vomiting in outpatients?

Nausea and vomiting are significant problems after ambulatory

surgery, causing patient discomfort and delayed recovery and discharge from the ambulatory center. Prolonged vomiting is one of the most frequent causes of unexpected hospital admission from the ambulatory surgical facility and is a major cause of patient dissatisfaction with their anesthesia care. Patients who have a history of motion sickness or PONV are more likely to develop postoperative symptoms of emesis, as are patients who are obese, pregnant, or have diabetes mellitus. PONV are common in children; the incidence decreases with age. Men and women are equally affected until puberty, when the incidence becomes considerably higher in women. Excessive anxiety and noncompliance with fasting can increase gastric volume and predispose patients to PONV. Interestingly, smoking has been shown to decrease the incidence of PONV.

The use of opioid analgesics, particularly morphine and meperidine, as premedication, as part of the anesthetic technique, or postoperatively to control pain, increases the incidence of PONV after outpatient anesthesia. Methohexital is less likely than either thiopental or etomidate to cause postoperative nausea. Propofol has a low incidence of emetic symptoms postoperatively and can be antiemetic, a desirable property in this setting.

Although the Apfel scoring system to predict the likelihood of PONV emphasizes female gender, nonsmoking status, history of PONV or motion sickness, and opioid administration as the major risk factors, there is no or insufficient evidence for a number of commonly held factors, such as preoperative fasting, menstrual cycle, and surgery type; using these factors may be counterproductive in assessing risk for PONV. In addition, pain, hypotension, and early ambulation are postoperative factors shown to increase nausea and vomiting.

Apfel CC, Heidrich FM, Jukar-Rao S, et al. Evidence-based analysis of risk

factors for postoperative nausea and vomiting. *Br J Anaesth*. 2012;109:742–753.

Apfel C, Kranke P, Eberhart LH, et al. Comparison of predictive models for postoperative nausea and vomiting. *Br J Anaesth*. 2002;88:234–240.

D.2. How would you pharmacologically prevent PONV in the susceptible ambulatory patient?

Because of concerns about medication cost and potential side effects, routine prophylactic administration of an antiemetic is not considered appropriate for all ambulatory surgical patients. Instead, antiemetic prophylaxis should be reserved for patients who are considered to be susceptible to developing PONV. Many medications have been used as prophylaxis for PONV in the outpatient, some with only limited success. Unfortunately, the ideal medication for each patient is not known. Serotonin antagonists, such as ondansetron 4 to 8 mg IV in adults and 0.1 mg per kg IV in children, are highly effective, but their use as single agents in high-risk patients may not suffice. Droperidol is effective, inexpensive, and without an increase in postoperative sedation when used in low doses, such as 0.625 to 1.25 mg in adults (or as low as 10 to 20 μg per kg). However, the U.S. Food and Drug Administration (FDA) issued a black box warning on the use of droperidol for antiemetic prophylaxis based on concerns about prolongation of the QTc interval and subsequent potentially dangerous ventricular arrhythmias. Charbit et al. reported that droperidol and ondansetron induce similar clinically relevant QTc prolongation and concluded that the safety of 5-hydroxytryptamine type 3 (5-HT_3) antagonists may not be superior to that of low-dose droperidol. Although the serotonin antagonists are classically believed to lack efficacy with regard to preventing or treating nausea, the newest 5-HT_3 blocker, palonosetron, appears to reduce its severity, and the extended benefits of palonosetron may last up to 3 days, given its long half-life. In addition, palonosetron purportedly has no

QT-interval issues.

Prophylactic administration of dexamethasone, 1 to 10 mg IV in adults and 0.5 to 1 mg per kg IV in children, is effective in the prevention of PONV and appears to offer no evidence of any clinically relevant toxicity. Combining dexamethasone with a serotonin antagonist further decreases the incidence of nausea and vomiting and may prove to be the best prophylactic regimen, although optimal doses of this combination are not currently known. Transdermal scopolamine effectively reduces PONV if given as a premedicant well in advance of the surgery, but the high incidence of anticholinergic side effects and prolonged residual effects on cognitive performance, especially in the elderly, detract from its usefulness in the ambulatory patient.

Aprepitant is a highly selective, brain-penetrating neurokinin-1 receptor antagonist that is effective against centrally induced emesis. A recent study showed that aprepitant was superior to ondansetron for prevention of vomiting in the first 24 to 48 hours, but no notable differences were detected between aprepitant and ondansetron for nausea control, use of rescue drugs, or complete response.

Because the etiology of PONV is multifactorial, there is increasing evidence that a multimodal approach may lead to improved outcomes. Double and triple antiemetic combinations, using drugs with different mechanisms of action, are recommended for patients at high risk of PONV. Moreover, liberal hydration and effective analgesia play an important role in reducing the incidence of PONV. General anesthesia with volatile agents should be avoided, if possible, in high-risk patients. If general anesthesia is necessary, a total IV approach with propofol may be advantageous. Moreover, if rescue therapy for PONV is needed within 6 hours of surgery, patients should not receive a repeat dose of the drug that was administered

prophylactically. Rather, a rescue drug with a different mechanism of action should be selected.

Apfel CC, Kranke P, Katz MH, et al. Volatile anaesthetics may be the main cause of early but not delayed postoperative vomiting: a randomized controlled trial of factorial design. *Br J Anaesth*. 2002;88:659–668.

Apfel CC, Läärä E, Koivuranta M, et al. A simplified risk score for predicting postoperative nausea and vomiting: conclusions from cross-validations between two centers. *Anesthesiology*. 1999;91:693–700.

Charbit B, Albaladejo P, Funck-Brentano C, et al. Prolongation of QTc interval after postoperative nausea and vomiting treatment by droperidol or ondansetron. *Anesthesiology*. 2005;102:1094–1100.

Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 3rd ed. Philadelphia, PA: Elsevier Saunders; 2013:294–300.

Gan TJ, Apfel CC, Kovac AL, et al. A randomized, double-blind comparison of the NK_1 antagonist, aprepitant, versus ondansetron for the prevention of postoperative nausea and vomiting. *Anesth Analg*. 2007;104:1082–1089.

Gan TJ, Diemunsch P, Habib AS, et al. Consensus guidelines for the management of postoperative nausea and vomiting. *Anesth Analg*. 2014;118:85–113.

Kovac AL, Eberhart L, Kotarski J, et al. A randomized, double-blind study to evaluate the efficacy and safety of three different doses of palonosetron versus placebo in preventing postoperative nausea and vomiting over a 72-hour period. *Anesth Analg*. 2008;107:439–444.

Kranke P, Eberhart LH. Possibilities and limitations in the pharmacological management of postoperative nausea and vomiting. *Eur J Anaesthesiol*. 2011;28:758–765.

Ruiz JR, Kee SS, Frenzel JC, et al. The effect of an anatomically classified procedure on antiemetic administration in the postanesthesia care unit. *Anesth Analg*. 2010;110:403–409.

Sinclair DR, Chung F, Mezei G. Can postoperative nausea and vomiting be predicted? *Anesthesiology*. 1999;91:109–118.

D.3. How is postoperative pain treated?

Pain control is one of the most important factors in determining when a surgical outpatient can be discharged. Pain should be treated rapidly and effectively to minimize postoperative symptoms so that ambulation and discharge are not delayed. The

optimal strategy is to use a preemptive, multimodal approach. Begin controlling postoperative pain intraoperatively by supplementing the anesthetic technique with a short-acting opioid analgesic or a regional block. IV fentanyl is usually the opioid of choice for postoperative pain relief. It may be given in small doses of 25 μg at 5-minute intervals and titrated to relief of pain. Ketorolac, a nonsteroidal anti-inflammatory drug, has become increasingly popular in the management of postoperative pain in the ambulatory patient because of its lack of opioid-related side effects (e.g., sedation, nausea, vomiting, respiratory depression). It is available for oral and parental administration, and its use may decrease a patient's requirement for opioid analgesics. Controversy still surrounds the perioperative use of ketorolac because of the potential for bleeding complications and renal dysfunction. Local and regional anesthetic techniques can be used to provide effective postoperative analgesia and, when used to supplement general anesthesia, facilitate a pleasant emergence and minimize the need for opioids. Commonly used techniques include local infiltration of the incision site, intra-articular injection, nerve blockade (e.g., dorsal nerve penile block for circumcision or ilioinguinal and iliohypogastric nerve blocks for inguinal hernia repair), and caudal blocks. Bupivacaine liposomal injectable suspension (Exparel®; Pacira Pharmaceuticals, Inc, Parsippany, NJ), formulated using the DepoFoam® (Pacira Pharmaceuticals, Inc, Parsippany, NJ) lipid-based delivery system, was approved for administration into the surgical site after bunionectomy and hemorrhoidectomy, offering long-acting analgesia without opioid-associated side effects. In February of 2018, the FDA approved a new indication for use in interscalene brachial plexus nerve block for postsurgical analgesia for shoulder surgery. One randomized study in 200 patients compared efficacy and safety of transversus abdominis plane (TAP) blocks with Exparel

versus epidural anesthesia using a continuous infusion of local anesthetic plus fentanyl. Systemic opioid use was less in patients with a TAP block, and there were no differences in postoperative complications or length of hospital stay.

When the patient has resumed intake of oral fluids, oral analgesics (e.g., acetaminophen, nonsteroidal anti-inflammatory drugs, oxycodone, hydrocodone, and other opioid analgesics) may be administered for control of pain after discharge.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:847–861.

Golf M, Daniels SE, Onel E. A phase 3, placebo-controlled trial of DepoFoam® bupivacaine (extended-release bupivacaine local analgesic) in bunionectomy. *Adv Ther*. 2011;28(9):776–788.

Joshi GP. Anesthetic management for enhanced recovery after major surgery (ERAS) in adults. https://www.uptodate.com/contents/anesthetic-management-for-enhanced-recovery-after-major-surgery-eras-in-adults. Updated January 15, 2019. Accessed June 1, 2019.

D.4. What criteria would you use to establish that a patient can be safely discharged after ambulatory surgery?

For patients to be discharged from an ambulatory facility, they must satisfy specific criteria that are usually summarized on simplified checklists. Although each ambulatory surgical facility must determine its own set of criteria, generally accepted guidelines for safe discharge home after ambulatory surgery include the following:

- Stable vital signs
- No evidence of respiratory depression
- Oriented to person, place, and time
- Able to walk unassisted
- Able to dress unassisted
- Minimal nausea or vomiting
- No active bleeding or oozing

- Pain controllable with oral analgesics
- Responsible adult to escort patient home and to remain with the patient overnight
- Discharge by both the person who administered anesthesia and the person who performed surgery, or their designees
- Written instructions for the postoperative period at home must be supplied to the patient before discharge as well as a phone number to call in the case of emergency.

The requirement for patients to drink and void before discharge is no longer considered mandatory, except in the case of certain patients who had central neuraxial blockade.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:847–861.

Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 3rd ed. Philadelphia, PA: Elsevier Saunders; 2013:343–351.

D.5. How would you decide when to discharge a patient after regional anesthesia?

Patients recovering from regional anesthesia must satisfy the discharge criteria listed earlier. In addition, if spinal or epidural anesthesia is used for outpatients, it is important to ensure recovery from the sympathetic and the motor blocks. Hypotension and syncope on standing may be signs that the sympathetic nervous system is still blocked. An indication that the motor block is no longer functioning is the ability to move the legs and feet freely. A simple test is to have the patient run each heel up and down the opposite leg from the big toe to the knee. Ability to walk to the bathroom and void are excellent recovery tests after epidural or spinal anesthesia because these abilities reflect recovery of both the motor and the sympathetic functions.

Mulroy et al. have suggested that delaying discharge for voiding after spinal or epidural anesthesia with *short-acting*

local anesthetics is unnecessary in *low-risk* patients (e.g., age younger than 70 years; no hernia, rectal, or urologic surgery; no history of voiding problems). Nonetheless, appropriate measures must be in place for bladder catheterization if the inability to void persists after discharge home. The use of ultrasonographic monitoring of bladder volume before discharge may reduce the incidence of urinary retention after discharge.

Darrah DM, Griebling TL, Silverstein JH. Postoperative urinary retention. *Anesthesiol Clin*. 2009;27:465–484.

Fleisher LA, ed. *Evidence-Based Practice of Anesthesiology*. 3rd ed. Philadelphia, PA: Elsevier Saunders; 2013:343–352.

Mulroy MF, Salinas FV, Larkin KL, et al. Ambulatory surgery patients may be discharged before voiding after short-acting spinal and epidural anesthesia. *Anesthesiology*. 2002;97:315–319.

Pavlin DJ, Pavlin EG, Gunn HC, et al. Voiding in patients managed with or without ultrasound monitoring of bladder volume after outpatient surgery. *Anesth Analg*. 1999;89:90–97.

D.6. What instructions should be given to an ambulatory surgical patients upon discharge?

Patients should be discharged to the care of a responsible adult. Additionally, they should be instructed that after surgery, they should not ingest an alcoholic beverage or depressant medication unknown to their surgeon or anesthesiologist, drive a car, or operate complex machinery for at least 24 hours. In addition, the discharge instructions should provide a list of problems that require immediate notification of the surgeon (e.g., bleeding that does not stop, inability to void, and persistent PONV).

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:847–861.

Marshall SI, Chung F. Discharge criteria and complications after ambulatory surgery. *Anesth Analg*. 1999;88:508–517.

62 Magnetic Resonance Imaging

Jayanth Swathirajan, Dana L. Gurvitch, and Hugh C. Hemmings Jr.

You are consulted by the pediatric intensive care unit (PICU) team on an 11-year-old, 35-kg boy for urgent magnetic resonance imaging (MRI). He is 2 days removed from a partial temporal lobectomy for seizure management and now has altered mental status and is thrashing in the PICU. The child has intractable seizures but no other medical history. He was able to cooperate enough to perform a computed tomography (CT) scan that showed no acute bleeding, but the team wants an MRI and does not believe he will stay still for the 1.5-hour scan. He is currently extubated, but on your review of his previous anesthetic record, you see that he required an oral airway to achieve adequate mask ventilation. On conventional direct laryngoscopy only the epiglottis was visualized (Cormack-Lehane grade III view), but when a video laryngoscope was used the epiglottis, arytenoid cartilages and posterior vocal cords were visualized (Cormack-Lehane grade IIa view) and an endotracheal tube was passed atraumatically. Your patient has a left hand 20 gauge peripheral intravenous catheter and a right radial arterial catheter for close blood pressure monitoring. He is current with all his antiepileptic medications and is otherwise appropriately nothing

orally (NPO).

A. Medical Disease and Differential Diagnosis

1. What is MRI, and how does it work?
2. What are some advantages of MRI?
3. What are some disadvantages associated with MRI? What are some safety concerns?
4. How do you manage patients with implanted devices?
5. What are the biologic effects of clinical MRI?
6. What are the anesthetic considerations for this procedure?
7. What is intraoperative MRI (iMRI)? What is real-time MRI, and in what setting can this be used?

B. Preoperative Evaluation and Preparation

1. What type of patients may require sedation or general anesthesia for MRI?
2. Do all children require sedation for MRI?
3. What preoperative laboratory testing would you require for this patient?
4. How would you premedicate this patient? What are some options that can be used to premedicate other patients for MRI?

C. Intraoperative Management

1. What are some of the anesthetic options for this patient?
2. How is an MRI conducted?
3. How would you monitor this patient?
4. What special considerations apply to monitoring equipment used during MRI?
5. How would you induce and maintain general anesthesia in this patient?
6. What are ways to maintain the airway during an MRI scan?
7. During the scan, you notice loss of end-tidal carbon dioxide.

You immediately go into the scanner, remove the patient from the MRI scanner and initiate bag ventilation. However, you are still unable to ventilate the patient, and asystole follows. What do you do next?

8. What is the risk to the patient of gadolinium administration in the presence of acute renal insufficiency?

D. Postoperative Management

1. How will you recover the patient from anesthesia?

A. Medical Disease and Differential Diagnosis

A.1. What is MRI, and how does it work?

MRI is a noninvasive diagnostic technique that uses the magnetic properties of atomic nuclei to produce high-resolution, multiplanar cross-sectional images of the body. MRI is utilized both as an interventional aid in diagnosis and in disease therapy in lieu of conventional approaches. Atoms having an odd number of protons and/or neutrons in their nuclei, most notably hydrogen, have an associated magnetic dipole. The net rotation of protons or neutrons produces a local magnetic field similar to the electromagnetic field produced by the flow of electrons in a wire loop. Biologic tissues have high water content and therefore have abundant hydrogen. The detection of hydrogen's single proton serves as the basis for MRI. Normally, the magnetic fields surrounding these nuclei are randomly oriented. When placed in the setting of a powerful static magnetic field of the MRI scanner, the nuclei align themselves longitudinally so they lie parallel or antiparallel (in line but moving in an opposite direction) to the magnetic field. The hydrogens aligned antiparallel have a slightly higher energy than those aligned parallel, thereby causing the tissue to have a slight net magnetic field that can be detected by the MRI scanner. The higher the

strength of the magnet used, the stronger the tissue magnetic field.

Within the MRI, a quick specific radiofrequency (RF) pulse of energy (a second magnetic field) is directed toward the patient at right angles to the tissue's generated static magnetic field, displacing the aligned nuclei from the longitudinal magnetic field. As the RF pulse is removed, the nuclei return to their original magnetic alignment positions. This is termed *relaxation*. The energy released from the tissue as the nuclei relax is termed an RF signal. It can be detected by the receiver coil of the scanner placed close to the patient and is used to produce the magnetic resonance (MR) image. There are two ways to measure relaxation time, T1 and T2; certain tissues and/or pathologies are best viewed either with T1 or T2 weighted imaging. This allows for differentiation of body structures as well as between normal and pathologic tissue.

Resolution of the image requires a strong magnetic field. The magnetic field strength used to quantify the scanners is in Tesla (T) units. One tesla is equivalent to 10,000 gauss. Most MRI scanners used now have a magnetic field of 0.5 to 3.0 T (the magnetic field of the earth is 5×10^{-5} T). Also, the smaller the opening to the scanner, the stronger the possible magnet. Therefore, although patients may prefer an "open" magnet, which induces less claustrophobia, this generates a weaker image.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:880–896.

A.2. What are some advantages of MRI?

The advantages of MRI include the lack of ionizing radiation; the capability of using noniodinated intravenous contrast agent, thereby reducing the risk of an anaphylactic or nephrotoxic reactions; and the production of multiplanar, temperature

sensitive, contrast amplified images. MRI also provides excellent resolution of normal tissues (e.g., gray and white matter and soft tissues) without image artifact from bone, and it can differentiate between normal and pathologic tissue. MRI may be used to evaluate blood and cerebrospinal fluid flow, to assess contraction and relaxation of organs such as the heart, and to provide images of tissues in proximity to bone. Specifically, brain MRI is indicated to evaluate for indicating developmental delay, cause of seizures, failure to thrive, apnea, cyanosis, and vascular lesions.

MRI-guided intervention is another major potential advantage in cases where conventional CT imaging is lacking. These images of the soft tissues and tumors are exceptionally delineated, thus facilitating interventions for biopsies of these areas. MRI offers better capture of the temperature-related changes that occur during cryoablation and has been effectively used in safely treating liver, kidney, breast, and prostate tumors as well as in uterine fibroids. MRI has also proven advantageous during interventional electrophysiology studies and catheter ablation procedures. MRI offers structural real-time three-dimensional (3D) images of the anatomy and presence of scar tissue in the heart and nearby structures, and exact localization of the ablation catheter. It can also delineate potential gaps in ablation. Delayed enhancement (DE) MRI is currently the gold standard for outlining scar/fibrosis in the heart that may serve as an arrhythmogenic source for patients with ventricular tachycardia (VT). Based on the staging of atrial fibrosis, DE MRI can also provide vital preprocedural information in identifying those patients who might be at risk for relapse of atrial fibrillation. In experienced hands and centers, real-time MRI provides vital information while eliminating the radiation required by conventional fluoroscopy.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:880–896.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier/Saunders; 2019:1077–1094.

Eitel C, Hindricks G, Grothoff M, et al. Catheter ablation guided by real-time MRI. *Curr Cardiol Rep*. 2014;16(8):511.

A.3. What are some disadvantages associated with MRI? What are some safety concerns?

There are many hazards associated with an MRI suite. The constant static magnetic field, the pulsed (time-varied) gradient magnetic fields, and the high-frequency RF waves all interact; when combined with a ferromagnetic object, this can pose significant risk to the patient or operator. Not only can attraction of external objects be fatal but also implantable objects can dislodge and malfunction or burn the patient. Depending on the distance from the core of the magnet, the magnetic field strength diminishes. Distances less than the 5-gauss line can make pacemakers malfunction, and less than 50-gauss line can make ferromagnetic gas cylinders lethal projectile missiles.

Owing to the potential for catastrophic events, recommendations for MRI safety have been proposed by the American College of Radiology. Briefly, the MRI suite should be separated into four zones: zone I is the public zone immediately outside the MRI suite, zone II is the reception area monitored by MRI personnel, zone III encompasses the control room with access restricted from the public, and zone IV is the physical MRI scanner room. To ensure safety, entry into zones III and IV must be screened by MRI personnel (**Fig. 62.1**). Ferromagnetic objects should not be brought into zone III, but if necessary, they should be brought in with extreme caution. Items such as credit cards, pens, keys, laryngoscopes, scissors, stethoscopes, paper clips, and ferromagnetic gas cylinders are

excluded from zone IV. One important way to ensure safety is to use aluminum oxygen E-gas cylinders instead of magnetic ones. Adherence to these zones must be maintained especially during emergent situations.

FIGURE 62.1. The MRI suite should be separated into four zones.

Safety terminology for devices and implants was developed by the ASTM International. *MR safe* refers to items with no known hazards in any MR environment. *MR conditional* refers

to items that pose no known hazards in a specified MR environment (i.e., the conditions present at your scanner). *MR unsafe* refers to items that pose definite hazards in all MR environments (i.e., ferromagnetic scissors). Concerns about a specific device and its potential hazards should be addressed by staff members, on-site radiologists, and/or manufacturer to determine whether the exam can be conducted in a safe manner.

Additional patient-related risks include (1) need for intensive or critical care (vasoactive infusion requirement), (2) comorbidities that may contribute to adverse MRI effects (burns, obesity-related temperature increases), and (3) impaired respiratory function (obstructive sleep apnea, tonsillar hypertrophy).

Other major disadvantages of MRI include the potential for malfunction of electronic equipment (e.g., monitors and infusion pumps) and the limited access to the patient. MR safe/conditional monitors and machines should be used in the scanner. Thermal injuries have been reported from electrocardiogram (ECG) electrodes and pulse oximeter probes. All cables and monitoring equipment should be placed in a straight manner without coiling to ensure no such injuries. MR safe/conditional infusion pumps can be used in zone IV, but otherwise, pumps can be left in zone III and the tubing passed through a wave guide. The relatively long scan time necessary to obtain images (as much as 15 minutes per image, with a total scanning period of 1 to 3 hours) and image degradation from any motion including cardiac contractions, respirations, cerebrospinal fluid flow, and bowel peristalsis are additional disadvantages. MRI safe anesthesia machines and monitoring equipment are available; however, cost may prove prohibitive for institutions that do not regularly do MRI under anesthesia. MR conditional anesthesia machines can cost $60,000, monitors $120,000 to $140,000, and infusion pumps $12,000 to $18,000.

Another potential hazard to both patients and operators is the high decibel level of sound emanating from the scanner due to RF pulses (>90 dB). Hearing protection for both is mandatory even if the patient is under anesthesia.

Quenching of the MRI machine is a rare hazard that refers to a sudden loss of superconductivity of the magnet, which can occur either spontaneously or be triggered by a significant safety event. During a quench, the temperature of the magnet coil suddenly rises, resulting in an explosive boil-off of surrounding liquid helium and deactivation of the magnet. In the event of a quench, the patient should be quickly removed from the now hypoxic room. The magnet should almost never be quenched on purpose because it creates a dangerous room for the patient as well as other providers. In the case of a medical emergency for a patient, the best practice would be to remove the patient to zone II or zone III and initiate resuscitation. Once the magnet is quenched, it cannot be reactivated for days.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:880–896.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier/Saunders; 2019:1077–1094.

Kanal E, Barkovich AJ, Bell C, et al. ACR guidance document on MR safe practices: 2013. *J Magn Reson Imaging*. 2013;37:501–530.

Ocazionez D, Dicks DL, Favinger JL, et al. Magnetic resonance imaging safety in cardiothoracic imaging. *J Thorac Imaging*. 2014;29:262–269.

Practice advisory on anesthetic care for magnetic resonance imaging: a report by the Society of Anesthesiologists Task Force on Anesthetic Care for Magnetic Resonance Imaging. *Anesthesiology*. 2009;110:459–479.

Safety Guidelines for Magnetic Resonance Imaging Equipment in Clinical Use. London, Medicines and Healthcare Products Regulatory Agency. 2014;16–17. http://www.ismrm.org/smrt/files/con2033065.pdf. Accessed December 21, 2019.

A.4. How do you manage patients with implanted

devices?

Patients with certain implanted biologic devices, such as pacemakers, implantable cardioverter-defibrillators (ICDs), and certain pumps, should be excluded from MRI studies because of the possibility of device malfunction, inactivation, or damage in the magnetic field. The safety of various cardiovascular devices for MR examination was reviewed based on ex vivo, animal, and in vivo studies and reported by the American Heart Association (AHA). Although many coronary stents, peripheral stents, sternal wires, inferior vena cava filters, prosthetic heart valves, and annuloplasty rings have been deemed MR safe or conditional, it is important to review each type carefully and decide whether the proposed MRI exam is in line with the specified safety of the particular device. Currently, the AHA and the American Society of Anesthesiologists (ASA) Practice Advisory Task Force on Anesthetic Care for Magnetic Resonance Imaging regard the presence of a pacemaker or an ICD as a strong relative contraindication to routine MRI examination. In 2011, MR conditional ICDs, pacemakers, and leads became available and are available in the United States; they are approved in certain settings and up to 1.5 T MRI examinations. Intact pacemaker leads are unlikely to move; however, an electrical current could be generated if fractured leads are exposed to the magnet, causing a lethal arrhythmia. MRI is currently contraindicated in patients with an artificial heart or ventricular assist device. Also see Chapter 8, section B.8.

If the benefits far outweigh the risks of the exam, MRI should be performed in an experienced center with collaboration between the cardiologist, radiologist, device manufacturer, and MRI technician. Written consent must detail all risks to the patient including death. Full resuscitation equipment must be readily accessible in the MRI suite in case of an arrhythmia or

equipment malfunction.

According to the Heart Rhythm Society (HRS), for MR conditional devices it is reasonable to proceed with standard monitoring but have external defibrillators and personnel capable to reprogram the cardiovascular implantable electronic device (CIED) available. If the device is not MR conditional and the patient is pacemaker dependent, then the device should be programed to asynchronous pacing and ICD features deactivated. The device should be interrogated before and after the scan.

Clips used in vascular surgery and neurosurgery must be verified and the model and type of clip documented. All intracranial aneurysm clips manufactured after 1995 that the company identifies it as MR conditional need no further testing. Clips manufactured before 1995 require some pretesting and may need approval of an MRI attending radiologist. Despite a prior history of MRI, variations can occur in different magnetic fields under the influence of different pulsed frequencies, so verification may still be needed.

Coronary artery stents, especially after 2007, are proven safe for patients having an MRI procedure at ≤3 T. Most aortic stent grafts are MR safe, but the Zenith AAA and TAA endovascular graft (Cook Medical, Bloomington, IN) are MR conditional, and their timing for scanning needs to be individualized. Coil embolization materials, such as platinum, iridium, and nitinol, are safe for MRI examinations. Most heart valves and annuloplasty rings can be safe under certain conditions, that is, ≤3 T, but if possible, delay the scan for up to 6 weeks after implantation.

Certain cochlear implants are MR conditional and may be safe if the patient is over 8 years of age and ≤1.5 T is used. Care must be taken for patients with retained shrapnel and bullets; there may be potential risks if it is ferromagnetic due to

movement and heating near vital organs. Patients with implanted stimulators need to be investigated, and some may be MR unsafe or conditional. MRI may be performed on a limited basis for patients with certain deep brain stimulators and vagal nerve stimulators. In each case, care must be individualized and decisions made with the on-site level 2 MRI attending radiologist.

For a more thorough evaluation of these devices, please refer to the website http://www.mrisafety.com, which has a thorough list of MR safe, conditional, and unsafe devices. Orthodontic braces and dentures and tattoos or cosmetics that contain metallic dyes, although safe, can degrade the image quality significantly.

Baikoussis NG, Apostolakis E, Papakonstantinou NA, et al. Safety of magnetic resonance imaging in patients with implanted cardiac prostheses and metallic cardiovascular electronic devices. *Ann Thorac Surg*. 2011;91:2006–2011.

Indik JH, Gimbel JR, Abe H, et al. 2017 HRS expert consensus statement on magnetic resonance imaging and radiation exposure in patients with cardiovascular implantable electronic devices. *Heart Rhythm*. 2017;14(7):e97–e153.

Kanal E, Barkovich AJ, Bell C, et al. ACR guidance document on MR safe practices: 2013. *J Magn Reson Imaging*. 2013;37:501–530.

Ocazionez D, Dicks DL, Favinger JL, et al. Magnetic resonance imaging safety in cardiothoracic imaging. *J Thorac Imaging*. 2014;29:262–269.

Practice advisory on anesthetic care for magnetic resonance imaging: a report by the Society of Anesthesiologists Task Force on Anesthetic Care for Magnetic Resonance Imaging. *Anesthesiology*. 2009;110:459–479.

A.5. What are the biologic effects of clinical MRI?

Although an area of controversy and ongoing investigation, most human data to date suggest that there are no significant deleterious effects to patients or health care professionals from exposure to the static magnetic field of an MRI machine. However, MRI capabilities were developed relatively recently

(the 1960s), and epidemiologic evidence of harmful exposure may not yet be apparent. It seems prudent, therefore, to limit repetitive and readily avoidable exposure to the magnetic field.

Also controversial is the use of MRI during pregnancy because the effects of magnetic fields on the human fetus cannot be easily determined. Current evidence does not support the suggestion that routine clinical exposure of the pregnant patient to MRI causes developmental abnormalities in the fetus. Pregnant patients have undergone MRI safely during all stages of pregnancy. Nevertheless, caution is advised. Studies have shown that gadolinium-based contrast agents enter the fetal circulation and are filtered in the fetal kidneys into the amniotic fluid, which can potentially form free gadolinium ions that can theoretically pose risks to the developing fetus. The appropriateness of MRI examination and the acuteness of the diagnostic need must be considered. Ultrasonography is preferred if it can provide equivalent diagnostic information, and consideration should be given to postponing the MRI until late in the pregnancy or until after delivery.

MRI contrast agents have fewer side effects compared to iodinated contrast agents. However, there are some potential reactions with gadolinium-based contrast agents in patients with moderate to severe chronic renal disease. Patients with severe chronic renal disease, hepatorenal syndrome, and/or perioperative liver transplant have developed “nephrogenic systemic fibrosis,” which can be fatal. Nephrogenic systemic fibrosis primarily involves the skin, but other organs such as the liver, heart, lungs, diaphragm, and skeletal muscle can be affected. Care must be taken when considering the use of MRI contrast agents in these patients. If a pediatric patient with advanced renal disease requires gadolinium, the US Food and Drug Administration (FDA) suggests prompt hemodialysis be considered.

Chernoff D, Stark P. Principles of magnetic resonance imaging. http://www.uptodate.com/contents/principles-of-magnetic-resonance-imaging. Accessed August 18, 2019.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier/Saunders; 2019:1077–1094.

Kanal E, Barkovich AJ, Bell C, et al. ACR guidance document on MR safe practices: 2013. *J Magn Reson Imaging*. 2013;37:501–530.

A.6. What are the anesthetic considerations for this procedure?

The problems that complicate anesthetic management of any patient outside the operating room environment exist for patients requiring sedation or general anesthesia for MRI. The MRI suite is often located some distance from the operating room and the anesthesia department, thus limiting the availability of backup assistance and supplies. As with any remote anesthetizing location, the personnel may not be familiar with the requirements of anesthetized patients, thereby decreasing their ability to provide assistance. Frequently, MRI suites have been designed without consideration for anesthetic needs, such as pipeline gases, suction, or an anesthetic exhaust system. Access to a recovery suite for postanesthesia care may not be readily available, thereby necessitating a trip to the main recovery room.

In addition, there are anesthetic challenges unique to the MRI suite. Because of the bulkiness of the unit, the patient is often far removed from the anesthesiologist, and access to the airway is limited. Intravenous lines, anesthesia circuits, oxygen tubing, and monitoring cables must be of sufficient length to reach the patient deep within the scanner. The strong magnetic field necessitates the exclusion of all ferromagnetic objects and equipment. The displays of standard monitoring devices can be distorted or displaced by the magnetic field and the monitors themselves can degrade the MR image by disturbing the signal/noise ratio. The ASA task force understands that the

interpretation of the ECG may be limited due to the superimposed voltages from blood flow in a high magnetic field (i.e., ST-segment interpretation unreliable even with filters). Safe monitoring conditions must be maintained with MR safe/conditional monitors and remote monitoring and must be in compliance with ASA standards. **Figure 62.2** shows that the anesthesiologist is watching the patient (in zone IV) and anesthesia monitors in zone III control room during MRI scan.

Finally, for a machine to be MR conditional, its components must be less than 2% ferromagnetic. Vaporizers themselves are not ferromagnetic so conventional ones can be used.

FIGURE 62.2. The anesthesiologist is watching the patient (in zone IV) and anesthesia monitors in zone III control room during MRI scan.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:880–896.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier/Saunders; 2019:1077–1094.

Practice advisory on anesthetic care for magnetic resonance imaging: a report by the Society of Anesthesiologists Task Force on Anesthetic Care for Magnetic Resonance Imaging. *Anesthesiology*. 2009;110:459–479.

A.7. What is intraoperative MRI (iMRI)? What is real-time MRI, and in what setting can this be used?

Since 1993, image-guided surgery systems have been introduced that combine the resources of an operating room with MRI technology and high-performance computing. Several low-, mid-, and high-field strength interventional MRI systems have been developed that permit access to the patient by surgeons and provide near real-time imaging during surgical procedures. Intraoperative MRI furnishes the surgeon with simultaneous combination of direct vision and beyond-the-surface MRI, allowing for more accurate localization and targeting during surgery. In addition, iMRI allows the surgeon to detect the full extent of lesions, to devise a surgical approach that is safe with less potential operative morbidity, and to monitor for unseen hemorrhage. In some cases, iMRI may obviate the need for postoperative imaging that may necessitate additional sedation for pediatric patients. In addition to tumor resections, iMRI can be utilized in the surgical revascularization of moyamoya arteriopathy and during the management of arteriovenous malformations (AVMs), placement of deep brain stimulator for Parkinson disease and other movement disorders, evaluation of hematoma, and resection of epileptogenic foci. Other fields of medicine that incorporate iMRI include surgeries of the liver,

pancreas, and kidney as well as radiation therapy guidance when tumors shift. Not surprisingly, iMRI systems are expensive and require MRI-compatible surgical instruments and monitoring equipment. One of the largest challenges anesthesiologists face in this setting is dealing with the high-energy iMRI-generated electrical noise that can interfere with the ECG. Unlike in an MRI suite, there are multiple people and objects to account for when the iMRI unit is brought out and engaged around the patient. All personnel working in an iMRI environment must take MRI safety courses to ensure patient safety as well as personal safety. For the duration of the scan, the anesthesiologist has limited or no access to the patient, and visualization of the patient may be limited when enclosed in an electrical noise shield. All ferromagnetic objects, such as laryngoscopes, stylets, and beepers, must be left outside the operating room or placed in a secure area. Lastly, as opposed to MRI in a dedicated suite, anesthetic considerations for iMRI must also include the needs of the ongoing complex surgical procedure.

As opposed to iMRI, real-time MRI integrates exceptional soft tissue visualization in a 3D anatomic and functional manner with delineation of suspected lesions without exposure to radiation. In the electrophysiology suite, use of real-time MRI allows a number of catheter ablation procedures for the treatment of and risk stratification of various arrhythmias, with reduction in fluoroscopy usage. In addition, DE MRI is the gold standard for scar and fibrosis mapping, which serves as an arrhythmogenic source for VT. This preprocedural MRI may be difficult to obtain because these patients often have ICDs that are contraindicated for MRI. DE MRI can also be used to predict potential atrial fibrillation ablation failure based on the amount of left atrial fibrosis that is present. After an intervention, MRI can help identify complications, such as pulmonary vein stenosis and esophageal injury. MRI thermography is another useful tool

used to show tissue heating during RF ablation.

There are many hazards associated with real-time MRI and iMRI. Special MRI conditional and safe monitors, devices, and catheters need to be utilized to avoid catastrophic complications.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier/Saunders; 2019:1077–1094.

Dzwonczyk R, Fujii JT, Simonetti O, et al. Electrical noise in the intraoperative magnetic resonance imaging setting. *Anesth Analg*. 2009;108:181–186.

Eitel C, Hindricks G, Grothoff M, et al. Catheter ablation guided by real-time MRI. *Curr Cardiol Rep*. 2014;16(8):511.

Henrichs B, Walsh RP. Intraoperative MRI for neurosurgical and general surgical interventions. *Curr Opin Anaesthesiol*. 2014;27:448–452.

B. Preoperative Evaluation and Preparation

B.1. What type of patients may require sedation or general anesthesia for MRI?

Although MRI is painless, patients must remain still throughout the time required to make each scan (as much as 15 minutes) in order to obtain images free of movement artifacts. Patients who are unable to cooperate adequately (e.g., infants, young children, and adults who are confused, mentally ill, or intellectually compromised) usually require an anesthesiologist to assist with the examination. Most children younger than 5 years of age and as old as 11 years of age require some form of sedation or general anesthesia. Not only children need anesthesia; 30% of adult patients experience some form of anxiety during MR scanning. Anesthesiologists are frequently managing claustrophobic or anxious adults as well as those requiring either airway protection (unconscious or critically ill patients) or mechanical ventilation (patients with head injuries or elevated intracranial pressure) to ensure that an adequate examination is

obtained safely and efficiently.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:880–896.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier/Saunders; 2019:1077–1094.

Wu J, Mahmoud M, Schmitt M, et al. Comparison of propofol and dexmedetomedine techniques in children undergoing magnetic resonance imaging. *Paediatr Anaesth*. 2014;24:813–818.

B.2. Do all children require sedation for MRI?

Performing general anesthetics in neonates and children with a potentially challenging airway in a remote location can be dangerous. In addition, due to the risks associated with potential neurotoxicity in the developing brain, there are many looking for methods to perform MRI scans without sedation. For instance, in small infants and neonates the "feed and swaddle" method can be used. Although this strategy is associated with an increased likelihood of obtaining inadequate images, it can be used as a first-line method with general anesthesia reserved as a backup. In older children, one can use multimedia, trained child life experts, and handheld device application-based technologies to calm children and help them stay still. This method can be sufficient in developmentally appropriate and cooperative children. It is important to discuss cases with the attending radiologist to determine whether MRI is appropriate for the clinical question. The harms from ionizing radiation on the developing child are well known; however, the amount of radiation required to obtain quality CT images has decreased with modern CT scanners. Because CT exams are far shorter (minutes instead of 1 hour for MRI), children likely do not need general anesthesia or sedation.

Callahan MJ, MacDougall RD, Bixby SD, et al. Ionizing radiation from computed tomography versus anesthesia for magnetic resonance imaging in

infants and children: patient safety considerations. *Pediat Radiol*. 2018;48:21–30.

Heller BJ, Yudkowitz FS, Lipson S. Can we reduce anesthesia exposure? Neonatal brain MRI: swaddling vs. sedation, a national survey. *J Clin Anesth*. 2017;38:119–122.

Runge SB, Christensen NL, Jensen JE, et al. Children centered care: minimizing the need for anesthesia with a multi-faceted concept for MRI in children aged 4–6. *Eur J Radiol*. 2018;107:183–187.

B.3. What preoperative laboratory testing would you require for this patient?

For this patient, it would be prudent to obtain a complete blood count (CBC) and a basic metabolic panel (BMP), the CBC to evaluate for postoperative bleeding and the BMP to evaluate electrolyte derangements (particularly sodium) as contributing to the patient's altered mental status. However, if the patient were otherwise healthy, no further laboratory studies would be warranted.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:880–896.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier/Saunders; 2019:1077–1094.

B.4. How would you premedicate this patient? What are some options that can be used to premedicate other patients for MRI?

The goal of premedication is to provide anxiolysis yet not precipitate hypoxemia or hypercarbia. In this patient who already has altered mental status, long-acting sedatives should be avoided. However, other children may be good candidates for premedication for anxiolysis.

At some centers, ambulatory pediatric patients are not routinely given pharmacologic premedication; rather, parents are allowed to be present at the time of induction in order to help

allay anxiety and ease the induction. The most commonly used premedication in pediatrics is oral midazolam. Although the standard dose is 0.5 mg per kg, some advocate for an increased dose in younger children, up to 1 mg per kg in children 1 to 3 years old. A relatively high dose is likely needed due to the poor bioavailability of the drug orally (15%). Midazolam should be administered at least 20 to 25 minutes prior to intended onset for maximal effect. The side effects include respiratory depression, bad taste, and in some patients paradoxical agitation.

There are other medications that can be used for anxiolysis in children, including dexmedetomidine and ketamine. Dexmedetomidine can be given either intranasally (2.5 to 3 μg per kg) or orally (4 μg per kg). Dexmedetomidine is a centrally acting α_2-agonist that is a sedative without respiratory depression. It is odorless and tasteless so can be much more palatable for children. Dexmedetomidine can also reduce the incidence of postoperative emergence delirium, an added benefit.

Ketamine can be given orally (6 mg per kg) or intramuscularly (1 to 2 mg per kg). The oral route is preferred because many children have a needle phobia. The side effects of ketamine include an increase in oral secretions. This can cause upper airway obstruction, bronchospasm, laryngospasm, and microaspiration, even in the presence of intact upper airway reflexes. Ketamine can also cause significant postsedation delirium, especially if the child is not pretreated with a benzodiazepine.

A novel premedication is melatonin (0.5 mg per kg), which can provide comparable anxiolysis as oral midazolam. Melatonin is an endogenous indolamine produced and secreted by the pineal gland that normally regulates circadian rhythm and promotes sleep. However, it can have sedative effects that have been well studied in adults. Melatonin can reduce the amount of

propofol needed for induction of anesthesia in pediatric patients.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:880–896.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier/Saunders; 2019:1077–1094.

Impellizzeri P, Vinci E, Gugliandolo MC, et al. Premedication with melatonin vs midazolam: efficacy on anxiety and compliance in paediatric surgical patients. *Eur J Pediatrics*. 2017;30:947–953.

Jannu V, Mane RS, Dhorigol MG, et al. A comparison of oral midazolam and oral dexmedetomidine as premedication in pediatric anesthesia. *Saudi J Anaesth*. 2016;10(4):390–394.

Lerman J. Preoperative assessment and premedication in paediatrics. *Eur J Anaesthesiol*. 2013;30(11):645–650.

Qiao H, Xie Z, Jia J. Pediatric premedication: a double-blind randomized trial of dexmedetomidine or ketamine alone versus a combination of dexmedetomidine and ketamine. *BMC Anesthesiol*. 2017;17(1):158.

C. Intraoperative Management

C.1. What are some of the anesthetic options for this patient?

There are many techniques used to anesthetize children undergoing MRI or other painless radiologic procedures. This can range from moderate sedation with intravenous boluses of midazolam or fentanyl to deep sedation, with various combinations of intravenous ketamine/propofol/dexmedetomidine, or general anesthesia with inhaled anesthetics or total intravenous anesthesia (TIVA). Because conscious sedation of children is frequently insufficient to prevent patient movement, deeper levels of sedation or general anesthesia are often required to successfully anesthetize the pediatric patient for MRI. The ideal anesthetic should allow the anesthesiologist the ability to titrate and maintain stable drug concentrations in order to prevent undesired patient movement

during the scan and to provide rapid rates of induction and recovery with a minimal requirement for special MRI-compatible equipment.

Intravenous anesthesia with propofol meets several of the aforementioned criteria, and it can be an excellent technique for MRI. Continuous intravenous infusion of propofol allows for a precise, rapid titration to the desired effect and has for a rapid recovery. Propofol use eliminates the need for a nonferromagnetic, MRI-compatible anesthesia machine and for scavenging of waste anesthetic gases, both of which are major drawbacks of an inhalational technique. Ketamine is another useful drug for deep sedation while maintaining airway reflexes. However, in addition to the issue with increased secretions mentioned earlier, ketamine may elicit undesirable myoclonic movements, increased intracranial pressure, and emergence delirium, especially at higher dosages and in ages younger than 2 and older than 13 years.

Dexmedetomidine can be used as a maintenance agent as well as a premedication. No major respiratory effects are known with this agent, although hemodynamic side effects can occur, especially at higher doses. Wu et al. compared propofol and dexmedetomidine infusions for sedation in MRI and concluded that for longer scans, the dexmedetomidine group had longer induction times and overall hospital times than the propofol group. Due to potential hemodynamic side effects, such as hypotension and bradycardia, and life-threatening complications when used with digoxin, dexmedetomidine should be used cautiously in patients with cardiac compromise. MRI scans performed under propofol sedation have been shown to have better image quality than those performed with dexmedetomidine alone. Dexmedetomidine is a good adjunct agent, especially in a patient where spontaneous ventilation is paramount, however may not be a suitable agent by itself.

Another viable alternative to deep sedation with intravenous agents would be general anesthesia with inhalational anesthetics. In children younger than 3 years of age or in patients with comorbidities requiring or necessitating airway management, general anesthesia may be the preferred choice.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:880–896.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier/Saunders; 2019:1077–1094.

Loh P-S, Ariffin MA, Rai V, et al. Comparing the efficacy and safety between propofol and dexmedetomidine for sedation in claustrophobic adults undergoing magnetic resonance imaging (PADAM trial). *J Clin Anesth*. 2016;34:216–222.

Schulte-Uentrop L, Goepfert MS. Anaesthesia or sedation for MRI in children. *Curr Opin Anaesthesiol*. 2010;23:513–517.

Wu J, Mahmoud M, Schmitt M, et al. Comparison of propofol and dexmedetomedine techniques in children undergoing magnetic resonance imaging. *Paediatr Anaesth*. 2014;24:813–818.

C.2. How is an MRI conducted?

The patient is placed on a long, thin table outside the scanner. After obtaining an adequate level of anesthesia, the patient is positioned. If the head is to be examined, it is often enclosed within a small coil or tube. Next, the table with the patient is moved into the long tube of the MRI magnet. The portion of the body to be examined is usually centered in the magnet approximately 1 m from the end of the tube. During the examination, delivery of the RF pulses produces a loud thumping noise, which can average 95 dB in a 1.5 T scanner. To obtain a high-quality scan, the patient must refrain from moving during the acquisition of an individual cut or from changing position at any time during the entire examination. An individual scan can take several minutes, and the total scanning time may range from 1 to 3 hours. Body surfaces can absorb some of the

RF energy during the sequence, although this is unlikely to increase core temperature by more than 1°C. Nevertheless, the specific absorption rate (SAR) of energy by the body as measured in watts per kilogram is monitored. Depending on the patient, if the SAR is too high the sequence may need to be aborted and adjusted.

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Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier/Saunders; 2019:1077–1094.

C.3. How would you monitor this patient?

Reliable and accurate monitoring of an unconscious individual during an MRI is essential because the patient cannot be seen adequately or accessed easily by the anesthesiologist. During sedation, the ASA standard monitors including blood pressure, pulse oximetry, and ECG must be used. ECG electrodes should be placed together and toward the middle of the magnetic field, and the leads should be insulated from the patient's skin to avoid any potential thermal injuries. During general anesthesia, capnography and temperature should also be monitored. The assessment of ventilation in a spontaneously breathing patient may be difficult especially when the patient is within the magnet and far from view. Monitoring end-tidal carbon dioxide from one limb of the nasal oxygen prongs or through a nasal catheter is frequently successful. Pulse oximetry is a marker for oxygenation and should not be used as a marker for ventilation. Hypothermia can be problematic, especially in pediatric patients. Because of the high airflow through the scanner cavity, the patient should be covered in blankets. Hyperthermia can also occur, and if suspected based on SAR, the sequence may need to be temporarily stopped. Temperature monitoring can be

accomplished by using nonferromagnetic temperature strips or probes with RF filters when feasible. It is currently not mandatory for the anesthesiologist to remain in the scanner room during the examination as long as remote monitoring with direct vision of the patient is possible.

The patient outlined in this case requires invasive blood pressure monitoring. However, one may need to place extension tubing as the transducer should be placed at least 50 gauss away from the scanner, potentially leading to a dampened signal.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:880–896.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier/Saunders; 2019:1077–1094.

Practice advisory on anesthetic care for magnetic resonance imaging: a report by the Society of Anesthesiologists Task Force on Anesthetic Care for Magnetic Resonance Imaging. *Anesthesiology*. 2009;110:459–479.

C.4. What special considerations apply to monitoring equipment used during MRI?

Unshielded ferromagnetic materials, such as those within monitors and cables, or metallic pieces on patient clothing can interfere with imaging signals causing distortion of MRI results and burns. Similarly, the RF signals can induce currents in ferromagnetic elements of monitors, causing a distortion of the monitoring signal and making the monitor unusable. Use of MR safe/conditional monitors and equipment (e.g., ECG electrodes) are preferable because they contain shielding nonferromagnetic components and filters to produce satisfactory results without major distortion of signal. To avoid magnetic pull, monitors should be placed at least 5 to 8 ft from the magnet bore or be permanently mounted.

The ECG may show significant changes within a static magnetic field. In particular, T waves and late ST segments can

mimic ECG changes associated with conditions such as hyperkalemia and pericarditis. This is due to an induced voltage in blood (a conducting fluid) flowing through the magnetic field. These changes are directly related to field strength, but they do not appear to represent any significant physiologic alteration.

Pulse oximeter cables must be nonconducting, fiberoptic, and MRI compatible. Traditional pulse oximeter probes may contain metal and when adjacent to the patient can cause burns.

The high RF power used in MRI poses the risk of excessive heat at monitoring sites. This can lead to thermal injury. To minimize the risk of burns, one should

- Inspect the insulation on all monitoring wires to ensure that it is intact.
- Place cables and lead wires in straight alignment. Do not allow monitoring wires to form loops.
- Remove all leads or wires not in use.
- Separate cables from patient's skin.
- Keep the cable and sensor out of the scanning area (e.g., place a pulse oximeter probe on the toe of a patient whose chest is being examined).
- Avoid excessive power.
- Remove patient gown or any clothing that may have metal.

It is the role of the anesthesiologist to confirm all monitors used in zone IV are MR compatible. In addition, a monitor should be available to view vital signs from zone III when the anesthesia provider is not in zone IV.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:880–896.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier/Saunders; 2019:1077–1094.

C.5. How would you induce and maintain general

anesthesia in this patient?

This patient will likely require general anesthesia to complete the MRI scan due to his altered mental status and the necessity to avoid hypoxia/hypercarbia in this postneurosurgical patient. General endotracheal anesthesia is the best option. However, the child was clearly difficult to intubate in the operating room and required use of a videolaryngoscope. Therefore, it would be prudent to ensure that help from experienced and trained anesthesiologists is available and to induce general anesthesia away from the scanner such that difficult airway equipment would be readily available. An intravenous induction should be performed to control oxygenation and carbon dioxide as quickly as possible. MRI-compatible monitors should be placed prior to induction to allow a smooth transition to the scanner. The pilot balloon on the cuff of the endotracheal tube (or supraglottic device, if used) must be taped away from the patient to minimize artifact from the cuff's spring. Once under general anesthesia, the child is moved into the scanner room and placed on the MRI table. The patient and monitors are carefully positioned before attempting to advance the table into the magnet bore. Anesthesia can be maintained with either a continuous intravenous infusion of propofol or an inhalational agent combined with oxygen.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:880–896.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier/Saunders; 2019:1077–1094.

Schulte-Uentrop L, Goepfert MS. Anaesthesia or sedation for MRI in children. *Curr Opin Anaesthesiol*. 2010;23:513–517.

Wu J, Mahmoud M, Schmitt M, et al. Comparison of propofol and dexmedetomedine techniques in children undergoing magnetic resonance imaging. *Paediatr Anaesth*. 2014;24:813–818.

C.6. What are ways to maintain the airway during an

MRI scan?

Securing the airway with an endotracheal tube is not required to successfully sedate a patient during an MRI scan, which can be performed with patients breathing spontaneously with a native airway. This should be considered in patients with a good natural airway whose ventilation is being monitored adequately. Infusions of propofol or dexmedetomidine can be considered in this situation. Placing a shoulder roll under the patient with the chin taped up may help prevent airway obstruction during the MRI scan. This should only be performed when there are no contraindications, such as potential spinal injuries with head and neck manipulations.

However, limited access to the patient's airway is one of the greatest challenges for the anesthesiologist during MRI. In patients whose airway may be problematic, it may be prudent to place either an endotracheal tube or supraglottic airway device. Respiration can be spontaneous or controlled depending on personal preference and the needs of the patient. However, supraglottic airway devices can alter the appearance of cervical soft tissue masses causing problems in diagnosis and should be used only after consulting with a radiologist if the neck is being imaged. The literature is not conclusive as to whether the use of a tracheal tube decreases the incidence of airway complications during MRI scans. As long as a plan is in place should emergencies occur, any type of anesthetic can be used to accomplish the scan.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:880–896.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier/Saunders; 2019:1077–1094.

Practice advisory on anesthetic care for magnetic resonance imaging: an updated report by the American Society of Anesthesiologists Task Force on

Anesthetic Care for Magnetic Resonance Imaging. *Anesthesiology*. 2015;122(3):495–520.

Simpao AF, Obsekov V, Galvez JA, et al. A retrospective study of the impact of supraglottic airway devices on the appearance of neck masses in children undergoing serial magnetic resonance imaging. *Paediatr Anaesth*. 2018;28(12):1123–1128.

C.7. During the scan, you notice loss of end-tidal carbon dioxide. You immediately go into the scanner, remove the patient from the MRI scanner and initiate bag ventilation. However, you are still unable to ventilate the patient, and asystole follows. What do you do next?

The initial picture represents severe bronchospasm. The management of bronchospasm includes increasing fraction of inspired oxygen (FIO_2) to 100%, checking the tracheal tube for kinking, secretions or obstruction, and deepening the anesthetic if the blood pressure allows. If this is unsuccessful, boluses of low-dose epinephrine should be used. However, as this patient has progressed to cardiopulmonary arrest, the patient should be removed from zone IV, if not done so already, as you initiate advanced cardiac life support (ACLS) and cardiopulmonary resuscitation (CPR). You should request additional assistance from other providers. It is important to remove the patient from the MRI scanner to have complete access as well as reduce the risk of bringing in magnetic devices such as oxygen tanks and defibrillator into zone IV.

Practice advisory on anesthetic care for magnetic resonance imaging: an updated report by the American Society of Anesthesiologists Task Force on Anesthetic Care for Magnetic Resonance Imaging. *Anesthesiology*. 2015;122(3):495–520.

C.8. What is the risk to the patient of gadolinium administration in the presence of acute renal

insufficiency?

For patients with acute renal insufficiency (serum creatinine >1.5 mg per dL), gadolinium should not be administered due to the increased risk of nephrogenic systemic fibrosis. Gadolinium based contrast should also be avoided in patients with previous allergic/anaphylactoid reaction and in patients who are or might be pregnant.

Ergün I, Keven K, Uruç I, et al. The safety of gadolinium in patients with stage 3 and 4 renal failure. *Nephrol Dial Transplant*. 2006;21(3):697–700.

Practice advisory on anesthetic care for magnetic resonance imaging: an updated report by the American Society of Anesthesiologists Task Force on Anesthetic Care for Magnetic Resonance Imaging. *Anesthesiology*. 2015;122(3):495–520.

D. Postoperative Management

D.1. How will you recover the patient from anesthesia?

Postanesthesia recovery care after MRI is the same as that required after any anesthetic. This can be accomplished in a designated area of the MRI suite provided that adequate facilities and trained personnel are available. For most, such a facility may not be available, and the patient will require transport to the main recovery room. To transport the patient quickly and safely, one must ensure that adequate personnel and the proper equipment are organized in advance. It is useful to have the location of recovery and logistics of transport (if necessary) planned before the procedure begins.

Barash PG, Cullen BF, Stoelting RK, et al, eds. *Clinical Anesthesia*. 8th ed. Philadelphia, PA: Wolters Kluwer; 2017:880–896.

Coté CJ, Lerman J, Anderson BJ, et al, eds. *Coté and Lerman's A Practice of Anesthesia for Infants and Children*. 6th ed. Philadelphia, PA: Elsevier/Saunders; 2019:1077–1094.

63 Morbid Obesity, Obstructive Sleep Apnea, and Bariatric Anesthesia

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A 27-year-old man was scheduled for elective robotic sleeve gastrectomy. He had a past medical history significant for morbid obesity (MO) (height, 182.9 cm; weight, 272.16 kg; body mass index [BMI], 81.4 kg per m^2), Pickwickian habitus, osteoarthritis, mild asthma, hypertension, adult-onset diabetes mellitus, peptic ulcer disease with symptomatic gastroesophageal reflux, and obstructive sleep apnea (OSA). He experienced daytime somnolence, heavy nighttime snoring, and had slept in a seated position for the previous 2 years. He was able to walk around the house with a cane but was unable to climb any stairs. A preoperative diagnostic polysomnography (PSG) was performed, and an apnea–hypopnea index (AHI) of 64 was calculated. Home oxygen therapy with bilevel positive airway pressure (BIPAP) settings had been started at the following settings, with symptomatic improvement: fraction of inspired oxygen (F_{IO_2}) of 0.40, respiratory rate 10 breaths per minute, inspired positive airway pressure (IPAP) of +12 cm H_2O, and expired positive airway pressure (EPAP) of +5 cm H_2O, spontaneous mode.

Cardiology clearance was obtained as a high-risk candidate, after an echocardiogram revealed mild right-sided cardiomegaly and mild pulmonary hypertension. The patient's blood pressure was 155/82 mmHg, pulse 60 beats per minute, and respirations 20 breaths per minute. The patient was determined to have a difficult airway. Prior to scheduling surgery, the patient was scheduled for an upper endoscopy and a Bravo procedure.

A. Medical Disease and Differential Diagnosis

1. What problems exist with this patient? The patient asks you if he is high risk. What is the evidence? Is surgical therapy a safe and viable alternative for this patient?
2. Define the terms overweight, obesity, MO, super obesity (SO), super-SO (SSO), normal weight, ideal body weight (IBW), and lean body weight (LBW). What is the impact of obesity on society?
3. What is OSA? What are the risk factors for OSA?
4. How is OSA diagnosed? What is a sleep study, or PSG? How are results obtained from a PSG used to grade the severity of OSA? What are the subtypes of OSA? Are there genetic disorders with a predisposition to OSA? What is the role of OSA screening tests in the preoperative setting?
5. How does OSA differ in the pediatric population in clinical presentation and pathogenesis?
6. What is the Pickwickian syndrome (PS)? What is obesity hypoventilation syndrome (OHS)? Describe the pathogenesis of severe OSA.
7. What is the association between obesity and OSA? What is the etiology of OSA in severe obesity?
8. What are the anesthetic implications of OSA?
9. What type of metabolic problems would you expect to find in morbidly obese patients? What are the roles of leptin and

ghrelin in obesity?

10. Describe the changes that occur in the following respiratory parameters in morbidly obese patients:
    - Pulmonary mechanics: tidal volume (V_T), functional residual capacity (FRC), residual volume (RV), vital capacity (VC), inspiratory reserve volume (IRV), expiratory reserve volume (ERV), and total lung capacity (TLC)
    - Flow–volume loops
    - Pressure–volume loops
    - Diffusing capacity for carbon monoxide (DLCO)
    - Compliances: lung (C_L), chest wall (C_{CW}), and total (C_{RS})
    - Resistance: airway and total respiratory system
    - Closing capacity (CC)
    - Work of breathing (WOB)
11. What changes occur in Pa_{O_2} and Pa_{CO_2} in morbidly obese patients?
12. What changes occur in intrapulmonary shunt (Q_S/Q_T) and dead space (V_D/V_T) in MO? Describe the Shunt equation and the physiologic dead space, or Bohr equation.
13. What changes occur in the cardiovascular system of the obese patient? Discuss cardiac output, blood volume, blood pressure, and pulmonary arterial pressure.
14. Are there any other disease entities commonly associated with obesity? What is their relationship?
15. What anatomic changes that affect the airway are associated with MO and OSA?
16. What derangements of the gastrointestinal system are associated with MO?

B. Preoperative Evaluation and Preparation

1. How would this patient be optimized for surgery preoperatively? Would you use preoperative screening questionnaires to diagnose OSA? Summarize the workup for

this patient.

2. One of the recent developments in bariatric surgery is that many patients are receiving prebariatric screening procedures performed in the endoscopy suite. Describe the anesthetic considerations.
3. Summarize the evidence-based workup, risk, chance of various adverse outcome, and expected length of stay for this patient.
4. What is the role of enhanced recovery after surgery (ERAS) in bariatric surgery? How does the public find a quality bariatric surgery team and surgical facility? What is the role of robotics in bariatric surgery?
5. Would you premedicate the patient?
6. Describe the mechanism of action of each premedication in the ENERGY protocol.
7. How would you adjust doses of anesthetics in the morbidly obese?

C. Intraoperative Management

1. How would you monitor this patient?
2. The American Society of Anesthesiologists' (ASA) Difficult Airway Algorithm (DAA) provides a guideline for management of the difficult airway. How do the comorbidities of MO and OSA modify implementation of the algorithm?
3. Why is it important to preoxygenate the obese patient? How would you do it? Compare the effectiveness of the four-maximum-breath and 3-minute techniques. What is the importance of continuous positive airway pressure (CPAP) during the induction of general anesthesia? Describe use of the nasal CPAP mask in the induction of general anesthesia.
4. There are many new airway devices on the marketplace. Which of these devices have been particularly successful on the morbidly obese or OSA patient?
5. How would you induce anesthesia? Describe the intubation

technique.

6. How would you maintain general anesthesia? What agents would you choose? How would you prepare for emergence?
7. Which muscle relaxants would you use?
8. Is postoperative pain severe after bariatric surgery? What are the pain generators? What is the role of regional anesthesia to decrease opioid requirements for bariatric surgery? What are the advantages and disadvantages of regional anesthesia? What are some of the newer techniques available?
9. What is the pathophysiology of pneumoperitoneum (PNP)? What is the effect on the cardiopulmonary system? How does it change perioperative care? What are the optimal ventilator strategies for morbidly obese patients undergoing bariatric surgery?
10. What are the devices that anesthesiologists place in the upper gastrointestinal canal during laparoscopic bariatric surgery? Are there risks associated with placement and management of these devices?
11. When will you extubate this patient? Describe weight-based extubation criteria.
12. What is apneic oxygenation?
13. What is diffusion hypoxia (DH)? How do you prevent it?

D. Postoperative Management

1. What are the early postoperative complications of bariatric surgical procedures?
2. What are the late complications of bariatric surgical procedures?
3. What is the effect of position on respiratory function in the obese patient?
4. How would you prevent postoperative atelectasis?
5. How long would you prescribe supplementary oxygen postoperatively?

6. How would you control postoperative pain?

A. Medical Disease and Differential Diagnosis

A.1. What problems exist with this patient? The patient asks you if he is high risk. What is the evidence? Is surgical therapy a safe and viable alternative for this patient?

Preoperative significant past medical history in this patient consists of MO, OSA, possible PS, right ventricular hypertrophy, early-onset coronary artery disease, mild pulmonary hypertension, systemic hypertension, adult-onset diabetes mellitus, osteoarthritis, and severe gastroesophageal reflux disease (GERD). Epidemiologically, this patient is at increased risk of coronary artery disease, cardiac arrhythmias, left- and right-sided congestive heart failure, peripheral vascular disease, venous thrombosis and pulmonary emboli, cerebrovascular disease, biliohepatic disease, hepatic steatosis, hepatic cirrhosis, degenerative joint disease, metabolic syndrome, and socioeconomic and psychosocial impairment.

This is a high-risk patient, with increased risk of both perioperative morbidity and mortality. Major anesthetic concerns include risk of difficult airway, difficult mask ventilation, decreased apneic threshold to anesthetics, sedatives and narcotics, prolonged anesthesia emergence, postemergence resedation, positional ventilatory collapse, restrictive and obstructive lung disease, ventilation/perfusion mismatch, worsening of reactive pulmonary hypertension, and cor pulmonale. This patient must receive continuation of his preoperative oxygen therapy with CPAP in the immediate recovery period, at the values determined by his sleep study (PSG), or greater. Additional anesthetic concerns include

difficult monitoring, difficult vascular access, and positioning issues. Additionally, there is a risk of postoperative massive pharyngeal collapse, rhabdomyolysis with renal failure, increased risk of infection including pneumonia, and positional injuries. Meticulous attention to acute pain management is essential.

Safe perioperative care for this patient requires triage to a specialized facility with additional personnel, surgeons with advanced laparoscopic training, and anesthesiologists with advanced airway skills and optimal equipment. Overall, the evidence for the long-term effectiveness of bariatric surgical therapy is quite compelling. The most widely quoted studies are on the gastric bypass, which has the longest track record; the Swedish Obese Subjects (SOS) study, and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)-National Institute of Health Longitudinal Assessment of Bariatric Surgery (LABS). Both of these seminal studies showed that compared with conventional treatment, the surgery group was associated with favorable short-term (low 30-day mortality of 0.3%, low rates of adverse outcomes comparable to a laparoscopic cholecystectomy) and long-term (reduction in overall mortality, decreased incidence of diabetes, myocardial infarction, stroke, cancer) outcomes. Bariatric surgery is the most effective long-term therapy for patients with severe obesity and has been recommended in all current guidelines.

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A.2. Define the terms overweight, obesity, MO, super obesity (SO), super-SO (SSO), normal weight, ideal body weight (IBW), and lean body weight (LBW). What is the impact of obesity on society?

Obesity is a multifactorial chronic disease involving social, cultural, physiologic, psychological, metabolic, endocrine, genetic, and behavioral components, resulting in excess adipose and tissue mass. The modern basis for the determination of demographics is the BMI, or Quetelet Index, after the Belgian statistician, Adolphe Quetelet, published in 1842, and is measured in body weight in kilograms divided by the height in meters squared (kg per m^2). The standard for *IBW*, the sex-specific desirable weight for persons with small, middle, and large frames, is published in the Metropolitan Life Insurance Tables. *LBW* accounts for the added muscle mass supporting the added weight, and corresponds to the well-perfused portion, of 120% to 140% of the IBW, or 1.3 times the IBW.

- *Anorexia* is defined as a BMI of less than 17.5 in males or females.
- *Underweight* is defined as a BMI of 17.6 to 19.0 in females or 17.6 to 20.6 in males.
- *Ideal (normal) weight* is defined as a BMI of 19.1 to 25.8 in females and 20.7 to 26.4 in males.
- *Marginally overweight* is defined as a BMI of 25.9 to 27.2 in females and 26.5 to 27.8 in males.
- *Overweight* is defined as a BMI of 27.3 to 32.3 in females

and 27.9 to 31.1 in males.

- *Obesity* is defined as a BMI of greater than 20% of IBW, 32.4 to 34.9 in females and 31.2 to 34.9 in males.
- *Severe obesity* is defined as a BMI of 35.0 to 39.9 in both sexes.
- *MO* is defined as a BMI of greater than 40 or greater than 35 with associated comorbidities such as hypertension and diabetes mellitus. MO is the accepted medical term for all cases of severe obesity.
- *SO*, a relatively new term, is defined as a BMI of 50 to 59.9. *SSO* is defined as a BMI of greater than 60.

There exist imperial and metric system BMI tables and web-based calculators.

Occasionally, an approximate, non–sex-specific system is used. In this system, a *healthy (normal) weight* is a BMI of 18.6 to 24.9, *overweight* is a BMI of 25 to 29.9, *obesity* is a BMI of 30 to 34.9, *severe obesity* is a BMI of 35 to 39.9, and MO is a BMI of more than 40.0.

The older definitions of obesity may occasionally suffice. Overweight was formerly defined as a body weight of up to 20% greater than the predicted ideal weight and obesity of more than 20%. MO was formerly defined as a body weight of 100 lb above the IBW, or alternatively, of twice the IBW. These definitions involved value judgments and inaccuracies and were later abandoned in favor of more objective terminology.

Alternative systems for the determination of obesity exist. In the triceps skinfold thickness test, for example, obesity is defined as a value of greater than 23 mm in males or greater than 30 mm in females. In the Broca Index (height in centimeters minus 100 for males and minus 105 for females), the IBW is calculated in kilograms.

- Males: IBW (kg) = height (cm) − 100
- Females: IBW (kg) = height (cm) − 105

There are different patterns of distribution of obesity. In *peripheral obesity* (e.g., gynoid or gluteal pattern), the individual has a pear shape, and adipose tissue deposition is predominantly in the lower body. In *central obesity* (e.g., android, or cushingoid), and especially upper body obesity, the individual has an apple shape, and adipose tissue deposition occurs predominantly in the upper body. Central obesity has greater associations with perioperative risk and OSA.

Much has been written on the obesity epidemic; according to the World Health Organization (WHO), obesity remains one of the most critical health challenges of the modern era. Obesity has reached epidemic proportions in the industrialized world and currently poses a greater worldwide health risk than malnourishment. In the United States alone, 65% of the U.S. population, or 127 million adults, are obese and is annually responsible for 300,000 premature deaths.

The financial impact on society of obesity is rue to *direct medical costs*, *increased incidence disease associated with* obesity, *associated medical costs*, *cost associated with lost* productivity, *absenteeism*, *presenteeism*, disability, increased health insurance issues, and increased indirect costs and have been discussed elsewhere. Together, the total cost of obesity has been estimated in 2010 at annual costs of $215 billion for the United States economy and $2 trillion a year for the world economy.

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Kopelman PG, Caterson ID, Dietz WH, eds. *Clinical Obesity in Adults and*

Children. 3rd ed. West Sussex, United Kingdom: Wiley-Blackwell; 2010:3–14.

A.3. What is OSA? What are the risk factors for OSA?

OSA is a sleep disorder. Sleep disorders may be grouped into the following types: conditions with excessive daytime somnolence (e.g., OSA), conditions with disorders initiating and maintaining sleep (e.g., insomnia), and circadian rhythm disorders (e.g., jet lag). In the older terminology, OSA referred to both OSA proper and to obstructive sleep hypopnea (OSH) syndrome, a milder variant. Today, it is more precise to refer to OSA and hypopnea syndrome (OSAHS) when naming the general condition.

OSA is defined as cessation of airflow for more than 10 seconds despite continuing ventilatory effort, five or more times per hour of sleep, associated with a decrease in arterial oxygen saturation (Spo_2) of greater than 4%. OSH is defined as a decrease in airflow of more than 50% for more than 10 seconds, 15 or more times per hour of sleep, associated with a decrease in Spo_2 of greater than 4%. Both forms of OSAHS are usually associated with snoring, sleep disruption from increased ventilatory effort–induced arousal, hypersomnolence (daytime sleepiness), altered cardiovascular function, and pathophysiologic alterations, of which hypoxemia and hypercarbia are primary events, and polycythemia, systemic and pulmonary hypertension, various cardiac arrhythmias, myocardial ischemia, right and left ventricular (LV) hypertrophy, and eventually failure are secondary events.

Severe obesity is a strong independent risk factor for OSAHS. Other risk factors include male gender, middle age, evening ingestion of alcohol, and drug-induced sleep. In nonobese individuals, risk factors are craniofacial dysostoses, particularly micrognathia (absolute or relative), cartilaginous abnormalities

(e.g., lingual tonsillar hyperplasia), chronic nasal obstruction, and tonsillar hypertrophy.

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A.4. How is OSA diagnosed? What is a sleep study, or PSG? How are results obtained from a PSG used to grade the severity of OSA? What are the subtypes of OSA? Are there genetic disorders with a predisposition to OSA? What is the role of OSA screening tests in the preoperative setting?

OSA may be suspected by history, physical examination, or comorbidities, but definitive diagnosis requires a sleep study. The hallmark of OSA is a history of heavy snoring. Nocturnal apnea, arousal during sleep, and daytime somnolence are commonly reported. Most adults with OSA have upper body obesity, increased neck circumference, micrognathia, and poor Mallampati scores on physical examination. Patient characteristics typically associated with OSA are a higher BMI, hypertension, and certain cephalometric measurements. In 90% of cases, the patient has a BMI in excess of 28 kg per m^2. OSA, however, may result from any condition that predisposes to upper airway obstruction. Some examples are pregnancy, upper airway abnormalities (e.g., deviated nasal septum, hypertrophic tonsils, and adenoids), cartilaginous abnormalities (e.g., lingual tonsillar hyperplasia), craniofacial dysostoses, certain congenital and genetic conditions (e.g., Prader-Willi syndrome, Down syndrome, Marfan syndrome, Pierre Robin sequence,

acromegaly, muscular dystrophy, cerebral palsy), as well as certain medical conditions (hypothyroidism). The absence of a typical or compelling presentation, however, does not rule out the possibility of OSAHS.

Adult OSA consists of a continuum from asymptomatic, to paroxysmal snoring, to severe nocturnal airway closure, requiring the patient to sleep in a sitting position, and daytime somnolence. The pathophysiology of OSAHS is central, peripheral, or mixed. Peripheral disease is caused by redundant adipose tissue in the upper airway, in the setting of severe obesity, sometimes with a superimposed craniofacial dysostosis. The symptomatology of OSAHS consists of intermittent snoring, apneic episodes, with daytime somnolence. *OSH*, a milder form of OSA, may be clinically indistinguishable. *OHS* is severe OSA with chronic daytime hypoventilation, SO, and hypercapnia not related to pulmonary disease. *PS* is OHS with cor pulmonale.

Definitive diagnosis of OSA is made by sleep specialists with a formal sleep study or a PSG. A PSG is an involved study, performed at sleep study centers, that examines nocturnal sleeping patterns by monitoring physiologic parameters. In its most comprehensive form, the following parameters are studied: two to six electroencephalographic (EEG) channels to measure electrical activity of the brain and to document sleep cycles, two electrooculogram (EOG) channels to distinguish rapid eye movement (REM) from non-REM sleep, chin electromyogram (EMG) to monitor arousal and activity of the upper airway (genioglossus and digastric muscles), an airway microphone to monitor airflow from the nose and mouth, elastic belts placed on the chest and abdomen to monitor respiratory effort, an infrared video camera to monitor body position, one channel of electrocardiogram (ECG) to monitor cardiac activity, a pulse oximeter to monitor oxygen saturation, and two-leg EMG

channels to monitor leg movements. A PSG may be ordered to definitively diagnose a sleep disorder, as part of medical management, or in the surgical workup of a high-risk population (e.g., preoperative screening of bariatric surgical candidates).

A PSG will diagnose the presence of OSAHS, type (central, peripheral, or mixed), and grade severity. Results are reported in as the total number of apneas and hypopneas per hour of sleep or the AHI. AHI values correspond to OSA severity as follows: 6 to 20 (mild), 21 to 40 (moderate), and greater than 40 (severe). The total number of arousals hourly is the arousal index (AI), which is the number of hourly arousals. The sum of the AHI and the AI is the respiratory disturbance index (RDI). Because the PSG is an expensive and time-consuming study that not covered by all insurance plans, simpler tests have been proposed, such as a partial (level 2) portable polysomnography and nocturnal oximetry. OSA is primarily a clinical diagnosis. Because only a very small percentage of patients presenting for surgery have been tested, have available results, and are compliant with recommendations, great importance is placed on preoperative sleep apnea screening tools and questionnaires. Of these, the STOP-BANG questionnaire is the most widely used and has been recently ratified in a meta-analysis across different populations.

The ASA has developed official policy for the perioperative management of OSA patients. In its most recent iteration of the practice guidelines for the Perioperative Management of Patients with Obstructive Sleep Apnea, all aspects of anesthetic care are described, including a scoring system for perioperative risk for OSA patients, based on OSA severity, invasiveness of surgery and anesthesia, and requirement for postoperative opioids.

American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Obstructive Sleep Apnea. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: an

updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Obstructive Sleep Apnea. *Anesthesiology*. 2014;120(2):268–286.

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A.5. How does OSA differ in the pediatric population in clinical presentation and pathogenesis?

Childhood OSA (COSA) consists of a continuum from snoring, to upper airway resistance syndrome, to the fully expressed syndrome. The pathophysiology of COSA is most commonly peripheral in origin due to nocturnal airway blockage from nasal pathophysiology, hypertrophic tonsils and adenoids, or craniofacial dysostoses. The symptomatology in COSA consists of snoring (usually continuous), rare daytime sleepiness, and frequent behavioral disturbances (e.g., attention deficit hyperactivity disorder [ADHD]). It is distinguished from adult OSA by the following: Snoring is more continuous, there is no sex predilection, and surgery (commonly adenotonsillectomy, rarely uvulopalatopharyngoplasty [UPPP]) is curative.

COSA occurs in 2% of young children and is frequently underdiagnosed. Most cases are idiopathic. COSA may be also related to severe chronic disease, such as chronic asthma, cystic fibrosis, pulmonary fibrosis, bronchopulmonary dysplasia, or chest wall abnormality. Rarely there is a genetic basis (see section A.4); and in these cases, apnea may be of central, or mixed, origin. The American Academy of Pediatrics (AAP) recommends that all children be screened for snoring. Polysomnography has been recommended as the most reliable diagnostic test and has been described elsewhere in detail. The American Academy of Otolaryngology—Head and Neck

Surgery has published guidelines clinical practice guidelines for polysomnography to screen children with sleep-disordered breathing prior to tonsillectomy.

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Wise MS, Nichols CD, Grigg-Damberger MM, et al. Executive summary of respiratory indications for polysomnography in children: an evidence-based review. *Sleep*. 2011;34(3):389–398AW.

A.6. What is the Pickwickian syndrome (PS)? What is obesity hypoventilation syndrome (OHS)? Describe the pathogenesis of severe OSA.

PS was so named by Burwell in 1956, as a reference to Joe, an obese, somnolent boy in *The Posthumous Papers of the Pickwick Club*, written in 1837 by Charles Dickens. In Joe, Dickens provided the first accurate description of the most severe type of OSA, consisting of a BMI over 50 kg per m^2 or SO, alveolar hypoventilation (hypoxemia and hypercarbia), heavy nighttime snoring with periodic respiration, hypersomnolence (daytime somnolence), secondary polycythemia, right and LV hypertrophy, and right-sided heart failure.

In these individuals with PS, there are repeated cycles of sleep, arousal, and sleep, accompanied by obstructed breathing, with snoring and restlessness. Hypoxemia and hypercarbia result from disruption of a normal sleep pattern, with loss of REM sleep and cardiovascular changes. Loss of REM sleep induces hypersomnolence, personality, behavior, and cognitive changes and predisposes these individuals to be accident-prone.

Eventually, severe OSA leads to OHS, with nocturnal, and later diurnal alterations in the control of breathing, manifested as central apneic events, or apnea without ventilatory efforts. They also develop an alveolar–arterial oxygen gradient by ventilation/perfusion mismatch and may develop pulmonary hypertension. The major factor in the pathogenesis of this syndrome is unknown but may be due to decreased hypoxic and hypercarbic ventilatory drive. Late in the disease process, there is progressive daytime hypoxia and hypercarbia. When cor pulmonale supervenes, PS is complete. Recently, the term *PS* has been abandoned in favor of OHS.

There are several cardiovascular changes in severe OSA, all related to the episodic airway closure, with hypoxemia and hypercarbia. Hypoxemia and alterations in autonomic tone may induce bradycardia during apneic episodes; in half of these patients, long sinus pauses, second-degree heart block, and ventricular ectopy may result. These arrhythmias may lead to nocturnal angina and myocardial infarction in susceptible individuals. Pulmonary hypertension may be caused directly by hypoxic pulmonary vasoconstriction, or indirectly by either increased transmural pulmonary artery pressures from negative thoracic pressure created by a sustained ventilatory effort against the upper airway obstruction, or by increases in pulmonary artery tone from increased sympathetic tone created by episodic hypoxemia. Pulmonary hypertension initially causes right ventricular hypertrophy, resulting in a higher right ventricular end-diastolic pressure (RVEDP), and later culminates in right ventricular failure, or cor pulmonale. The systemic circulation is also affected by episodic increases in sympathetic tone, with systemic hypertension presenting early, and LV hypertrophy, followed by LV failure, presenting much later. Systemic hypertension may also lead to increased stroke volume.

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Klinger J. Diagnosis and management of pulmonary hypertension associated with pulmonary fibrosis. *Adv Pulm Hypertens*. 2009;8:141–147.

A.7. What is the association between obesity and OSA? What is the etiology of OSA in severe obesity?

Obesity and OSAHS are both common, coexisting diseases. The prevalence of severe obesity, a strong risk factor for OSAHS, is 3.15% in males and 6.70% in females, according to U.S. population data. Incidence and severity of OSAHS correlates loosely with BMI, better with neck circumference, and most closely with waist circumference. OSAHS is 2.6 times more likely when the waist-to-hip ratio exceeds 1.0 in obese males and 0.85 in obese females.

Sixty percent to 90% of OSA patients are obese, and it has been estimated that 9% of women and 24% of men in the United States suffer from the syndrome, a total of 18 million individuals, of which 2% of women and 4% of men, are symptomatic. These figures will almost certainly increase, as the demographics shift toward an older and more obese population. Many of these patients do not have diagnosis of OSA on their medical record at the time of surgery, representing potential perioperative complications. The prevalence of OSA in morbidly obese patients presenting for weight loss surgery is 78%.

There are three reasons why severe obesity per se may cause or exacerbate OSAHS. First, there is an inverse relationship

between obesity and pharyngeal volume. The pharyngeal area decreases in obesity from deposition of adipose tissue into pharyngeal structures, in particular, the uvula, the tonsils, the tonsillar pillars, the tongue, the aryepiglottic folds, and, most importantly, the lateral pharyngeal walls. The volume of adipose in the lateral pharyngeal walls correlates with the clinical severity of airway obstruction. Increased deposition of pharyngeal adipose increases the likelihood that relaxation of the upper airway muscles will result in collapse of the soft-walled retroglossal space, between the uvula and the epiglottis. The shape of the pharynx remodels from an ellipse with the long axis transverse to an ellipse with the long axis anterior-posterior. The muscles that open the collapsible pharynx on expiration during sleep (e.g., tensor palatini, genioglossus, hyoid muscles) in response to stretch receptors in the pharynx are located in the anterior pharynx and do not function well with a remodeled pharynx.

Second, patency of the collapsible pharynx is determined by the transmural pressure (the difference between the extraluminal and intraluminal pressure) and compliance of its wall. If the compliance of the pharyngeal wall and intraluminal pressure (inspiratory pressure) is constant, then the remaining important determinant of upper airway patency is extraluminal pressure. In obese patients, extraluminal pressure is increased by superficially located fat masses; that is, the upper airway is compressed externally. Therefore, neck circumference is greater in obese patients with OSAHS compared with obese non-OSAHS patients.

Third, pharyngeal patency is partially determined by lung volume. The collapsible (particularly in a supine position), soft-walled pharynx is kept patent during sleep by lung volumes above the FRC, which pulls on the carina, tenting open the pharynx. This is known as *the lung volume hypothesis*. Smaller

lung volumes allow a cephalad displacement of the carina, approximately 0.5 to 1.5 cm, resulting in collapse or even telescoping of the pharynx, with a smaller circumferential area.

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Martinez-Rivera C, Abad J, Fiz JA, et al. Usefulness of truncal obesity indices as predictive factors for obstructive sleep apnea syndrome. *Obesity (Silver Spring)*. 2008;16:113–118.

Squier SB, Patil SP, Schneider H, et al. Effect of end-expiratory lung volume on upper airway collapsibility in sleeping men and women. *J Appl Physiol (1985)*. 2010;109:977–985.

A.8. What are the anesthetic implications of OSA?

Management of anesthesia in patients with severe OSAHS poses significant risks. These patients are extremely sensitive to minimal doses of central nervous system–depressant drugs, such as anesthetics, sedatives, and analgesics, and may exhibit prolonged sedation, resedation, or apnea as well as upper airway obstruction or, rarely, massive pharyngeal collapse. For these reasons, premedication with benzodiazepines or narcotics is used sparingly if at all, and sedation is generally reserved for painful or unpleasant situations (e.g., placement of invasive lines) where the patient is under the direct observation of a trained clinician.

Difficult tracheal intubation is expected in 13% to 24% of obese patients with OSAHS. In this particular case, the patient presents for laparoscopic bariatric surgery. Although the “ideal

general anesthetic" regimen for these patients is a matter of some discussion, the literature does support the following: a safe induction, a deep maintenance anesthetic with muscle relaxants, and a smooth emergence with rapid offset devoid of active metabolites or trace anesthetic. Anesthetic gases should be insoluble, resistant to metabolic degradation, and without lipid depot compartmentalization, combined with rapid return of airway reflexes. The only weak inhalation anesthetic, nitrous oxide (N_2O), has the advantage of being relatively insoluble, as measured by blood–gas solubility coefficient (0.46), but it causes intestinal inflation, may be emetic, and is not recommended in the presence of pulmonary hypertension, a condition that is more common in MO. Of the available potent inhalation anesthetics (desflurane, sevoflurane, and isoflurane), desflurane combines the quickest wake-up; fastest return of airway reflexes; lowest solubility, as measured by the blood–gas solubility coefficient (desflurane, 0.45; sevoflurane, 0.65; isoflurane, 1.4); and lowest percentage of hepatometabolization (desflurane, 0.02%; isoflurane, 0.2%; sevoflurane, 2% to 3%). Intravenous agents should be either lipophobic (hydrophilic), spontaneously degrade in vivo, or be ultrashort-acting.

Sedation or awake fiberoptic intubation: Ketamine and dexmedetomidine are optimal agents. *Induction of general anesthesia*: All agents have been utilized. *Maintenance agents*: air/oxygen mixtures, desflurane, cisatracurium, and remifentanil. *Last hour of general anesthesia and emergence*: N_2O (except in the presence of pulmonary hypertension), remifentanil, and hydromorphone. Use of regional anesthesia decreases opioid requirements and facilitates extubation.

Tracheal extubation is considered only when patients are fully awake with intact upper airway reflexes. Episodic arterial hypoxemia may occur early, in the first 24 hours, or late, from the second to the fifth day, postoperatively. Postoperative pain

management must take into account the exquisite sensitivity of these patients to the ventilatory-depressant effects of opioids.

Discharge from the postanesthesia care unit (PACU) may be made in the morbidly obese OSA, per protocol, after they have been started on CPAP or BIPAP and have been observed for at least 30 minutes, without stimulation, and found to be free of respiratory arrests. If respiratory arrests occur, PACU stay is extended for an additional 3 hours, and consideration is made to transfer the patient to a monitored bed.

Intravenous patient-controlled analgesia (IV-PCA) appears to be well tolerated in the morbidly obese, without deleterious effects on oxygen saturation, respiratory function, blood pressure, or heart rate. Hydromorphone is the most commonly used opioid for IV-PCA, morphine and fentanyl are second-line agents. It is important to individualize therapy. Use of multimodal analgesia, combined with the transversus abdominis plane (TAP) block after surgery, decreases opioid requirements. Recently, eliminating IV-PCA has been shown to accelerate hospital discharge after bariatric surgery.

American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Obstructive Sleep Apnea. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Obstructive Sleep Apnea. *Anesthesiology*. 2014;120(2):268–286.

Apfelbaum JL, Hagberg CA, Caplan RA, et al. Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. *Anesthesiology*. 2013;118:251–270.

Bosworth T. Eliminating patient-controlled analgesia accelerates discharge after bariatric surgery. Published 2017. https://www.mdedge.com/acssurgerynews/article/151134/bariatric-surgery/eliminating-patient-controlled-analgesia-accelerates. Accessed December 31, 2018.

Mittal T, Dey A, Siddhartha R, et al. Efficacy of ultrasound-guided transversus abdominis plane (TAP) block for postoperative analgesia in

laparoscopic gastric sleeve resection: a randomized single blinded case control study. *Surg Endosc*. 2018;32(12):4985–4989.

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A.9. What type of metabolic problems would you expect to find in morbidly obese patients? What are the roles of leptin and ghrelin in obesity?

In MO, there is an increase in both low metabolically active tissue (e.g., adipose) and normally active tissue (e.g., muscle). In general, LBW is equal to IBW plus 20% to 40% IBW. IBW is a value, based on population demographics, which could never be realized through weight reduction, in a severely obese individual.

Morbidly obese individuals have an increase in total oxygen consumption and carbon dioxide (CO_2) production due to an increased tissue mass. Increased metabolism demonstrates a linear relation with body weight and body surface area. Basal metabolic rate, however, remains normal in obese individuals.

Severely obese patients often have nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) increasing long-term risk of hepatic cirrhosis, dyslipidemia, inflammation, insulin resistance, and atherosclerosis. Metabolic syndrome, defined as a collection of central obesity, hypertension, dyslipidemia, and impaired glucose tolerance, is present in severe cases and increases perioperative risk of morbidity and death. Metabolic syndrome is mediated through adipocytokines, such as acute phase reactants (increases in C-reactive protein and serum amyloid A [SAA]), adipokines (decreased adiponectin, or increases in leptin or resistin), macrophage-derived factors (increased resistin or interleukin-1 beta [IL-1β]), proinflammatory cytokines and chemokines (increases in tissue necrosis factor-alpha [TNF-α], several

interleukins [IL-1, IL-6, IL-8, IL-10, IL-18]), chemokine (C-C motif), and prothrombotic factors (increases in plasminogen activator inhibitor-1 [PAI-1], fibrinogen, and factor VII).

Leptin is a satiety hormone secreted by adipocytes. Most obese adults have high inappropriate leptin levels or hyperleptinemia. Leptin levels are increased by overfeeding, insulin, glucocorticoids, endotoxin, and cytokines and are decreased by fasting, testosterone, thyroid hormone, and exposure to cold temperature. In the heart, increased leptin expression is seen following reperfusion after ischemia, and leptin concentration in cardiomyocyte culture serum is increased with endothelin (ET)-1 and angiotensin II treatment. Congenital leptin deficiency is a rare cause of obesity, caused by mutations in the LEP gene in an autosomal recessive pattern. Although polymorphism in leptin receptor gene expression has been identified in many diseases, such as diabetes, coronary artery disease, metabolic syndrome, and cancer, it also exists in healthy populations. Ghrelin is the hormonal stimulant of short-term hunger. In MO, there is a resistance to both leptin and ghrelin. The cellular and molecular basis for the interplay between leptin and ghrelin has been discussed in detail and is an area of intense research.

Cui H, López M, Rahmouni K. The cellular and molecular bases of leptin and ghrelin resistance in obesity. *Nat Rev Endocrinol*. 2017;13:338–351.

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Matsuzawa Y. Therapy insight: adipocytokines in metabolic syndrome and related cardiovascular disease. *Nat Clin Pract Cardiovasc Med*. 2006;3:35–42.

Ragin CC, Dallal C, Okebia M, et al. Leptin levels and leptin receptor polymorphism frequency in healthy populations. *Infect Agent Cancer*.

2009;4(suppl 1):S13.

Yang R, Barouch LA. Leptin signaling and obesity: cardiovascular consequences. *Circ Res*. 2007;101:545–559.

A.10. Describe the changes that occur in the following respiratory parameters in morbidly obese patients:

- **Pulmonary mechanics: tidal volume (V_T), functional residual capacity (FRC), residual volume (RV), vital capacity (VC), inspiratory reserve volume (IRV), expiratory reserve volume (ERV), and total lung capacity (TLC)**
- **Flow–volume loops**
- **Pressure–volume loops**
- **Diffusing capacity for carbon monoxide (DLCO)**
- **Compliances: lung (C_L), chest wall (C_{CW}), and total (C_{RS})**
- **Resistance: airway and total respiratory system**
- **Closing capacity (CC)**
- **Work of breathing (WOB)**

Morbidly obese patients have reduced lung volumes, increased WOB, and alterations in control of breathing and gas exchange. Body fat distribution, as well as BMI, determines the effect of obesity on pulmonary function.

Pulmonary mechanics. Pulmonary function tests (PFTs), or lung volumes, are uniformly altered in obesity. V_T is normal or increased in the obese and is decreased in Pickwickian obesity. IRV is decreased. ERV is markedly decreased because the increased weight of the torso decreases the normal expansive tendency of the rib cage and pulmonary parenchyma. RV is normal. FRC or ERV plus RV is markedly decreased because of the decrease in ERV. VC or ERV + V_T + IRV is decreased because of decreased ERV. TLC or RV + ERV + V_T + IRV is decreased for the same reason as VC. Individuals with central, as opposed to peripheral, fat distribution have greater decreases

in the forced vital capacity (FVC), forced expiratory volume (FEV), and TLC. The maximum voluntary ventilation (MVV) may also be reduced.

Diffusing capacity for carbon monoxide. The DLCO is usually normal in individuals with obesity and mildly reduced in those with OHS because the lung parenchyma is normal, and changes in PFTs are due to abnormal chest wall mechanics and lower lung volumes. DLCO is a useful test to separate intrinsic lung pathology from obesity.

Compliance. There is a decrease in the total respiratory system compliance ($1 / C_{RS} = 1 / C_L + 1 / C_{CW}$), where C_{RS} is the total compliance, C_L is the compliance of the lung, and C_{CW} is the compliance of the chest wall. Total compliance is always decreased because of the weight of the torso and abdominal contents pressing against the diaphragm creating a restrictive component, markedly decreasing the C_{CW}. Lung compliance is often normal but is decreased when pulmonary and circulatory comorbidities are present (e.g., pulmonary hypertension).

Resistance. There are increases both in the airway resistance (reduced elastic tension of the lung) and in the total respiratory system resistance (increased elastic tension of chest wall) at lower lung volumes, which leads to reduction in the caliber of the smaller airways. The increase in total resistance is approximately 30% in simple obesity and 100% in OHS. Resistance increases further in the supine position, possibly due to extrinsic adipose pressure of the supralaryngeal airway and a decreased FRC.

Closing capacity. FRC is reduced in the morbidly obese patient and may be below the CC; resulting in small airway closure; ventilation/perfusion mismatch; right-to-left shunting; and possibly hypoxemia, the so-called positional ventilatory collapse. This may be worsened in the supine position,

Trendelenburg position, by general anesthesia and muscle relaxants, and improved by the use of lung recruitment strategies (e.g., positive end-expiratory pressure [PEEP]), and reverse Trendelenburg position.

Increased work of breathing. MO is associated with a 70% increase in the WOB and a fourfold increase in the oxygen cost of breathing (oxygen consumed by the respiratory muscles per liter of ventilation, used as a surrogate for the energy cost of breathing). This is due to decreased lung compliance, increased respiratory resistance, and threshold inspiratory load from adipose tissue mass. Obese individuals with obstructive sleep apnea syndrome (MO-OSAHS) have elevated pharyngeal and nasopharyngeal resistance, raising the WOB 60% above the obese and 250% above the nonobese.

Al Ghobain M. The effect of obesity on spirometry tests among healthy non-smoking adults. *BMC Pulm Med*. 2012;12:10.

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Piper A, Yee B. Clinical manifestations and diagnosis of obesity hypoventilation syndrome. http://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-obesity-hypoventilation-syndrome. Accessed December 31, 2018.

A.11. What changes occur in PaO_2 and $PaCO_2$ in morbidly obese patients?

In the awake patient, positional reduction in lung volume and respiratory system compliance occur when moving from an upright position to a supine position. These changes are exaggerated in the severely obese patient, particularly ERV and FRC. FRC declines both with obesity and with induction of general anesthesia.

Hypoxemia is the most common blood gas abnormality in the

severely obese patient. The etiology is most commonly due to a low ventilation:perfusion ($\dot{V}/\dot{Q}$) ratio and less commonly as a result of hypoventilation. Pulmonary perfusion is increased in the obese as a result of increased cardiac output, increased circulating blood volume, and, occasionally, pulmonary hypertension. Alveolar ventilation is decreased in the obese as a result of upper airway closure and spirometric changes (decreased ERV and FRC). In addition, the closing volume is often greater than the ERV, particularly in the supine position, causing airway closure, resulting in right-to-left shunt and hypoxemia. These patients frequently develop atelectasis, both from cephalad position of the diaphragm and increased weight of thoracic adipose tissue. Many obese patients develop a restrictive respiratory pattern, with mild small-volume tachypnea, and increased use of accessory muscles of respiration.

The second most common blood gas abnormality in the severely obese is a variable change in the CO_2 tension ($PaCO_2$), not related to lung disease, and dependent on the alveolar ventilation. There are three patterns of ventilatory derangement described:

- *Alveolar hyperventilation* in response to a hypoxic drive. This occurs in young, active subjects. $PaCO_2$ is approximately 35 mmHg.
- *Periodic*, *nocturnal*, *alveolar hypoventilation* with normal daytime values. This is the hallmark of OSAHS.
- *Daytime, or constant, alveolar hypoventilation*. This occurs in OHS and PS.

In addition, lung disease, such as asthma and chronic obstructive pulmonary disease (COPD), is more common in the obese patient population, when compared with age- and sex-matched controls. Preexisting lung disease may become exacerbated perioperatively.

Alvarez A, Brodsky JB, Lemmens HJM, et al, eds. *Morbid Obesity: Peri-operative Management*. 2nd ed. Cambridge, United Kingdom: Cambridge University Press; 2010:125–126.

Onofri A, Patout M, Kaltsakas G, et al. Neural respiratory drive and cardiac function in patients with obesity hypoventilation syndrome following initiation of non-invasive ventilation. *J Thorac Dis*. 2018;10(suppl 1):S135–S143.

Shetty S, Parthasarathy S. Obesity hypoventilation syndrome. *Curr Pulmonol Rep*. 2015;4(1):42–55.

A.12. What changes occur in intrapulmonary shunt (Q_S/Q_T) and dead space (V_D/V_T) in MO? Describe the Shunt equation and the physiologic dead space, or Bohr equation.

Q_S/Q_T is normally less than 5%. In the MO, this is increased, because of the following:

- Lower $\dot{V}/\dot{Q}$ ratio
- Upper airway closure (e.g., OSAHS)
- Decreased FRC from abdominal compression
- Hypoventilation (e.g., OSAHS)
- Increased pulmonary circulation, from increased cardiac output, increased blood volume, and occasionally pulmonary hypertension

Shunt equation: $Q_S / Q_T = (CcO_2 - CaO_2) / (CcO_2 - CvO_2)$

where Q_S is pulmonary physiology shunt (milliliter per minute), Q_T is cardiac output (milliliter per minute), CcO_2 is end pulmonary capillary oxygen content, CaO_2 is arterial oxygen content, and C_VO_2 is mixed venous oxygen content.

Dead space is anatomic, alveolar, or physiologic. *Anatomic dead space* is the volume of the lung and upper airway that is not involved in gas exchange. Ventilation of this area does not result in gas exchange. The volume of the anatomic dead space in milliliters is approximately equal to the IBW in pounds.

Fowler's method of measuring anatomic dead space is by analyzing nitrogen concentration after single breath 100% oxygen. *Alveolar dead space* is the area of alveoli with ventilation and no perfusion, which has a $\dot{V}/\dot{Q}$ equal to infinity, or West Zone 1. *Physiologic dead space*, the sum of anatomic and alveolar dead space, is the total area of lung plus airways not involved in gas exchange. Physiologic dead space is approximately 30% of the V_T. It is decreased in the supine position, and increased with disease states that alter, and in OHS, because the latter individuals adopt a shallow ventilatory pattern. Physiologic dead space is decreased in SO due to increased V_T ventilation and unchanged anatomic dead space. Physiologic dead space, or V_D/V_T, is measured by the Bohr equation, with Enghoff modification.

$$\text{Bohr equation: } V_D/V_T = (Pa\text{CO}_2 - P\text{ECO}_2) / P\text{ECO}_2$$

where V_D is the physiologic dead space volume (mL), V_T is the tidal volume (mL), $Pa\text{CO}_2$ is the partial pressure of carbon dioxide in arterial blood, and $P\text{ECO}_2$ is the partial pressure of carbon dioxide in the average mixed expired air.

There are no changes in the physiologic dead space-to-V_T ratio or the alveolar–arterial oxygen gradient in obese patients undergoing laparoscopic gastric bypass surgery during general anesthesia compared with baseline.

Lumb AB, ed. *Nunn's Applied Respiratory Physiology*. 8th ed. Philadelphia, PA: Elsevier; 2017:119–123, 133–134, 135.e2, 306–307, 318.e1.

A.13. What changes occur in the cardiovascular system of the obese patient? Discuss cardiac output, blood volume, blood pressure, and pulmonary arterial pressure.

MO produces changes in cardiac morphology and ventricular

function.

As BMI increases, both total and circulating blood volume increase. Although absolute blood volume is expanded, relative blood volume is decreased. Increase in circulating blood volume and decrease in systemic vascular resistance results in augmentation in cardiac output. Cardiac output increases by increased stroke volume, and heart rate remains unchanged. Cardiac output and stroke volume increase in proportion to oxygen consumption and the degree of obesity but more closely to the LBW. LV wall stress increases according to the law of Laplace ($P_2 - P_1 = 2T / R$), where P is the change in pressure produced by the increased volume, T is the LV wall stress, and R is the radius. Increase in afterload from hypertension produces eccentric LV hypertrophy and eventually LV dysfunction. They are thus sensitive to acute changes in preload and afterload. Morbidly obese patients presenting to the operating room (OR) require an ECG, chest x-rays, and an echocardiogram. Seventy percent of the echocardiograms in morbidly obese patients contain abnormalities.

Hypertension is more prevalent because of increased cardiac output and increased blood volume. Hypertension is more commonly systolic than diastolic in the obese. Obese patients without comorbidity have normal pulmonary artery filling pressures. Those individuals with OHS and PS, however, commonly have pulmonary hypertension, as a result of hypoxic pulmonary vasoconstriction and increased cardiac output. Hypertension and increased cardiac output lead to congestive heart failure in approximately 10% of obese individuals. There are two mechanisms in the pathogenesis of heart failure. In the first, pulmonary and systemic vascular congestion develops as a consequence of chronic volume overload superimposed on diminished diastolic compliance, caused by long-standing ventricular hypertrophy. In the second, chronic volume overload

and high cardiac output results in LV hypertrophy. The ventricular wall/cavity ratio decreases, and LV systolic dysfunction results. Echocardiography demonstrates LV hypertrophy in these patients, often in the absence of electrocardiographic evidence. Obesity leads to fatty infiltration of the cardiac conduction system, predisposing to sudden death, with a peak incidence occurring at 2:00 AM. Obesity is not a direct predictor of coronary artery disease. As an indirect predictor, obesity is linked to coronary artery disease via hyperlipidemia and systolic hypertension. Incidence of congestive heart failure and stroke are elevated.

Obese patients develop a particular pattern of ventricular remodeling. Centrally obese normotensives develop eccentric ventricular remodeling from chronic volume overload, increased diastolic pressure, increased diastolic wall stress, and chamber enlargement. This is in contrast to lean hypertensives, with concentric hypertrophy. The hypertensive obese may have both systolic and diastolic pressure overload and potentially earlier heart failure.

The term "syndrome Z" has been used to describe the association of components of the metabolic syndrome, including central obesity, type 2 diabetes with insulin resistance, hypertension, atherogenic dyslipidemia, increased sympathetic nerve activity, and OSA.

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Poirier P, Giles TD, Bray GA, et al. Obesity: association with cardiovascular disease. https://www.uptodate.com/contents/obesity-weight-reduction-with-cardiovascular-disease. Accessed December 11, 2019.

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Silventoinen K, Magnusson PKE, Neovius M, et al. Does obesity modify the effect of blood pressure on the risk of cardiovascular disease? A population-

based cohort study of more than one million Swedish men. *Circulation*. 2008;118:1637–1642.

A.14. Are there any other disease entities commonly associated with obesity? What is their relationship?

Secondary obesity may be associated with hypothyroidism, Cushing disease, insulinoma, hypogonadism, and hypothalamic disorders. Although most obese patients are not diabetic, 80% to 90% of nonketotic diabetics are obese. Increased insulin secretion and insulin resistance resulting from peripheral tissue insensitivity are well-characterized features of obesity. Obesity exacerbates the diabetic state. Furthermore, malignancies of breast, prostate, cervix, uterus, colon, and rectum are more common in the obese.

In addition, there is a disproportionate increase in health-related risks from obesity. Above a BMI of 25, the risk of coronary artery disease more than doubles. Above a BMI of 29, there is an increased perioperative risk of pulmonary embolus. Above a BMI of 35, there is more than a 40-fold increase in adult-onset diabetes mellitus, respiratory disease, osteoarthritis, and OSAHS. Perioperative mortality during weight reduction surgery is statistically correlated with BMI, preoperative hypertension, anastomotic leak, and pulmonary embolus.

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Karam JG, McFarlane SI. Secondary causes of obesity. *Therapy*. 2007;4(5):641–650. https://www.openaccessjournals.com/articles/secondary-causes-of-obesity.pdf. Accessed December 31, 2018.

Lauby-Secretan B, Scoccianti C, Loomis D, et al. Body fatness and cancer—viewpoint of the IARC Working Group. *N Engl J Med*. 2016;375(8):794–798.

A.15. What anatomic changes that affect the airway are associated with MO and OSA?

Patient-specific anatomic changes in the MO are related to the

BMI, type of obesity (peripheral vs. central), and presence or absence of OSAHS. Not all MO patients have airway involvement. The anatomic changes affecting the airway are not always easily diagnosed on routine physical examination. At a given BMI, there is more airway involvement in central obesity compared with peripheral obesity, and the most severe airway involvement occurs in patients with OSAHS.

Anatomic alterations in the MO and OSA include the following:

- Deposit of adipose tissue in the lateral pharyngeal walls, and to a lesser extent in the uvula, the tonsillar pillars, the tongue, and the aryepiglottic folds, causing a decreased in the pharyngeal area
- Deposit of adipose tissue external to the upper airway (lateral parapharyngeal fat pads or jowls), extrinsically compressing the airway
- Presence of hypopharyngeal adipose tissue not evident on external examination that acts as a ball valve, obstructing the upper airway and interfering with the line-of-sight (LOS) at direct laryngoscopy (DL)
- Presence of pretracheal adipose tissue, which pushes the hyoid bone posteriorly into a less favorable position, causing the epiglottis to partially override the glottic entrance, worsening the laryngoscopic view
- Alteration in shape of the pharynx from an ellipse with the long axis lateral transverse to an ellipse with the long axis anterior-posterior
- Decreased efficiency of the anterior pharyngeal dilator muscles (tensor palatini [nasopharynx], genioglossus [oropharynx], hyoid muscles [laryngopharynx]), which promotes snoring
- The “lung volume hypothesis.” Decreased FRC in the asleep or anesthetized patient translates the tracheal carina cephalad

0.5 to 2 cm, relaxing the soft-walled hypopharynx and decreasing the internal volume. In severe cases, it may passively seal or telescope. Noninvasive positive pressure ventilation (NIPPV) tents open the hypopharynx, promoting gas exchange.

The anatomic changes that occur with MO are important for three reasons. First, these patients may obstruct their airway with light-to-moderate sedation (peripheral OSAHS). Various surgical procedures have been developed to improve this problem, such as the UPPP. Second, these patients may be difficult to mask ventilate, both because of external adipose tissue and internal collapse of redundant upper airway adipose. Third, there is a higher incidence of difficult intubation (DI) and failed intubation in the MO. When coupled with the precipitous desaturation, there is a need to revise the ASA DAA.

The literature is inconclusive on the relationship between obesity and difficult airways. According to some authorities, obesity is an independent risk factor for DI due to a disproportionately large tongue base or a short, thick neck. Other authors found that a higher BMI is not an indicator of DI but that increased neck circumference and poor Mallampati scores (classes 3 and 4) are. MO-OSAHS patients with other risk factors for DI (e.g., micrognathia) develop worsening of airway closure to an even greater degree than their counterparts.

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Feng Y, Keenan BT, Wang S, et al. Dynamic upper airway imaging during wakefulness in obese subjects with and without sleep apnea. *Am J Respir Crit Care Med*. 2018;198(11):1435–1443. https://www.atsjournals.org/doi/abs/10.1164/rccm.201711-2171OC. Accessed December 31, 2018.

Hagberg CA, Vogt-Harenkamp C, Kamal J. A retrospective analysis of airway management in obese patients at a teaching institution. *J Clin Anesth*. 2009;21:348–351.

Isono S. Obstructive sleep apnea of obese adults: pathophysiology and perioperative airway management. *Anesthesiology*. 2009;110:908–921.

Kheterpal S, Martin L, Shanks AM, et al. Prediction and outcomes of impossible mask ventilation: a review of 50,000 anesthetics. *Anesthesiology*. 2009;110(4):891–897.

A.16. What derangements of the gastrointestinal system are associated with MO?

There are several changes in the upper gastrointestinal tract that place severely obese individuals at risk of acid aspiration pneumonitis upon induction and emergence of general anesthesia: linear increase in intra-abdominal pressure with increasing body weight, increased incidence of GERD, decreased gastric pH, increased incidence of hiatal hernia, and impaired gastroesophageal antireflux mechanism, especially with foregut surgery. Ninety percent of fasting morbidly obese patients exceed Mendelson criteria, a gastric volume of greater than 0.35 mL per kg total body weight (TBW), with a pH less than 2.5. Severely obese patients have a normal gastric emptying rate with a larger pouch, so that after a controlled fasting (e.g., 2-day liquid diet for bariatric surgery), patients should have an empty stomach.

There is a substantially higher incidence of hepatobiliary disease in the morbidly obese, such as cholelithiasis, hepatitis, intra- and extrahepatic cholestasis, hepatic steatosis, and cirrhosis. Seventy-five percent of the morbidly obese have hepatic steatosis. Although there is a 25% incidence of severe hepatic dysfunction in the morbidly obese, there is no clear correlation between liver function tests (LFTs) and hepatic dysfunction, complicating medical and anesthetic management. There is a natural, step-wise progression from NAFLD, to NASH, to fibrosis and hepatocellular carcinoma. Typically,

NAFLD is stable and benign, with 1% to 2% risk of developing cirrhosis over 15 to 20 years. NASH is more progressive, with 3% to 15% progressing to cirrhosis over 10 to 20 years. Pancreatic disease is also more common in this population, specifically gallstone pancreatitis, adult-onset diabetes mellitus, and insulinoma. There is a higher incidence of colorectal malignancies in the morbidly obese. Long-standing central obesity in the presence of metabolic syndrome is associated with erosive esophagitis, Barrett esophagus, and esophageal adenocarcinoma. This is probably related to (1) dysfunctional gastroesophageal junction; (2) altered metabolism from visceral fat, with resulting lower levels of adiponectin and higher levels of IL-1β and TNF-α; and (3) the insulin-like growth factor (IGF) axis, particularly IGF-1 receptor (IGF-1R) gene polymorphism at G1013A.

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National Cancer Institute. Obesity and cancer. https://www.cancer.gov/about-cancer/causes-prevention/risk/obesity/obesity-fact-sheet. Accessed December 31, 2018.

Singh M, Lee J, Gupta N, et al. Weight loss can lead to resolution of gastroesophageal reflux disease symptoms: a prospective intervention trial. *Obesity (Silver Spring)*. 2013;21(3):284–290.

B. Preoperative Evaluation and Preparation

B.1. How would this patient be optimized for surgery preoperatively? Would you use preoperative

screening questionnaires to diagnose OSA? Summarize the workup for this patient.

Key to a successful outcome in any high-risk surgery is a multidisciplinary approach, and bariatrics is no exception. After the initial visit, the patient was assigned an internal medicine physician, specializing in obesity medicine, with a plan to defer surgical intervention until medical optimization. Complete, comprehensive care, consisting of rehabilitation medicine, pharmacologic and nonpharmacologic interventions, behavior modification, and medically supervised diet, was accompanied by psychological evaluation to determine motivation and long-term perception of patient goals. This resulted, after roughly 1 year, in a functional improvement to 2 metabolic equivalents (METs) and weight loss to 204.12 kg, with a BMI of 61.0 kg per m^2, a roughly 25% decrease. Once the patient had been deemed optimized for surgery, and after at least 6 months, the preoperative workup is conducted and surgery was scheduled.

Preoperative evaluation includes a detailed history, review of systems, physical examination, and laboratory tests. Special attention is paid to circulatory, pulmonary, and hepatic functions. Circulatory evaluation includes signs and symptoms of left or right ventricular failure, history of hypertension, and electrocardiographic abnormalities. Respiratory evaluation includes smoking history, exercise tolerance, history of hypoventilation and somnolence, PFTs with spirometry and baseline arterial blood gases, and chest x-ray results. Hepatic function tests include serum albumin and globulin, serum aspartate aminotransferase, serum alanine aminotransferase, direct and total bilirubin, alkaline phosphatase, prothrombin time, and cholesterol levels.

A cardiology consultation was conducted, with a noninvasive assessment of cardiac function by echocardiogram. Patients

without an adequate echocardiographic window require radionucleotide ventriculography to assess ventricular function and morphology, as in this case. It is important to obtain a full assessment by the cardiologist to determine whether this patient is optimized and which invasive lines, if any, are appropriate. This patient was found to have mild right ventricular hypertrophy and mild pulmonary artery hypertension. Pertinent negatives were the absence of demonstrated coronary artery disease and left or right ventricular failure. In this case, it was determined that the patient was optimized, and that an arterial line would be helpful.

Physical examination focuses on the cardiovascular, pulmonary, and the upper airway. The upper airway assessment, in particular, should be thorough. In addition to the routine parameters, atlanto-occipital joint extension, modified Mallampati class (MMC), temporomandibular joint (TMJ) assessment with inter-incisor distance, mento-hyoid distance, and dentition, the following parameters should be checked: pretracheal adipose thickness, neck circumference, and hypertrophic tonsils and adenoids. Nonreassuring findings related to the latter three variables are a large neck, an abundance of anterior neck soft tissue, and obligate mouth breathing. Neck circumference is an independent predictor of DI; the odds ratio is 1.13 (The odds of a problematic intubation in a particular patient with a neck circumference 1 cm larger than that of another patient are 1.13 times the odds of the patient with a 1 cm smaller neck circumference.). At 40 cm (15.75 in.), there is a 5% chance of DI; at 60 cm (23.62 in.), this increases to 35%. Pretracheal adipose greater than 2.5 cm at the level of the vocal cords, determined by ultrasound is an independent predictor of DI. Obligate mouth breathing may be a clue that the patient has adenotonsillar hypertrophy, nasal septal blockage, or a craniofacial dysostosis. Factors that render mask ventilation

problematic, such as a heavy beard, should be noted.

Prior anesthetic records should be obtained. Patients with a history of heavy snoring should have a formal sleep study or PSG. Severity of OSAHS, AHI, home oxygen therapy with CPAP or BIPAP, response, and compliance should be noted.

The obesity surgery mortality risk score (OR-MRS) is a ratified tool consisting of BMI >50 kg per m^2, male gender, hypertension, pulmonary embolus risk (previous thrombus, inferior vena cava (IVC) filter, right-sided heart failure, OHS), and age >45 years old. The STOP-BANG questionnaire is a widely used ratified tool to screen patients for OSA. An acronym, it consists of response to the following questions:
Snoring: louder than talking, heard through closed doors
Tired: daytime hypersomnolence
Observed cessation of breathing during sleep
High Blood **P**ressure: with or without treatment
BMI: >35 kg per m^2
Neck circumference: >40 cm (15.75 in.)
Gender: male

Predictive value of the STOP-BANG questionnaire is as follows.
High risk of OSA: Yes, three or more out of eight items.
Low risk of OSA: Yes, less than three items.

The sensitivities of the STOP questionnaire with AHI greater than 5, greater than 15, and greater than 30 as cut-offs were 65.6%, 74.3%, and 79.5%, respectively. When incorporating BMI, age, neck circumference, and gender into the STOP questionnaire, sensitivities were increased to 83.6%, 92.9%, and 100% with the same AHI cut-offs.

In this case, of the STOP-BANG acronym, each letter is positive, except for age, so the score is *7*.

ASA has devised a ratified patient- and procedure-specific perioperative scoring system that measures OSA risk based on

points:

A. OSA severity based on clinical indicators (0 to 3)
B. Invasiveness of surgery and anesthesia (0 to 3)
C. Need for postoperative opioids (0 to 3)

Score is based on A + B versus A + C, whichever is greater. Expert consensus: Agree that patient is at increased perioperative risk of OSA complications if the score is >3. In this case, A. *3 − 1 = 2 (due to patient compliance)*, B. *2*, C. *0.* OSA risk: *4 (mild increase)*. Recommendation: *Continue CPAP/BIPAP*, no need for monitored bed. It is acceptable to be cautious and send a patient to a monitored bed, it just does not match the expert consensus.

American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Obstructive Sleep Apnea. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Obstructive Sleep Apnea. *Anesthesiology*. 2014;120(2):268–286.

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Wolkove N, Baltzan M, Kamel H, et al. Long-term compliance with continuous positive airway pressure in patients with obstructive sleep apnea. *Can Respir J*. 2008;15(7):365–369.

B.2. One of the recent developments in bariatric surgery is that many patients are receiving prebariatric screening procedures performed in the endoscopy suite. Describe the anesthetic considerations.

Sleeve gastrectomy has emerged over the last few years to be an

ideal bariatric procedure because it is simpler than the Roux-en-Y gastric bypass (RYGB), yet still highly effective. More than half of the annual bariatric surgical procedures performed in the United States in 2017 (228,000) are now sleeve gastrectomy (59.39%). Patients with severe, chronic GERD, however, may have worsening of symptoms after a sleeve gastrectomy. The RYGB is an alternate procedure that may improve symptoms of GERD.

Endoscopic prescreening for bariatric surgery is becoming more widely used, being used in roughly 50% of cases.

Upper endoscopy (esophagogastroduodenoscopy [EGD]) and Bravo (Bravo Reflux Testing System®; Medtronic, Minneapolis, MN) may help determine the appropriate surgical procedure, documenting lower esophageal pH and demonstrating signs of chronic severe GERD. The Bravo® pH testing system is usually placed via upper endoscopy: A capsule is imbedded into the mucosa of the lower esophagus, where it remains for 48 hours and then either falls out or is retrieved endoscopically. Continuous pH readings may be obtained via an external device using Bluetooth wireless technology.

Anesthesia for bariatric prescreening procedures is typically deep sedation via propofol bolus or infusion only. In all patients for upper endoscopy, the mortality rate is 0.03% and a serious morbidity rate is 0.54%, but it may be higher in the obese patient population.

The SuperNO_2VA® (Vyaire Medical, Mettawa, IL) nasal CPAP device facilitates spontaneous, assisted, or controlled ventilation for numerous indications. Among the possible oxygen sources (anesthesia circuit, wall supply, E-cylinder, flow-inflating resuscitator), the lightweight, highly complaint Mapleson F (Jackson Rees circuit) has been particularly successful. At Weill Cornell Medical Center, the SuperNO_2VA® has been used successfully in over 1,000

procedures as well as most bariatric screening procedures, for the provision of deep sedation in the Endoscopy Suite.

American Society for Metabolic and Bariatric Surgery. Estimate of bariatric surgery numbers, 2011-2017. https://asmbs.org/resources/estimate-of-bariatric-surgery-numbers. Accessed December 31, 2018.

De Palma GD, Forestieri P. Role of endoscopy in the bariatric surgery of patients. *World J Gastroenterol*. 2014;20(24):7777–7784.

Hendricks L, Alvarenga E, Dhanabalsamy N, et al. Impact of sleeve gastrectomy on gastroesophageal reflux disease in a morbidly obese population undergoing bariatric surgery. *Surg Obes Relat Dis*. 2016;12:511–517.

Thereaux J, Barsamian C, Bretault M, et al. pH monitoring of gastro-oesophageal reflux before and after laparoscopic sleeve gastrectomy. *Br J Surg*. 2016;103:399–406.

B.3. Summarize the evidence-based workup, risk, chance of various adverse outcome, and expected length of stay for this patient.

The American College of Surgeons National Surgery Quality Improvement Project (NSQIP) Surgical Risk Calculator provides the latest, nationally risk-adjusted database for tracking surgical outcomes and has an on-line risk calculator. The Calculator estimates adverse outcomes for a given surgical procedure and is based on their database. Our patient is having a *laparoscopic sleeve gastrectomy* (CPT code 43775, 2018/2019 ICD-10-CM Z.98.84) and has risk factors (*severe systemic disease, diabetes [oral], hypertension, class 3 obese*). A panel of expected outcomes is generated, which compares *case-specific risk* to average being risk and chance of outcome, as follows: serious complication *3.1%* (2.6%), *above average*; any complication *3.8%* (3.3%), *above average*; pneumonia *0.2%* (0.2%); cardiac complication *0.1%* (0.1%); surgical site infection *1.4%* (1.2%), *above average*; urinary tract infection *0.4%* (0.5%), *below average*; venous thromboembolism *0.5%* (0.4%), average; renal failure *0.4%* (0.2%), *average*;

readmission *3.8%* (3.2%), *above average*; return to OR *1.1%* (0.9%), *above average*; death *0.1%* (0.1%); discharge to nursing or rehabilitation facility *0.4%* (0.4%); and predicted length of hospital stay *2 days*.

American College of Surgeons. National Surgery Quality Improvement Project (NSQIP) Surgical Risk Calculator. http://www.riskcalculator.facs.org/RiskCalculator/. Accessed December 31, 2018.

Greenstein AJ, Wahed AS, Adeniji A, et al. Prevalence of adverse intraoperative events during obesity surgery and their sequelae. *J Am Coll Surg*. 2012;215(2):271.e3–277.e3.

B.4. What is the role of enhanced recovery after surgery (ERAS) in bariatric surgery? How does the public find a quality bariatric surgery team and surgical facility? What is the role of robotics in bariatric surgery?

ERAS is a multiprofessional and multidisciplinary approach to the care of the *surgical* patient. The multimodal approach to *recovery* was first outlined by a Danish surgeon, Henrik *Kehlet*, in 1995 for colorectal surgery.

ERAS quickly evolved from several perioperative elements into a cohesive multidisciplinary team approach and has been adopted into several surgical subspecialties, such as urology, obstetrics and gynecology, vascular surgery, orthopedics, spine surgery, cardiac surgery, and, most recently, bariatric surgery. Although originally used for laparoscopic procedures, ERAS has been used on open and robotic surgery. ERAS implementation has radically changed the surgical experience and results in net health care cost savings. Subsequently, this idea evolved into a multidisciplinary instrument integrating several perioperative elements which is now recognized as the ERAS protocol with a number of official ERAS Society Guidelines for Perioperative Care in Bariatric Surgery. ERAS for bariatric surgery has been

termed ENERGY, for *EN*hanc*E*d *R*ecovery *G*oals in Bariatric Surger*Y*.

In 2017, The American College of Surgery (ACS) launched a major surgical quality improvement initiative in collaboration with the Johns Hopkins Medicine Armstrong Institute for Patient Safety and Quality and the Agency for Healthcare Research and Quality (AHRQ). Separate programs of the ACS and the American Society for Metabolic and Bariatric Surgery (ASMBS) have since been combined into a single unified program to achieve one national accreditation standard for bariatric surgery centers, the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP). Participating medical centers are subjected to rigorous ongoing criteria, data registry, and reaccreditation surveys, and are high-quality. The ACS website, and their publication, *Bariatric Times*, provides timely information to the public.

Initial robotic bariatric surgery results are promising, for even the highest risk candidates. A recent review revealed that robotics led to a similar or lower complication rate compared with laparoscopic technique as well as shorter learning curve, lower leak rate, similar operative time, superior visualization, more degrees of freedom, and better ergonomics.

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Bariatric Times. http://bariatrictimes.com/. Accessed December 31, 2018.

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Cooke FE, Samuels JD, Pomp A, et al. A randomized, double-blind, placebo-controlled trial of intravenous acetaminophen on hospital length of stay in obese individuals undergoing sleeve gastrectomy. *Obes Surg*. 2018;28(10):2998–3006.

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super obese and super-super obese patients. *Surg Endosc*. 2018;32(12):4867–4873.

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Thanh NX, Chuck AW, Wasylak T, et al. An economic evaluation of the enhanced recovery after surgery (ERAS) multisite implementation program for colorectal surgery in Alberta. *Can J Surg*. 2016;59(6):415–421.

B.5. Would you premedicate the patient?

Current practice is not to give sedatives or hypnotics until these patients are on the OR table, as part of preparation for painful procedures (e.g., arterial line placement), or airway management (e.g., airway topicalization and cranial nerve blocks V, IX, and X). A well-conducted preoperative visit is more important than is sedation. This patient was not sedated before surgery.

Nonrespiratory depressant premedication may be used as part of multimodal analgesia in patients with MO; this has the potential to decrease preinduction anxiety, lower anesthetic requirements, and decrease immediate postoperative depressant effects of opioids in a high-risk population. A single loading dose of intravenous dexmedetomidine in the OR suite blunts the hemodynamic responses during laryngoscopy, reduces opioid and anesthetic requirements; it also decreases blood pressure and heart rate as well as the recovery time after the operation. Other pre- and perioperative medications that have been considered include acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs) including ketorolac, lornoxicam, diclofenac, pregabalin, tramadol, ketamine, magnesium, and others. More research needs to be conducted in this area before a standard of care emerges; however, preemptive analgesia has not been

adopted as a standard in bariatric surgical population.

Other drugs that have been advocated as intravenous premedicants include the anticholinergic, drying agent glycopyrrolate, prokinetic, antiemetic metoclopramide, and H_2-blockers, such as famotidine. Aprepitant, a selective human substance P/neurokinin 1 receptor antagonist, has recently been advocated as prophylaxis of postoperative nausea and vomiting (PONV). PONV is often severe following bariatric surgery and requires polypharmacy, including oral preoperative medications, such as aprepitant. Nonsedative premedicants (e.g., glycopyrrolate, metoclopramide, famotidine) are rarely used because these patients are on a liquid diet for 2 days preoperatively.

At our institution, we follow the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) on all cases, unless contraindicated. Two hours prior to surgery, in the holding area, subcutaneous heparin 5,000 mg, and the ENERGY protocol medications: celecoxib 400 mg oral, acetaminophen 975 mg oral, gabapentin 300 mg oral, aprepitant 40 mg oral. Despite best practice, the incidence of PONV, the most common postoperative complication in bariatric surgery, is high.

Jones SB. Multimodal analgesia in patients with morbid obesity. http://bariatrictimes.com/multimodal-analgesia-in-patients-with-morbid-obesity. Published November 26, 2013. Accessed December 31, 2018.

King AB, Spann MD, Jablonski P, et al. An enhanced recovery program for bariatric surgical patients significantly reduces perioperative opioid consumption and postoperative nausea. *Surg Obes Relat Dis*. 2018;14(6):849–856.

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Sawyer J, Morningstar B, Chung F, et al. Enhanced recovery after surgery guideline: perioperative pain management in patients having elective colorectal surgery. https://www.sages.org/wp-content/uploads/2013/09/toronto-

iERAS_Pain_Mangement_Guideline_March_2014.pdf. Accessed December 31, 2018.

Thorell A, MacCormick AD, Awad S, et al. Guidelines for perioperative care in bariatric surgery: Enhanced Recovery After Surgery (ERAS) Society recommendations. *World J Surg*. 2016;40(9):2065–2083.

B.6. Describe the mechanism of action of each premedication in the ENERGY protocol.

- The combination of a highly selective reversible inhibitor of the COX-2 isoform of cyclooxygenase, *celecoxib*, inhibits the transformation of arachidonic acid to prostaglandin precursors, exhibiting antipyretic, analgesic, and anti-inflammatory properties.
- *Acetaminophen*, a centrally acting cyclooxygenase inhibitor (COX-1 to 3), increases the pain threshold, decreasing opioid requirements.
- Gabapentinoid (*gabapentin* or pregabalin) is structurally related to the neurotransmitter GAB (gamma-aminobutyric acid), an anticonvulsant, works on the centrally located auxiliary subunit of the voltage-activated calcium channels, functioning as an anticonvulsant, treating neuropathic pain, and decreasing perioperative analgesic requirements.
- *Aprepitant* works as a selective human substance P/neurokinin 1 receptor antagonist and has been used as powerful antiemetic therapy to treat chemotherapy-induced nausea and vomit.

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U.S. Food and Drug Administration. Neurontin. https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/020235s041,0208

Accessed December 31, 2018.

B.7. How would you adjust doses of anesthetics in the morbidly obese?

Anesthetizing MO patients requires careful consideration regarding changes in the pharmacokinetic and pharmacodynamic properties of numerous drugs used in anesthesia. Physiologic and anthropometric changes, such as increases in cardiac output, changes in regional blood flow, and increases in the body composition affect pharmacokinetic properties. In addition, respiratory pathophysiology such as the increased incidence of OSA and fat deposition in the oropharynx and chest wall alters pharmacodynamic properties of anesthetics.

Weight-based dosing scalars other than TBW must be considered when administering drugs to MO patients. Administration of drugs based on TBW can result in an overdose, whereas administration based on IBW can result in a subtherapeutic dose.

With the exceptions of succinylcholine (where TBW is appropriate) and the nondepolarizing neuromuscular blocking agents (where IBW is appropriate), LBW is the optimal dosing scalar for most anesthetic agents including opioids and anesthetic-induction agents, especially as cardiac output is significantly correlated to LBW, except in individuals with obesity cardiomyopathy (**Table 63.1**).

TABLE 63.1 Weight-Based Dosing Scalar Recommendation for Commonly Used Intravenous Anesthetics

Drug	Dosing Scalar	Comments
Thiopental	Induction: LBW Maintenance: TBW	Simulations showed a 60% decrease in peak plasma concentration in MO subjects compared with lean subjects after a 250 mg dose. Induction dose adjusted to LBW results in same peak plasma concentration as dose adjusted to CO. Volumes and clearances increase proportionally with TBW.

Propofol	Induction: LBW Maintenance: TBW	MO subjects given an induction dose based on LBW required similar amounts of propofol and similar times to loss of consciousness compared with lean subjects given propofol based on TBW. Volume of distribution and clearance at steady state increases with increasing TBW.
Fentanyl	LBW	Clearance increases linearly with 'PK mass', an arbitrary scalar highly correlated to LBW.
Remifentanil	LBW	An infusion based on LBW results in similar plasma concentrations as normal weight subjects were given an infusion based on TBW.
Succinylcholine	TBW	Administration of 1 mg kg^{-1} based on TBW resulted in a more profound block and better intubating conditions compared with doses based on IBW or LBW.
Vecuronium	IBW	Doses based on TBW result in a prolonged duration of action in obese *vs* non-obese subjects.
Rocuronium	IBW	There is an increased duration of action when the drug is given based on TBW *vs* IBW.
Atracurium, Cisatracurium	IBW	The duration of action is prolonged in obese subjects when given on the basis of TBW *vs* IBW.

CO, cardiac output; IBW, ideal body weight; LBW, lean body weight; MO, morbid obesity; PK, pharmacokinetic; TBW, total body weight.

Reprinted from Ingrande J, Lemmens HJM. Dose adjustment of anaesthetics in the morbidly obese. *Br J Anaesth*. 2010;105(suppl 1):i16–i23. Copyright © 2010 The Author(s). With permission.

Volatile anesthetics are sequestered in adipose tissue based on lipid solubility. Desflurane has faster washout and recovery than sevoflurane; sevoflurane is useful for short-duration titration of anesthetic depth and in selected patients (e.g., smokers, asthma).

Barras M, Legg A. Drug dosing in obese adults. *Aust Prescr*. 2017;40(5):189–193.

Ingrande J, Lemmens HJM. Dose adjustment of anaesthetics in the morbidly obese. *Br J Anaesth*. 2010;105(suppl 1):i16–i23.

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Nightingale CE, Margarson MP, Shearer E, et al. Peri-operative management of the obese surgical patient 2015. *Anaesthesia*. 2015;70(7):859–876.

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C. Intraoperative Management

C.1. How would you monitor this patient?

In addition to the routine ASA-mandated monitors of ECG, noninvasive blood pressure, pulse oximetry, end-tidal CO_2, and temperature, an arterial line may be inserted for frequent assessment of blood gases for continuous blood pressure tracing in the patient with cardiac disease (as in our patient). An esophageal stethoscope with thermistor is placed in the tympanic membrane, or in the axilla, to monitor temperature because any device placed in the esophagus may be inadvertently included in the surgical anastomosis. Urinary drainage catheters are not typically placed. A peripheral nerve stimulator is used to monitor the effects of muscle relaxants. A processed EEG, such as the bispectral index or BIS® (Medtronic, Minneapolis, MN), was used to monitor depth of anesthesia. BIS monitoring has been shown to be useful in laparoscopic bariatric surgery, both because blood pressure and heart rate are inadequate surrogate proxies of anesthetic depth, due to patients positioned in the standing position with frequent sympathomimetic support (in this case, phenylephrine infusion), and because total intravenous anesthesia (TIVA) is frequently used. Obese patients are at higher risk of perioperative awareness under general anesthesia. Intraoperative spirometry and the use of flow–volume loops (GE Datex S/5 [System 5] series monitor [GE Datex Ohmeda, Helsinki, Finland]) are highly useful and will alert the anesthesiologist to change in surgical conditions and patient status. Automatic peripheral nerve stimulator (IntelliVue® NMT; Phillips, Amsterdam, The Netherlands) simplifies data acquisition and charting on the electronic medical record (EMR, CompuRecord®; Philips, Amsterdam, The Netherlands).

The advantages of invasive monitoring have to be weighed against the possible complications. Laparoscopic bariatric

surgeries have minimal blood loss (typically less than 100 to 200 mL) and fluid shifts. These are elective cases, and patients are optimized preoperatively. Invasive arterial monitoring is used for the super obese with severe cardiopulmonary disease or poor fit of the noninvasive blood pressure cuff because of the conical shape of the upper arms or unavailability of appropriately sized cuffs. Accurate blood pressure readings may be obtained from the wrist or the ankle. Central venous access is typically used when there are difficulties obtaining peripheral access. A pulmonary artery catheter is reserved for the rare patient with severe pulmonary hypertension, cor pulmonale, or LV failure.

Cook TM, Woodall N, Frerk C. Major complications of airway management in the UK: results of the Fourth National Audit project of the Royal College of Anaesthetists and the Difficult Airway Society. Part 1: anaesthesia. *Br J Anaesth*. 2011;106:617–631.

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Leykin Y, Brodsky JB, eds. *Controversies in the Anesthetic Management of the Obese Surgical Patient*. Milan, Italy: Springer-Verlag Italia; 2013:131–138.

National Audit Projects. NAP5 report. https://www.nationalauditprojects.org.uk/NAP5report. Accessed December 31, 2018.

Schumann R. Anesthesia for the obese patient. https://www.uptodate.com/contents/anesthesia-for-the-obese-patient. Accessed December 31, 2018.

C.2. The American Society of Anesthesiologists' (ASA) Difficult Airway Algorithm (DAA) provides a guideline for management of the difficult airway. How do the comorbidities of MO and OSA modify implementation of the algorithm?

The ASA DAA provides a guideline for management of the

difficult airway. It was created by a panel of experts under the direction of the ASA in 1993 and modified in both 2003 (to include the laryngeal mask airway [LMA]) and 2013 (to include the supraglottic airway [SGA] and videolaryngoscopes). Implementation of the algorithm will be altered in different patient populations, according to factors such as location, patient demographics, comorbidities, surgical requirements, equipment availability, presence of additional personnel, and, probably most importantly, the skill set of the anesthesiologist.

In the bariatric surgical population, with demonstrated or suspected OSA, considerations include bariatric surgical patients are considered "empty stomach" in most cases; they are generally vulnerable to precipitous apneic deoxygenation; the standard airway assessment may not be sufficient, there is a higher incidence of difficult mask ventilation and DI, and redundant adipose tissue may obstruct the line of sight on laryngoscopy. Each of these points deserves clarification.

First, bariatric surgical candidates typically receive an upper endoscopy. We therefore know whether they have conditions associated with the need for aspiration prophylaxis, such as GERD, hiatal hernia, a gastric hypersecretory state, or achalasia. Obesity produces a moderate increase in gastric accommodation and an increase in emptying rate. Foregut surgical patients are placed on a liquid diet for 2 days and should have an empty stomach. As part of the ERAS protocol for bariatrics, or ENERGY, patients receive an energy drink prior to midnight on the day prior to surgery and upon awakening. Studies have shown that gastric fluid volume and pH are unchanged after drinking a nonparticulate drink 2 hours prior to surgery.

Second, severely obese patients are at higher risk of early arterial apneic desaturation during induction of anesthesia. This is due to several factors, including derangement of pulmonary mechanics (decreased ERV and FRC) by cephalad displacement

of the diaphragm, increased incidence of atelectasis, airway modifications, and increased frequency of hypotensive events. This is discussed further in section C.3.

Third, the standard airway assessment may not be sufficient. Physical findings suggestive of peripheral OSA (such as pretracheal adipose thickness, neck circumference, and hypertrophic tonsils and adenoids) should be sought out. Craniofacial dysostoses (e.g., relative micrognathia) may be hidden behind facial adipose or hair. This is discussed further in section B.1. In consequence, there is a higher incidence of both difficult mask ventilation and unanticipated difficult airway. The latest guidance is from the Difficult Airway Society 2015 guidelines for management of unanticipated DI in adults. Videolaryngoscopes and alternative airway devices, including fiberoptic bronchoscopes (FOB), have been shown to improve laryngeal view during intubation. It is important, in this patient population, to have options when the primary airway management technique fails.

Fourth, and last, the importance of additional personnel needs to be stressed. The attending surgeon needs to be present at induction of anesthesia, and an unopened tracheostomy set should be available. When indicated, an additional anesthesia attending may be helpful. With the evolution of videolaryngoscopic devices, and our collective extensive experience, use of the FOB and awake techniques for securing the airway have become a rarity. The FOB remains an important part of our arsenal, however, and should be available as part of a backup plan.

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Airway. *Anesthesiology*. 2013;118:251–270.

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Kheterpal S, Martin L, Shanks AM, et al. Prediction and outcomes of impossible mask ventilation: a review of 50,000 anesthetics. *Anesthesiology*. 2009;110(4):891–897.

Kruisselbrink R, Arzola C, Jackson T, et al. Ultrasound assessment of gastric volume in severely obese individuals: a validation study. *Br J Anaesth*. 2017;118(1):77–82.

Tanoubi I, Drolet P, Donati F. Optimizing preoxygenation in adults. *Can J Anaesth*. 2009;56(6):449–466.

C.3. Why is it important to preoxygenate the obese patient? How would you do it? Compare the effectiveness of the four-maximum-breath and 3-minute techniques. What is the importance of continuous positive airway pressure (CPAP) during the induction of general anesthesia? Describe use of the nasal CPAP mask in the induction of general anesthesia.

In this patient population, preoxygenation (pre-O_2) is essential due to precipitous apneic deoxygenation on induction of anesthesia. Pre-O_2 is optimized by semirecumbent position and a tight-fitting face mask. In the past, two techniques of pre-O_2 have been used: full, or "slow" (V_T breathing for 3 minutes), and "fast" (four-maximum-breath over 30 seconds). "Slow" pre-O_2 produces higher oxygen tension; the "fast" is to be discarded. When time is of the essence, however, a modified "fast" pre-O_2 technique (eight-maximum-breath over 60 seconds) compares

favorably with the "slow" pre-O_2, both in terms of fraction of expired oxygen (FEO_2) and duration of apnea without desaturation in seconds (DAWD). The vast majority of the oxygen reserve is in the FRC. The amount of time for onset of hypoxia (SpO_2 of 90%) has been calculated for a healthy nonobese adult when breathing room air and when breathing 100% oxygen both at onset of apnea. The subject could sustain a period of apnea of 0.9 minutes versus 9 minutes. The vast majority of the oxygen reserve is in the FRC, and the first 8.1 minutes are spent consuming the FRC reserve. For the MO patient, time to hypoxia will be significantly shorter.

Continuous positive pressure ventilation (CPAP) increases FRC and further raises the oxygen reserve, compared with nasal oxygen. This occurs both during sedation and induction of general anesthesia. CPAP works by tenting open the hypopharynx and increasing the FRC, both particularly important in the MO patient population. Recent meta-analysis of perioperative noninvasive ventilation in obese patients suggest that CPAP is well tolerated and effective before induction of general anesthesia and after extubation in improving CO_2 clearance and decreasing the risk of respiratory complications.

Recently, the SuperNO_2VA® (Vyaire Medical, Mettawa, IL), a modified nasal CPAP mask, has been favorably trialed during the induction of general anesthesia. Nasal positive pressure ventilation is conducted via the anesthesia ventilator during the induction sequence without steric hindrance, due to the low-profile mask, and patients may be effectively ventilated while being intubated, as was our patient. This may be helpful in the event of an unexpected difficult airway. This device requires further study but has the potential to be incorporated into the guidelines of the Difficult Airway Society for the unexpected difficult airway.

Cabrini L, Nobile L, Plumari VP, et al. Intraoperative prophylactic and therapeutic non-invasive ventilation: a systematic review. *Br J Anaesth*. 2014;112(4):638–647.

Carron M, Zarantonello F, Tellaroli P, et al. Perioperative noninvasive ventilation in obese patients: a qualitative review and meta-analysis. *Surg Obes Relat Dis*. 2016;12(3):681–691.

Difficult Airway Society. DAS guidelines for management of unanticipated difficult intubation in adults 2015. https://das.uk.com/guidelines/das_intubation_guidelines. Accessed December 31, 2018.

Ghebremichael S, Gumbert SD, Vanga N, et al. Evaluation of SuperNO_2VA® mask technology in a clinical setting: a pilot study. *Trends Anesth Crit Care*. 2017;16:54–61.

Tanoubi I, Drolet P, Donati F. Optimizing preoxygenation in adults. *Can J Anaesth*. 2009;56(6):449–466.

C.4. There are many new airway devices on the marketplace. Which of these devices have been particularly successful on the morbidly obese or OSA patient?

In the 2013 iteration of the DAA, the SGA was introduced, in place of the LMA (Teleflex, Limerick, PA), to reflect further developments in the marketplace. Inclusion of the SGA into the algorithm emphasized that being able to ventilate through a temporary airway (1) returns the patient to the elective branch of the algorithm because they are being ventilated and oxygenated, (2) may often be all that is required for patient management, and (3) provides a bridge for insertion of a definitive airway. As used in the algorithm, “SGA” should not be interpreted as endorsement of any particular manufacturer or product. In addition, since publication of the first two DAAs, many new and diversified SGAs have been developed. Other types of airway devices have been developed as well. At the present time, there are no large prospective, randomized studies comparing the newer devices on the MO or OSA subject, and the choice of device on a given patient may be driven by the clinician. The

skill set of the clinician still appears to be the most relevant factor until the literature provides more guidance.

Several noteworthy advances in airway management devices have occurred. The first is the advent of affordable, high-quality video laryngoscopes (VL), mentioned in the 2013 DAA. Particularly promising of these for the MO/OSA patient appears to be the McGrath® MAC VL (Ambu, Ballerup, Denmark) and the C-MAC® (Karl Storz Endoskope, Tuttlingen, Germany). The McGrath® is totally portable, unchanneled, low profile (e.g., TMJ dysfunction), and both a DL, in which the operator looks in the mouth, or indirect laryngoscopy (IDL), in which the operator looks on the screen. It may therefore be referred to as a DL/IDL device. Complementary metal oxide semiconductor (CMOS) technology, similar to a cell phone camera, ensures high-quality optical resolution. Originally intended as a routine DL replacement, it may well be the first airway device capable of replacing DL. The C-MAC® (Karl Storz Endoskope, Tuttlingen, Germany) is also an unchanneled, DL/VL, CMOS device. Attached to a semiportable electronic module, and possessing the highest quality optical resolution, it is a true difficult airway device and may also be connected to a fiberoptic scope. Single-use or reusable blades come in different sizes; most MO/OSA patients may be intubated with either the no. 3 or the D (Doerges) blades. The D-blade is particularly suited to patients with increased neck circumference, who are prone to lateral pharyngeal collapse. The electronic module comes either mounted on an intravenous pole, freestanding, or totally portable (the C-MAC Pocket Monitor®). Digital photographs or video clips of a C-MAC® intubation may be taken by the laryngoscopist without advance preparation and uploaded to a memory card. The C-MAC® electronic module may be used for flexible, fiberoptic, and rigid (Storz Bonfils®; Karl Storz SE & Co. KG, Tuttlingen, Germany) or articulating (Videostylet®;

Karl Storz SE & Co. KG, Tuttlingen, Germany) scopes; in addition, a C-HUB adaptor serves as a CMOS-digital convertor for either a fiberoptic intubating tower or the surgeon's operative tower. Other unchanneled VL devices which have been used for the MO/OSA patient population include the GlideScope® Videolaryngoscope (GVL) suite of products. Most of the GVL products are IDL devices. Although glottic visualization is frequently successful with the GVL, intubation may be problematic, and right palatopharyngeal arch perforation has been reported secondary to blind insertion of the tracheal tube from the back of the pharynx to resurfacing within the camera's visual field at the laryngeal inlet. This complication is more likely to occur when lateral pharyngeal wall crowding occurs, as in MO with jowls, or severe OSA.

The second advance in airway management is the development of a new class of airway devices: the channeled, disposable optical laryngoscope. The Airtraq® (AT) (Prodol Systems, Viscaya, Spain) and the King Vision® (KV) (Ambu, Ballerup, Denmark) are in this category. These devices have been very successful in the MO/OSA patient. Advantages include portability, being able to intubate in unusual positions (such as semi-Fowler position or "face-to-face"), or with limited access. There is a high retention success rate for the novice or infrequent practitioner, and being an excellent conduit for FOB. Intubating is accomplished in a neutral neck position with little mouth opening, so TMJ limitation and cervical spinal pathology are indications. The KV has technical advantages over the AT. Both the KV and the AT are channeled devices, although they have different operating profiles. The advantages of KV include totally portable organic light-emitting diode (OLED) display (similar to the GVL), needing no special charger (three AAA batteries provide 1 hour of light), improved channel with J-curve sliding off tracheal tube easily, guiding channel with loaded

tracheal tube serving as an ideal fiberoptic ramp, absence of distal “tooth” at end of channel facilitating removal of tracheal tube, distal light and optical inlet with “fish-eye” lens with antifog lens, and wide angle of aperture. However, patients with a short jaw or TMJ dysfunction will benefit from the more compact profile of the original AT, an optical scope similar to a flashlight with two mirrors.

The third advance in airway management is the development of better airway “bridges” and short-term ventilatory support devices. The LMA Fastrach® (LMA-FT), or intubating LMA® and the LMA EVO® (Teleflex Medical, Research Triangle Park, NC; LMA, North America, San Diego, CA), provides a method of oxygenating and ventilating while obtaining a definitive airway. The I-Gel® (Intersurgical Complete Respiratory Systems, Berkshire, United Kingdom) provides an uncuffed perilaryngeal airway with a gastric decompression lumen. The LMA Supreme® (Teleflex Medical, Research Triangle Park, NC; LMA, North America, San Diego, CA) is an SGA salvage device with a gastric decompression port that incorporates features of the LMA Unique®, ProSeal®, and LMA-FT. In practice, these “bridges” are not utilized as often as they were before because the aforementioned devices (VL, channeled airway devices) rarely fail. Other than routine indications, they are useful for either airway salvage or as conduits for fiberoptic intubation. An airway salvage that has had success out-of-hospital by first responders and military medics, particularly in the event of gastrointestinal bleeding or for the difficult to manage airway (e.g., OSA), is the King Laryngo-Tracheal-Suction-Disposable® (King LTS-D®) (Ambu, Ballerup, Denmark).

The final advance in airway management is the development of high-quality, single-use metal laryngoscope blades, which appear to have superior success rates compared with their

reusable counterparts (both in terms of blade and handles and plastic) when used during the induction of anesthesia, due to a predictable degree of brightness.

For the MO/OSA patient with a challenging airway, FOB remains the gold standard. FOB has substantial limitations, however, such as limited availability, a long learning curve, a low retention rate, equipment fragility, longer setup time, longer intubation time, and few absolute indications (mostly lower airway pathology). As the advanced airway management devices improve, and clinician experience grows, the need for FOB should continue to decline.

Amour J, Le Manach YL, Borel M, et al. Comparison of single-use and reusable metal laryngoscope blades for orotracheal intubation during rapid sequence induction of anesthesia: a multicenter cluster randomized study. *Anesthesiology*. 2010;112(2):325–332.

Aziz MF, Dillman D, Fu R, et al. Comparative effectiveness of the C-MAC video laryngoscope versus direct laryngoscopy in the setting of the predicted difficult airway. *Anesthesiology*. 2012;116:629–636.

Buléon C, Parienti JJ, Lesage A, et al. Comparison of plastic and metallic single-use and metallic reusable laryngoscope blades: a randomised controlled trial. *Eur J Anaesthesiol*. 2013;30(4):163–169.

Hoshijima H, Denawa Y, Tominaga A, et al. Videolaryngoscope versus Macintosh laryngoscope for tracheal intubation in adults with obesity: a systematic review and meta-analysis. *J Clin Anesth*. 2018;44:69–75.

C.5. How would you induce anesthesia? Describe the intubation technique.

The OR should be set up with appropriate alternative noninvasive and invasive airway devices.

On arrival in the OR, the patient is positioned on the OR table in a ramp position (Troop Elevation Pillow®; Sharn Anesthesia Inc, Tampa, FL), placed on monitors, and administered an F_{IO_2} of 100% nasal CPAP with the SuperNO_2VA® (Vyaire Medical, Mettawa, IL) for 3 to 5 minutes at a fresh gas flow (FGF) rate of 15 L per minute, in both the mask and the auxiliary oxygen port,

attached to the anesthesia circuit. General anesthesia is gradually induced with propofol 2 mg per kg TBW, after setting the anesthesia ventilator to pressure control, and assuring the ability to positive pressure ventilate. At this point in the induction, intraoperative spirometry (e.g., flow–volume loop) is helpful; look for an open loop without signs of obstruction or restriction. Failure to obtain a capnogram usually indicates upper airway obstruction requiring jaw thrust or an oral airway. The goal is to have an expired V_T of 3 to 5 mL per kg LBW while maximizing FRC and arterial oxygen and pulmonary oxygen reserve in preparation for induction of general anesthesia. Once it has been ascertained that mask ventilation is feasible, nondepolarizing neuromuscular blockade is induced.

This patient was considered to be a moderately DI and, possibly, difficult mask ventilation. A videolaryngoscope such as channeled King Vision Laryngoscope® (KVL_C) (Ambu, Ballerup, Denmark) was used for intubation. A C-MAC® (Karl Storz Endoskope, Tuttlingen, Germany) electronic module coupled with the Doerges®, or D-blade, and FOB was available as a backup. If needed, the FOB could either be used to "peer and steer" the channeled tracheal tube or, more rarely, to cannulate the upper trachea and advance the tracheal tube in a Seldinger maneuver over the KVL_C blade.

If the physical examination and past anesthetic record demonstrated easy orotracheal intubation or the patient was at high risk of aspiration, a rapid sequence intubation could be contemplated using propofol (2 mg per kg TBW) with succinylcholine (1 to 1.5 mg per kg TBW), with the patient positioned on a ramp. This was not the case with our patient.

Chau EHL, Mokhlesi B, Chung F. Obesity hypoventilation syndrome and anesthesia. *Sleep Med Clin*. 2013;8(1):135–147.

Isono S. Obstructive sleep apnea of obese adults: pathophysiology and

perioperative airway management. *Anesthesiology*. 2009;110:908–921.

C.6. How would you maintain general anesthesia? What agents would you choose? How would you prepare for emergence?

The ideal maintenance anesthetic for morbidly obese patients undergoing laparoscopic surgical procedures is a matter of some discussion; there is support in the literature for a technique comprising insoluble anesthetic gases resistant to metabolic degradation and without lipid depot compartmentalization, combined with rapid return of airway reflexes, plus intravenous agents that are either hydrophilic, spontaneously degrade in vivo, or are ultrashort-acting. For the maintenance phase of general anesthesia, both inhalation and total intravenous techniques have been used successfully.

Of the potent inhalation agents, desflurane has several advantages; it is insoluble, has a faster wake-up, a faster return of airway reflexes, and a decreased amount of hepatic metabolism. Obesity increases the biotransformation of the inhalation anesthetics, resulting in increased serum toxic products of metabolism. Because of the frequent presence of coexisting liver dysfunction in the morbidly obese (75% have hepatic steatosis and 25% have severe hepatic dysfunction) and the absence of a clear correlation between LFTs and hepatic dysfunction, it would seem logical to use the agent with the lowest percentage of hepatometabolism, desflurane (0.02%), compared with isoflurane (0.2%) and sevoflurane (2% to 3%). An agent with a low blood–gas solubility coefficient also appears better because there will be a smaller body reservoir available for metabolism, and a faster time to steady state at the target organ, the brain. Of the inhaled agents, desflurane has the fastest wake-up, followed by sevoflurane and then by isoflurane. Desflurane also has the fastest return of airway reflexes,

followed by sevoflurane. All of the inhalational anesthetics will accumulate in the lipid compartment, creating a two-compartment model and lengthening the emergence. All of the inhalation agents, however, have been used successfully.

N_2O, a weak inhalation anesthetic, has a low blood–gas solubility coefficient (0.46) but is not recommended for maintenance use because it causes intestinal inflation; is emetogenic; and is contraindicated in the presence of severe pulmonary hypertension, a condition more common in the MO. Short duration use of N_2O, particularly during the surgical closure, facilitates offset of relatively lipid-soluble agents.

Of the intravenous anesthetics, remifentanil is an attractive choice because of its rapid onset, consistent profile, and rapid offset. Although it is lipophilic, it has a half-life of 5 minutes and therefore does not compartmentalize in the lipid compartment. The dose of remifentanil is therefore calculated by using LBW. It is dosed by infusion, in the range of 0.05 to 0.2 μg/kg/min LBW. The lipophilic opioids, fentanyl and sufentanil, that are dosed by LBW and may cause delayed respiratory depression in the high-risk patient, especially OSAHS, are less than ideal in larger doses. They may, however, be used in reasonable doses (fentanyl up to 5 μg per kg LBW). Dexmedetomidine, a centrally acting α_2-agonist, has also been used successfully in these cases. It decreases anesthetic and opioid requirements and may continue through the emergence phase and extubation because it only marginally raises the CO_2 apneic threshold.

For our patient, an inhalation technique was chosen with desflurane, and once a deep level had been reached (minimum alveolar concentration [MAC] of 1.2), low flow (FGF of 0.65 L per minute) was established. For this patient, we assessed anesthetic depth by end-tidal desflurane concentration,

hemodynamics, and a processed EEG (BIS®, Medtronic, Minneapolis, MN). Blood pressure was supported and maintained at the patient's baseline range with a phenylephrine infusion because operative position is steep reverse Trendelenburg. Roughly an hour from the end of the procedure, desflurane was discontinued, hydromorphone is administered, FGF is increased, and switched to oxygen/N_2O at 50%, and the BIS is maintained at acceptable levels (under 50) with small boluses of propofol for the remainder of the case. The ventilator was switched to a patient-assisted modality.

Recently, ENERGY, or ERAS for bariatric surgery (see section B.4), has changed both the surgical and anesthetic experience. More than half of the cases are sleeve gastrectomies (57% of 233,000 in 2017), a simpler surgical procedure with no anastomoses lasting about 2 to 3 hours. In consequence, anesthetic requirements are decreased, particularly for opioids. This patient received fentanyl 200 mcg, with a pain score of 0/10 on arrival in the PACU. TAP blocks decrease postoperative analgesic requirements, negating the need for postoperative opioid infusions (e.g., IV-PCA). Lighter anesthetics, consisting of less opioid, desflurane, and muscle relaxants, translate into less PONV and less opioid-induced nausea and vomiting (OINV) as well as a more awake patient who is less likely to require a NIPPV modality.

Alvarez A, Brodsky JB, Lemmens HJM, et al, eds. *Morbid Obesity: Peri-operative Management*. 2nd ed. Cambridge, United Kingdom: Cambridge University Press; 2010:100–109.

Awad S, Carter S, Purkayastha S, et al. Enhanced recovery after bariatric surgery (ERABS): clinical outcomes from a tertiary referral bariatric centre. *Obes Surg*. 2014;24(5):753–758.

McKay RE, Large MJ, Balea MC, et al. Airway reflexes return more rapidly after desflurane anesthesia than after sevoflurane anesthesia. *Anesth Analg*. 2005;100(3):697–700.

Thorell A, MacCormick AD, Awad S, et al. Guidelines for perioperative care

in bariatric surgery: Enhanced Recovery After Surgery (ERAS) Society recommendations. *World J Surg*. 2016;40(9):2065–2083.

Tufanogullari B, White PF, Peixoto MP, et al. Dexmedetomidine infusion during laparoscopic bariatric surgery: the effect on recovery outcome variables. *Anesth Analg*. 2008;106:1741–1748.

C.7. Which muscle relaxants would you use?

For intubation, a nondepolarizing muscle relaxant (NDMR) would be used. Patients presenting for bariatric surgery are generally on a liquid diet for a couple of days. The rate of gastric emptying is identical to that of the nonobese subjects, although MO patients have a larger gastric pouch. Cisatracurium has a predictable dose-response curve and no prolongation of recovery due to organ-independent recovery, or Hoffman elimination; dosage is by IBW. Cisatracurium is, however, relatively expensive. For this reason, rocuronium and vecuronium are more commonly used; both are dosed by IBW.

For the occasional subject requiring rapid sequence induction, succinylcholine or rocuronium are acceptable choices. Succinylcholine is dosed by TBW because the plasma cholinesterase activity increases in proportion to the BMI. When an awake technique is chosen for securing the airway, an NDMR may be administered, once tracheal intubation has been confirmed.

Dense muscle relaxation is required for laparoscopic bariatric surgical procedures to facilitate ventilation, to maintain adequate intraperitoneal space for visualization and manipulation of the surgical instruments, and to permit the introduction of surgical instruments and the removal of excised tissues.

Intraoperative contracture of the abdominal musculature, due to inadequate muscle relaxants, may increase intra-abdominal pressure during PNP, driving CO_2 out from the inflated abdominal cavity through the trocar sites. Adequacy of neuromuscular blockade is assessed by the anesthesiologist, by

following both peripheral nerve stimulation data and the inflation pressures necessary for excellent surgical conditions.

A peripheral nerve stimulator should be used to monitor the extent of relaxation and to avoid underdosing or overdosing. Extubation should only occur after documentation of full baseline train-of-four (T_4/T_1 >0.9) and return of extubation criteria. Reversal agents should be given in appropriate doses. Sugammadex, a modified γ-cyclodextrin, which was developed to reverse muscle relaxation by amino-steroid NDMRs, has had a huge impact on bariatric surgery, allowing dense anterior abdominal wall muscle relaxation until the end of surgery. It is dosed by TBW.

Alvarez A, Brodsky JB, Lemmens HJM, et al, eds. *Morbid Obesity: Peri-operative Management*. 2nd ed. Cambridge, United Kingdom: Cambridge University Press; 2010:107–108.

Lemmens HJM, Ingrande J. Effects of obesity on anesthetic agents. https://ispcop.net/index.php/14-publications/education/19-effects-of-obesity-on-anesthetic-agents. Accessed December 31, 2018.

Monk TG, Rietbergen H, Woo T, et al. Use of sugammadex in patients with obesity: a pooled analysis. *Am J Ther*. 2017;24(5):e507–e516.

C.8. Is postoperative pain severe after bariatric surgery? What are the pain generators? What is the role of regional anesthesia to decrease opioid requirements for bariatric surgery? What are the advantages and disadvantages of regional anesthesia? What are some of the newer techniques available?

Today, the majority of bariatric surgical procedures are performed laparoscopically. Postoperative pain is not usually severe and is of short duration, typically a few days.

Laparoscopic bariatric surgical procedures cause pain due to surgical portholes (somatic pain), from PNP (carbonic acid deposited on the parietal peritoneum) and from mild tugging on

the gastroesophageal junction (referred visceral pain). Porthole pain may be treated by intravenous opioids, infiltration of local anesthetics, and regional anesthesia. The other pain generators, described as a colitis-like cramping and a retrosternal "sticking" sensation, are milder and respond to intravenous NSAIDs.

Several regional anesthetic techniques may be used in bariatric surgery to decrease opioid requirements. Neuraxial techniques, used in the past, include thoracic epidurals for patient-controlled epidural analgesia (PCEA), the best studied of these, as well as continuous spinal anesthesia and analgesia (CSAA), and intrathecal opioids. Although they have a good side effect profile and reduce general anesthetic requirements, their use has been restricted to the rare open procedure. Until recently, IV-PCA was the standard of care. With the overwhelming majority of bariatric surgery being performed laparoscopically, analgesic postoperative analgesic requirements are decreased, and the emphasis is on getting patients out of bed, shortening hospital stay, and returning to baseline functional status. In consequence, neuraxial analgesic techniques are not currently used.

Techniques adopted from multimodal perioperative analgesia (MMPA) use nonopioid receptors (e.g., *N*-methyl-D-aspartate receptor antagonists [NMDA]) instead of, and synergistically with, the standard anesthetic pharmacopoeia. Nonopioid analgesia (NOA) has been used with varying agents such as dexmedetomidine, NSAIDs (e.g., ketorolac,) clonidine, lidocaine, ketamine infusion, and magnesium sulfate infusion in an attempt to decrease side effect profile and speed recovery.

The introduction of ENERGY (see section B.4) has changed the analgesic regimen for bariatric surgery. In the ENERGY protocol: *premedication* consists of a "cocktail" of oral nonopioid analgesics (e.g., COX-2 inhibitor, COX-3 inhibitor, gabapentinoid, an anticonvulsant, and a substance P/neurokinin

1 receptor antagonist); *intraoperative analgesics* consist of judicious opioids, with either infusions of intravenous lidocaine or the TAP block. In this technique, local anesthetics are deposited between the internal oblique and transversus abdominis muscles, blocking the anterior rami of spinal nerves T7–L1, which innervate the anterolateral abdominal wall. The TAP block has been hugely successful and has replaced other regional techniques. It is performed bilaterally with ultrasound guidance percutaneously by anesthesiologists and at the end of surgery with laparoscopic, or robotic, guidance by surgeons. Both techniques have been used successfully. Whether the TAP block is superior to surgical porthole infiltration is controversial. Our patient received surgical porthole infiltration. *Postoperative analgesics*, for both the PACU and the floor consist of oral acetaminophen (650-mg or a 975-mg tablet), an oxycodone (5-mg or 10-mg immediate release tablet), with dose-dose parenteral opioids (hydromorphone 0.2 mg) for breakthrough pain.

Brodsky JB, Mariano ER. Regional anaesthesia in the obese patient: lost landmarks and evolving ultrasound guidance. *Best Pract Res Clin Anaesthesiol*. 2011;25:61–72.

Leykin Y, Brodsky JB, eds. *Controversies in the Anesthetic Management of the Obese Surgical Patient*. Milan, Italy: Springer-Verlag Italia; 2013:227–236.

Jakobsson J, Wickerts L, Forsberg S, et al. Transversus abdominal plane (TAP) block for postoperative pain management: a review. Version 1. *F1000Res*. 2015;4:F1000 Faculty Rev-1359. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4754005/. Accessed December 31, 2018.

Ultrasound Guided Regional Anesthesia. Transversus abdominal plane (TAP) block. http://www.usra.ca/regional-anesthesia/specific-blocks/trunk/tapblocks.php. Accessed December 31, 2018.

C.9. What is the pathophysiology of pneumoperitoneum (PNP)? What is the effect on the cardiopulmonary

system? How does it change perioperative care? What are the optimal ventilator strategies for morbidly obese patients undergoing bariatric surgery?

Currently, the vast majority of bariatric surgical procedures are performed laparoscopically and now robotically. Benefits of laparoscopy include much smaller surgical incisions, decreased postoperative pain requirements, shorter hospital stay, and faster recovery time to baseline level of activity. CO_2 is the universally accepted gas choice for abdominal insufflation during laparoscopy. CO_2 has documented advantages, including short half-life, due to high tissue diffusion across all tissue beds and less flammability and morbidity, compared with other agents trialed (oxygen, N_2O).

PNP with CO_2, however, alters physiology and complicates intraoperative anesthetic management. Altered physiology due to PNP is both primary (due to CO_2 absorption) and secondary (due to increased intra-abdominal pressure). Primary physiologic changes arise from acidification of tissues from CO_2 absorption (approximately 30 to 42 mL per minute), which increases ventilator requirements (approximately 30%).

Cerebral effects arise from changes in cerebral vasoregulation due to hypercarbia: increased intracranial pressure from increased intrathoracic pressure and cerebral vasodilation, decreased cerebral oxygen saturation, and initiation of a hormonal cascade, with catecholamine and vasopressin release.

Cardiovascular effects arise from CO_2, which mildly depresses myocardial contractility and sensitizes myocardium to the arrhythmogenic effects of catecholamines. Most of the pathophysiologic changes occur as a result of increased intra-abdominal pressure, which decreases venous return, decreasing

cardiac output and blood pressure. Other *cardiac effects* are those typical of increased sympathetic output from hypercarbia, although bradycardia may result from initial peritoneal insufflation.

Pulmonary effects are due to cephalad shift of the diaphragm, decreased FRC, increased physiologic dead space, greater ventilation/perfusion mismatch, decreased pulmonary compliance, and increased airway pressures especially peak airway pressure.

Renal effects are due to decreased renal perfusion; decreased urine output; and increased release of antidiuretic hormone, plasma renin, and aldosterone levels.

Hepatic effects are due to decreased portal venous flow, which may lead to hepatic hypoperfusion, acute hepatocellular injury, and increased transaminase levels. Increased intra-abdominal pressure causes decreased venous drainage of the abdominal viscera and the lower extremities, which may result in deep venous thrombosis.

Most of the intraoperative changes caused by PNP are well tolerated, provided that the insufflation pressure is maintained at the lowest acceptable level, approximately an intra-abdominal pressure of less than 20 mmHg, an intraoperative recruitment maneuver is provided when indicated, and the following precautions are taken: loading of intravenous fluids (typically 500 to 1,000 mL), use of sequential compression devices, optimal ventilator settings as described in the following text, and intraoperative spirometry to monitor flow– and pressure–volume loops, and plateau airway pressure. In comparison with volume control ventilation, pressure control ventilation appears to improve oxygenation, produce lower airway pressures, greater dynamic compliance, and better preserve ventilation/perfusion matching.

- *Management of ventilation in MO patients*

- CPAP during induction
- F_{IO_2} <0.8
- Recruitment maneuver after induction, then periodically
- Pressure control-volume guarantee (PC-VG)
- V_T = 6 to 10 mL per kg IBW
- PEEP 10 to 12 cm H_2O
- Inspiration : expiration (I:E) = 1:1 longer inspiratory time to minimize atelectasis and improve gas exchange
- Inspiratory pressure <30 cm H_2O
- CPAP or BIPAP after extubation, if used preoperative, or deemed high-risk (as our patient)

Hodgson LE, Murphy PB, Hart N. Respiratory management of the obese patient undergoing surgery. *J Thorac Dis*. 2015;7(5):943–952.

Jaju R, Jaju PB, Dubey M, et al. Comparison of volume controlled ventilation and pressure controlled ventilation in patients undergoing robot-assisted pelvic surgeries: an open-label trial. *Indian J Anaesth*. 2017;61(1):17–23.

Sen O, Umutoglu T, Aydın N, et al. Effects of pressure-controlled and volume-controlled ventilation on respiratory mechanics and systemic stress response during laparoscopic cholecystectomy. *SpringerPlus*. 2016;5:298.

Wang JP, Wang HB, Liu YL, et al. Comparison of pressure- and volume-controlled ventilation in laparoscopic surgery: a meta-analysis of randomized controlled trial. *Clin Invest Med*. 2015;38(3):E119–E141.

C.10. What are the devices that anesthesiologists place in the upper gastrointestinal canal during laparoscopic bariatric surgery? Are there risks associated with placement and management of these devices?

Various devices have been placed in the upper gastrointestinal canal during laparoscopic bariatric surgery. All of these devices are single use and are placed orally by the anesthesiologist. The surgeon laparoscopically visualizes transit of the device through the gastrointestinal tract by gut distension and may help guide passage. *Orogastric tubes* are used both to decompress the stomach at the beginning of surgery and for “a leak test” after

completion of the anastomosis, in which a vital dye, such as methylene blue, is injected, the stomach is inflated, and lack of "leak" documented. The amount of vital dye is documented and serves as a rough estimate of neogastric pouch size. Both *bougies* or *calibration tubes* serve as templates to delineate the feeding channel, identify landmarks for the anastomosis, and choose the staple line. Bougies come as either *graduated-tip*, which are easier to insert, or *blunt-tip*. Gastroesophageal *anvils*, OrVil® (Medtronic, Minneapolis, MN), are used to create the gastrojejunostomy anastomosis in RYGB.

The ViSiGi 3D® (Boehringer, Ingelheim, Germany) can perform all of these functions and is becoming the preferred device for the laparoscopic sleeve gastrectomy. Both the anesthesiologist who places these devices and the surgeon are responsible for monitoring proper function and lack of trauma at removal. When the anesthesiologist is unable to place the indicated device, there are three options: The surgeon may try, gastroscopy may be attempted, or surgery may be converted to an open procedure.

Some of the pooled specific procedural risks with these devices are as follows: improper disinfection, incidence 1 per 100,000 cases; accidental stapling of tubes, incidence 1 per 132 cases; esophageal perforation, incidence 1 per 810 cases. Single-use devices can eliminate the first of these. The OrVil® is composed of a curved metal section joined to a modified orogastric tube; as a fairly sharp device, it is easy to understand how it may traumatize the esophagus.

Clearly, placement of these devices is a crucial portion of the anesthetic and surgical risk. Regardless of which device is chosen, the attending anesthesiologist should be present at the time of placement and document his or her findings. Orogastric tubes and esophageal temperature probes are strictly prohibited for patient monitoring during bariatric surgery; they may be

stapled and left as foreign bodies, resulting in major morbidity or death.

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C.11. When will you extubate this patient? Describe weight-based extubation criteria.

Bariatric surgery and anesthesia experience has evolved to the point where postoperative ventilatory support is rarely necessary, due to changing surgical technique (higher percentage of sleeve gastrectomies), with a simpler, shorter surgical time, and to the advent of ENERGY (see section B.4). Patients treated preoperatively with NIPPV should be returned to their therapy. Patients with an unfavorable OSA questionnaire response, STOP-BANG score of 4 or more (see section B.1) should be given consideration to NIPPV therapy. Our patient received BIPAP +12/5 cm H_2O at 40% oxygen via a full-face mask.

The vast majority of patients, however, are extubated in the OR at the conclusion of surgery as soon as the following extubation criteria are met:

- Intact neurologic status, fully awake and alert, with head lift >5 seconds
- Hemodynamic stability
- Normothermia, above 36°C
- Full reversal of neuromuscular blocking agents confirmed

with train-of-four (T_4/T_1 >0.9)

- Respiratory rate (breaths per minute) >10 and <30
- Baseline peripheral oxygenation, as judged by pulse oximeter (Spo_2 >95% on Fio_2 of 0.4)
- Acceptable blood–gas results, if available (Fio_2 of 0.4; pH, 7.35 to 7.45; Pao_2, >80 mmHg; $Paco_2$, <50 mmHg)
- Acceptable respiratory mechanics: negative inspiratory force (NIF) >25 to 30 cm H_2O; VC >10 mL per kg IBW; V_T >5 mL per kg IBW
- Acceptable pain control
- No demonstrated or suspected laboratory abnormalities

Patients with OSAHS, OHS, and PS have higher incidence of postoperative respiratory dysfunction. They require special attention during tracheal extubation, and occasionally, warrant a monitored bed for observation.

Extubation criteria should be used systematically in obese patients; in all cases, an attending anesthesiologist with advanced airway skills must be in attendance, in case tracheal reintubation becomes necessary, and the surgeon must be immediately available. Patients with documented difficult airway should be extubated per protocol of the individual institution. A significant percentage of settled malpractice cases in the ASA Closed Claims Database (67% upon induction, 15% during surgery, 12% at extubation, and 5% during recovery) occurred at the end of surgery. Death and brain damage decreased in the time periods of 1985–1992 and 1993–1999 during induction but not during extubation and recovery.

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Neligan PJ, Malhotra G, Fraser M, et al. Noninvasive ventilation immediately after extubation improves lung function in morbidly obese patients with

obstructive sleep apnea undergoing laparoscopic bariatric surgery. *Anesth Analg*. 2010;110:1360–1365.

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C.12. What is apneic oxygenation?

Draper and Whitehead conducted the pioneer study on apneic oxygenation in 1944. Apneic oxygenation (formerly known as diffusion respiration) is actually caused by mass movement oxygenation. When the lungs are completely denitrogenized with oxygen and the airway is connected to an oxygen source, continuous oxygenation takes place by mass movement. Normally, every minute, 250 mL of oxygen is removed from the alveoli for metabolism, and 200 mL of CO_2 is produced and eliminated from the lungs. When a person is apneic, only 10% of CO_2 accumulates in the alveoli, and 90% of CO_2 stays in the blood as bicarbonate. Consequently, 250 mL of oxygen is removed from the lungs and 20 mL of CO_2 accumulates in the lungs, creating a 230-mL vacuum effect and sucking in oxygen. CO_2 tension continues to rise because no elimination occurs during apnea. The total pressure in the alveoli is constant, so the decrease in P_{O_2} equals the rise in P_{CO_2}, ranging from 3 to 6 mmHg per minute. If the patient had been breathing 100% oxygen before respiratory arrest, the starting alveolar P_{O_2} would be about 650 mmHg, and therefore, the patient could theoretically maintain Pa_{O_2} above 100 mmHg for about 100 minutes of apnea provided that the airway remained clear and connected to 100% oxygen. However, patients will die of severe

respiratory acidosis (pH <6.80) before hypoxemia occurs. Moreover, as seen in suffocation, gross hypoxia supervenes after about 90 seconds if apnea with airway occlusion follows air breathing at the FRC. When the airway is patent and the ambient gas is air, gross hypoxia supervenes after about 2 minutes of apnea, as seen during intubation without pre-O_2. However, if the patient is preoxygenated for 3 minutes, gross hypoxia will not occur until 6 minutes of apnea for normal-weight patients and until about 3 minutes of apnea for morbidly obese patients. Apneic oxygenation is an older technique that is not recommended for obese patients. Aside from hypoxia and hypercarbia, it may lead to atelectasis or derecruitment of West Zone 3.

A much more useful maneuver in severely obese patients is to utilize 100% oxygen and PEEP, during both induction and emergence from general anesthesia. We did this with the SuperNO_2VA®, both on induction and on extubation.

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Gander S, Frascarolo P, Suter M, et al. Positive end-expiratory pressure during induction of general anesthesia increases duration of nonhypoxic apnea in morbidly obese patients. *Anesth Analg*. 2005;100:580–584.

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Semler MW, Janz DR, Lentz RJ, et al. Randomized trial of apneic oxygenation during endotracheal intubation of the critically ill. *Am J Respir Crit Care Med*. 2016;193(3):273–280.

C.13. What is diffusion hypoxia (DH)? How do you prevent

it?

Fink and colleagues in 1954 first reported DH during recovery from N_2O–oxygen anesthesia. A mild degree of hypoxia can develop for more than 10 minutes when N_2O–oxygen anesthesia is concluded and the patient is allowed to breathe room air. The arterial oxygen saturation can fall 5% to 10% and often reaches values less than 90% (Pa_{O_2} <60 mmHg). This occurs at the times when nitrous oxide is eliminated rapidly through the lungs. N_2O is 35 times more soluble in blood than nitrogen. Therefore, the amount of nitrous oxide diffused from blood to alveoli is much more than the amount of nitrogen diffused from alveoli to blood. Hence, alveolar oxygen is diluted by nitrous oxide.

DH, called the Fink effect, is explained by movement down a concentration gradient: Recovery from a high concentration of nitrous oxide leads to high partial pressure in the alveolus, which dilutes both the partial pressure of oxygen and CO_2 and may lead to hypoxia. Hypoxia is more likely in the presence of hypoventilation (e.g., residual anesthetics). DH may be prevented by simply increasing the inspired oxygen concentration prior to emergence, or by using, at most, a 50:50 mixture of N_2O:oxygen.

DH should not be allowed to occur in obese patients. There is no room for deep extubations in the MO/OSA patient. Patients should be fully awake, with baseline respiratory function. All anesthetics and analgesics should be stopped. Many of the newer anesthesia ventilators allow the use of pressure support ventilation during the emergence phase, which minimizes atelectasis. One hundred percent oxygen prior to, and during, extubation followed by a tight-fitting face mask with pressure support aids the patient in reestablishing ventilatory function, and assists in removal of trace anesthetic gas, until the patient is

fully recovered.

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D. Postoperative Management

D.1. What are the early postoperative complications of bariatric surgical procedures?

All-cause mortality within 30 days of bariatric surgery is rare (0.3%), with the majority of causes being of nonanesthetic origin: Most common cause of death was sepsis (33% of deaths), followed by cardiac causes (28%) and pulmonary embolism (17%). Early surgical complications include anastomotic closure with bowel obstruction, anastomotic or staple line leak, intestinal obstruction, gastrointestinal bleeding, and wound infection. The most commonly quoted source of statistics is the LABS, a 10-center observational cohort study of bariatric surgical outcomes, consisting of 6,118 bariatric surgical patients from March 2005 to April 2009, at academic centers of excellence. Obesity cardiomyopathy was highlighted in this study, predisposing to congestive heart failure and arrhythmias and emphasizing the need to perform risk assessment on all bariatric candidates. The LABS revealed the relationship between surgical volume and adverse outcome, at least for the RYGB.

Anesthetic early postoperative complications are mostly

related to the pulmonary and cardiovascular systems. Postanesthetic hypoxemia is more common in the MO patient, with or without the presence of OSA, despite supplemental oxygen therapy. This may be due to atelectasis, or reversion to a restrictive breathing pattern, with increased use of accessory muscles, as well as decreased FRC from pain ("splinting"), residual PNP, parietal peritoneal irritation from carbonic acid, air in the stomach, as well as pain. Other potential early postoperative complications include respiratory depression from residual anesthetic or muscle relaxant, early ventilatory failure with need for reintubation, positional ventilatory collapse, hemodynamic instability, PONV, positional injury, and venous thromboembolism. PONV, the single most common postoperative patient complaint after bariatric surgery, is distinguished from OINV, which is more severe and more difficult to treat. Bariatric surgical procedures are highly emetogenic and frequently require prophylaxis with multiple agents. They are foregut surgical operations and interrupt peristalsis and the gastroesophageal antireflux mechanism. Severe, resistant, or recurrent PONV may be due to anastomotic kink, leak, or iatrogenic esophageal injury; the surgical team should be called to examine the patient. In-hospital postoperative ventilatory insufficiency is always a risk; patients should be triaged by the perioperative team for postsurgical care. Very high-risk patients include those with severe cardiopulmonary disease, or severe OSA, by either STOP questionnaire, or who are noncompliant with NIPPV (CPAP or BIPAP). They should be triaged from the PACU to a step-down unit postoperatively or rarely to an intensive care unit. These patients should be transported wide-awake, whenever possible, and with oxygen (nasal cannula or face mask), as well as a NIPPV device if needed. The SuperNO_2VA® nasal CPAP device was used to transport our patient to the PACU. Our

patient was placed on NIPPV and later transferred.

At any given weight, the perioperative risk is greater for central obesity than for peripheral obesity, and for patients with preexisting severe comorbidity, especially OSA. All OSA patients should be given OSA precautions. The major perioperative risk of death correlates statistically with BMI, preexisting hypertension, pulmonary embolus, and anastomotic leak. Etiology is surgical, anesthetic, mixed, or undetermined.

Although perhaps difficult to objectively measure, it may well be that blinded peer review of surgical skill is the most important determinant of bariatric surgical outcome.

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D.2. What are the late complications of bariatric surgical procedures?

Late (after 30 days) complications of bariatric surgical procedures are mostly surgical and may occur in up to 40%. Some of these complications are general, and some procedure-specific, occurring with more complex procedures possessing one or more anastomosis, such as the RYGB or the biliopancreatic diversion duodenal switch. Some of the general complications are ventral incision hernia, internal hernia, hiatus hernia, marginal ulcers, small bowel obstruction, cholelithiasis, and metabolic and nutritional derangements. Some of the

procedure-specific complications are gastric remnant distension, stomal stenosis, marginal ulcers, nephrolithiasis and renal failure, gastric remnant distension, short bowel syndrome, dumping syndrome, postoperative hypoglycemia, failure to lose weight, weight regain, internal (usually gastro-gastric) fistulas, and others.

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D.3. What is the effect of position on respiratory function in the obese patient?

In the supine position, intra-abdominal contents shift the diaphragm rostrally, resulting in diaphragmatic dysfunction, decreased functional residual reserve (FRC), airway closure, increase in venous admixture (Q_S/Q_T), decreased Pa_{O_2}, and, possibly, positional ventilatory collapse. The FRC, the body's oxygen reserve, decreases 30% in the supine position. Pre-O_2 is more effective in the semi-Fowler position (head up 30 to 45 degrees) than in the supine position in severely obese patients, both for preinduction of general anesthesia, and for eventual postoperative reintubation. Recovery should take place in this position as soon as these patients are hemodynamically stable. Other benefits of a semi-sitting position are decreased superior vena cava pressure and decreased incidence of positional

injuries, which are more common in the MO, especially ulnar neuropathy. Patients recovered in the semi-Fowler position who are in need of eventual emergent mask ventilation or tracheal reintubation present better conditions for the laryngoscopist. There is a higher incidence of tracheal tube misplacement in the morbidly obese; care should be taken when positioning intubated morbidly obese patients in a semi-Fowler position.

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Smetana G. Postoperative pulmonary complications: an update on risk assessment and reduction. *Cleve Clin J Med*. 2009;76(suppl 4):S60–S65.

D.4. How would you prevent postoperative atelectasis?

In the past, bariatric surgical procedures were often performed open, with an incidence of postoperative atelectasis of 45%. Approximately 90% are now performed laparoscopically, so the incidence would be expected to decline substantially.

Early ambulation, chest physical ambulation with incentive spirometry, and effective coughing are encouraged to improve respiratory function. Prolonged recumbency is avoided whenever possible because of its adverse effects on the $\dot{V}/\dot{Q}$ ratio and to minimize circulatory congestion of the recumbent lung. Careful titration of postoperative analgesics is emphasized to prevent splinting from pain and hypoventilation from excessive sedation.

A recruitment maneuver followed by PEEP before extubation does reduce atelectasis and improve oxygenation in morbidly obese patients.

Neligan PJ, Malhotra G, Fraser M, et al. Continuous positive airway pressure via the Boussignac system immediately after extubation improves lung function in morbidly obese patients with obstructive sleep apnea undergoing laparoscopic bariatric surgery. *Anesthesiology*. 2009;110(4):878–884.

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Zoremba M, Dette F, Gerlach L, et al. Short-term respiratory physical therapy treatment in the PACU and influence on postoperative lung function in obese adults. *Obes Surg*. 2009;19(10):1346–1354.

D.5. How long would you prescribe supplementary oxygen postoperatively?

The incidence of postanesthetic hypoxemia (Pa_{O_2} <60 mmHg) is increased from a baseline of 25% to 30% in the nonobese to 75% in the obese. For a routine case on an otherwise healthy patient with simple obesity, supplemental oxygen in the PACU is probably sufficient. In most MO patients with comorbidities, oxygen should be prescribed for 24 to 72 hours. The MO patient with severe OSAHS on CPAP or BIPAP will usually have continuation of his or her therapy overnight, be recovered in a semi-Fowler position (30 to 45 degrees), and should have individualized care in an appropriate setting with continuous pulse oximetry and respiratory monitoring. At the New York-Presbyterian Hospital, the majority of these patients are discharged to home on the second or third postsurgical day.

Leykin Y, Brodsky JB, eds. *Controversies in the Anesthetic Management of the Obese Surgical Patient*. Milan, Italy: Springer-Verlag Italia; 2013:241–253.

D.6. How would you control postoperative pain?

Until recently, postoperative analgesia was provided by PCA in more than 90% of bariatric surgical procedures. PCA has been shown to be safe and effective in the MO patient population. It has many advantages: PCA is simple to use, saves nursing time,

and involves minimal time delay between patient perception of pain and therapy. There is less splinting and derangement of PFTs. PCA also facilitates early ambulation and shortens hospital stay. Hydromorphone is the gold standard. Morphine, once commonly used, has fallen out of favor due to histamine release, higher rates of nausea, and more interpatient variability. Dose regimens need to be individualized according to pain control and side effect profile. There have been rare cases of respiratory complications in the MO-OSAHS patient, so extra vigilance is needed in this group. PCA dosages for the MO in the opioid naive, based on IBW, are as follows:

- Morphine sulfate 20 μg per kg IBW
- Hydromorphone 4 to 5 μg per kg IBW
- Fentanyl 1 μg per kg IBW
- Methadone 20 μg per kg IBW

All settings are every 10 minutes, without continuous rate, at 80% of the calculated maximum doses. Although the opioids have different lipid solubilities, for IV-PCA, all have been dosed by IBW because the doses were originally formulated using IBW. Meanwhile, as we are titrating to individual patient satisfaction, there is room for posttreatment dose modification.

Intravenous infusions of opioids may also be administered in a monitored setting. In the past, opioids have been administered intramuscularly. Although this route has been shown to be effective, intramuscular injection is not advisable in the MO because of unpredictable pharmacodynamics, arising from inadvertent injection into lipid tissue.

There are three regional anesthetic/analgesic options: thoracic epidural analgesia and anesthesia/patient-controlled epidural analgesia (TEAA/PCEA), intrathecal opioids, and continuous spinal anesthesia/patient-controlled intrathecal analgesia (CSA/PCIA). All of these may be used with or without light general anesthesia. They offer similar side effect profiles and

will be described together. *PCEA*, the most commonly used of these, has numerous theoretical advantages. At a lower dose compared with parenteral opioids, there are few side effects and serious complications, effective analgesia, faster recovery, less respiratory complications, decreased total body oxygen consumption, improved cardiac function, and shorter hospitalization times compared with PCA. PCEA dosages in the MO should be decreased 75% to 80% due to decreased volume of the epidural space from increased intra-abdominal pressure. PCEA is strongly recommended when feasible yet remains underutilized. Patients should be positioned in a sitting position for epidural catheter insertion, and ultrasound guidance is recommended. Disadvantages include a higher rate of wound infection, possibly because of microdehiscence from faster return of gastrointestinal function, and the risk of neural injury. There is frequent technical difficulty with catheter insertion, which slows OR case flow. There is a higher rate of inadequate function, catheter migration and replacement, and variable block level. Side effects include excessive drowsiness, PONV, pruritus, and urinary retention. Respiratory depression occurs rarely and is more common with hydrophilic (e.g., preservative-free morphine sulfate [PFMS]) than with hydrophilic agents. With PFMS, it may occur from 1 hour until 18 hours. With fentanyl or sufentanil, it may occur from minutes until 2 hours. Neuraxial opioid respiratory depression risk factors include advanced age, excessive or repeated doses, lack of opioid tolerance, use of concomitant sedatives or hypnotics, increased intra-abdominal pressure (e.g., PNP), and severe OSAHS, which may precipitate massive pharyngeal collapse. *CSA/PCIA* with light general anesthesia has been used for gastroplastic surgery. It is technically easier to perform than TEAA/PCEA and produces a denser block with motor component, which is more predictable and controllable. *Intrathecal* opioids, with or without

local anesthetics, are technically easier to administer and offer an excellent alternative for appropriate surgical procedures. Other methods of controlling postoperative pain in bariatric surgery include preemptive analgesia via local anesthetic wound infiltration before and after surgery, pre- and intraoperative nonopioid drug combination (ketorolac, clonidine, lidocaine, ketamine, magnesium sulfate, and methylprednisolone), and perioperative dexmedetomidine.

Some bariatric patients will develop esophageal spasm-like pain in the postoperative period, which may mimic myocardial ischemic pain. These usually respond to antacids and H_2-receptor antagonists.

With the advent of Enhanced Recovery After Surgery (ERAS) techniques, postoperative pain is substantially less. In consequence, except for complex surgical cases or reoperations, no opioids are prescribed. The mainstay of postoperative analgesics today is non-opioid analgesics. Intravenous opioid analgesics are reserved for break-through pain. Aside from decreasing postoperative nausea and vomit, the most significant side effect after these cases, and decreasing respiratory depression, minimizing opioid exposure is associated with substantial societal benefits.

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A.5. What are the indications for IABP placement?
A.6. What are the contraindications and potential complications of IABP placement?
A.7. What are the pitfalls of IABP timing?
A.8. What are the main advantages and disadvantages of IABP support?
A.9. What is mechanical circulatory support?
A.10. What is a ventricular assist device (VAD)?
A.11. What are the types of percutaneous/temporary VADs?
A.12. What are the types of permanent VADs?
A.13. How does VAD work?
A.14. When is circulatory support needed?
A.15. What are the physiologic considerations in patients requiring a VAD?
A.16. What are the reasons for suboptimal VAD support?
A.17. What are common complications from VAD?
A.18. How long can VADs remain in the patient?
B. Preoperative Evaluation and Preparation
B.1. What is the focus of the preoperative assessment of an LVAD patient?
C. Intraoperative Management
C.1. Detail the anesthetic management for a patient undergoing LVAD placement.
C.2. How is a VAD patient monitored during a general anesthetic?
C.3. Prescribe an anesthetic for a VAD patient.
C.4. What is ECMO? What are the indications for ECMO? What

are the different types of ECMO?
C.5. What are the contraindications of ECMO?
C.6. What are the main complications of ECMO?
C.7. What are the necessary equipment and teams required to place ECMO? What are the pros and cons of different venoatrial ECMO (VA-ECMO) cannula placement?
C.8. How are patients monitored and managed while on ECMO?
C.9. What are the complications of ECMO?
C.10. How frequently is VA-ECMO being used and how effective is it in cardiogenic shock?
D. Postoperative Management
D.1. When and how is a patient weaned off IABP support?
D.2. How is weaning from ECMO accomplished?
7 Valvular Heart Disease
A. Medical Disease and Differential Diagnosis
A.1. What are the major etiologies of AS, AI, mitral stenosis (MS), and MR?
A.2. What are the major changes in the loading conditions of the LV that result from the four different lesions? Why do they occur? What changes result from them?
A.3. What are pressure–volume (P–V) loops? What do the different inflection points represent?
A.4. What are representative P–V loops for the four valvular lesions?
A.5. Draw the pressure/time curves for the LV, left atrium, pulmonary artery, and aorta for a normal patient and for patients with each of the four valvular lesions.
Aortic Stenosis
Aortic Insufficiency
Mitral Stenosis
Mitral Regurgitation
A.6. What are the basic principles of echocardiography? What are M-mode, B-mode, and Doppler color modalities? How do TTE and transesophageal echocardiography (TEE) differ?
A.7. What are the three TEE vantage points for the comprehensive imaging of the LV? How are pressure gradients measured by echocardiography? How do the pressure gradients derived from

Doppler echocardiography differ from those obtained in the catheterization laboratory by direct pressure measurement?
A.8. What is the role for three-dimensional (3D) echocardiography in the operating room?
A.9. What are the echocardiographic and cardiac catheterization criteria for the four valvular lesions?
Aortic Stenosis
Aortic Insufficiency
Mitral Stenosis
Mitral Regurgitation
B. Preoperative Evaluation and Preparation
B.1. What are the presenting signs and symptoms of the four valvular lesions listed previously?
Aortic Stenosis
Aortic Insufficiency
Mitral Stenosis
Mitral Regurgitation
B.2. What is the New York Heart Association classification of heart failure?
B.3. Discuss the role of premedication for patients with the four different valvular lesions.
B.4. How would you premedicate the patient with severe AS and MR?
C. Intraoperative Management
C.1. Outline the hemodynamic management goals for each of the four valvular lesions. What are the anesthetic goals with respect to heart rate and rhythm, preload, afterload, and contractility?
Aortic Stenosis
Aortic Insufficiency
Mitral Stenosis
Mitral Regurgitation
C.2. What are the hemodynamic goals for this patient with the combination of severe AS and MR?
C.3. How would you monitor this patient with severe AS and MR?
C.4. Should the patient have a pulmonary artery catheter placed before induction?
C.5. Is a pulmonary artery catheter with pacing capabilities

indicated?
C.6. What anesthetic technique would you employ? Why?
C.7. What muscle relaxant would you use for this patient?
C.8. What are the usual TEE findings in a patient with AS or MR? How do you grade the severity of AS by TEE? How do you quantify the severity of MR? What is the impact of AS on the severity of MR?
C.9. What special considerations particular to cardiopulmonary bypass (CPB) operations do you have for each of the four lesions? Focus on these concerns with respect to the induction and prebypass, bypass, and postbypass periods.
Aortic Stenosis
Aortic Insufficiency
Mitral Stenosis
Mitral Regurgitation
C.10. The patient cannot be weaned from CPB following an AV replacement and MV replacement. What are the possible causes?
C.11. How would you diagnose right-sided heart failure and pulmonary hypertension? How would you treat it?
C.12. How does an intra-aortic balloon pump (IABP) work to benefit the failing heart?
C.13. What role does the IABP have in this setting?
C.14. What role does TEE play in the placement, timing, and demonstration of efficacy of an IABP?
C.15. How would you properly time the IABP cycle?
C.16. What are the contraindications to the use of an IABP?
C.17. What is the role for ventricular assist devices?
D. Postoperative Management
D.1. In the intensive care unit (ICU) 4 hours later, the patient became hypotensive with a low cardiac output. How could you distinguish between cardiac tamponade and pump failure? How would the TEE images differ?
D.2. Would you extubate this patient early in the ICU? Why?
D.3. What are the advantages and disadvantages of early extubation?
E. Alternative Treatments
E.1. What are the percutaneous options for MV repair?

E.2. How is percutaneous MV repair performed?
E.3. What are the percutaneous options for AV repair and replacement?
E.4. How is percutaneous AV replacement performed?
E.5. What anesthetic techniques and monitors are used?
E.6. What is minimally invasive cardiac valve surgery?
8 Pacemakers, Implantable Cardioverter-Defibrillators, and Cardiac Resynchronization Therapy Devices
A. Medical Disease and Differential Diagnosis
A.1. What are the indications for PPMs?
A.2. What is sick sinus syndrome? What is chronotropic incompetence?
A.3. How would you diagnose first-, second-, and third-degree AV block; bifascicular block (right bundle branch block [RBBB] with left anterior fascicular hemiblock or left posterior fascicular hemiblock); and trifascicular block?
A.4. Is it necessary to insert a temporary pacemaker before general anesthesia for an asymptomatic patient with bifascicular or trifascicular block?
A.5. What are the three-letter and five-letter identification codes of the North American Society of Pacing and Electrophysiology (NASPE) and British Pacing and Electrophysiology Group (BPEG) generic (NBG) code for pacemaker classification?
A.6. How many modes of pacing are available in modern PPMs? How do they work? What is the difference between DDD pacing and DDI pacing?
A.7. The patient was mechanically hyperventilated during surgery, and her pacemaker gradually increased her heart rate. What feature of the PPM is accounting for this?
A.8. What are the advantages and disadvantages of atrial pacing only? What are the disadvantages of right ventricular pacing only?
A.9. What are the indications for and complications associated with AV sequential PPMs?
A.10. How would you know if the patient’s PPM was atrially, ventricularly, or atrioventricularly sequentially pacing?
A.11. What is a biventricular PPM or CRT device? What are the indications for such a device?

A.12. What are the usual lifespans of PPMs and implantable cardioverter-defibrillators (ICDs)?
A.13. What is an ICD? How does it work? What is a subcutaneous ICD?
A.14. What are the indications for ICDs?
A.15. What is the NASPE and BPEG generic defibrillator (NBD) code?
B. Preoperative Evaluation and Preparation
B.1. How would you preoperatively evaluate the patient described earlier?
B.2. How do you determine whether the patient has a cardiac implantable electronic device (CIED) and define what type of CIED?
B.3. How do you determine whether the patient is dependent on the pacing from the CIED?
B.4. How do you know if the implanted PPM or ICD is working?
B.5. What information would you like to obtain from interrogating this device?
B.6. How do you preoperatively prepare the patient for surgery and anesthesia?
B.7. Would you recommend reprogramming this device to asynchronously pace before surgery? What would you recommend regarding the ICD functions of the device?
B.8. The patient requires an abdominal magnetic resonance imaging (MRI) prior to the surgery. What considerations should you make regarding her CIED?
C. Intraoperative Management
C.1. How would you monitor this patient?
C.2. What drugs and equipment would you like to have on hand in the operating room?
C.3. How would you set up the transcutaneous external pacer and defibrillator?
C.4. Had this patient’s ICD been implanted the day before surgery, would you consider avoiding certain inhalational gases for anesthesia?
C.5. Electromagnetic interference (EMI) from electrocautery results in significant noise on your cardiac monitor. You recall that EMI

also can inhibit pacing function from the PPM. In this pacemaker-dependent patient, how can you determine whether inappropriate inhibition of the PPM is occurring?
C.6. What are the potential responses of pacemakers and ICDs to electrocautery?
C.7. How would you prevent the effects of EMI on the pacemaker or ICD from the electrocautery?
C.8. What are the effects of a magnet on pacemakers and ICDs?
C.9. In the middle of surgery, the patient developed ventricular tachycardia. What would you do?
C.10. What precautions should be taken when a patient with a CIED is undergoing extracorporeal shock wave lithotripsy (ESWL)?
C.11. Is electroconvulsive therapy (ECT) contraindicated in patients with pacemakers or ICDs?
C.12. What precautions should be taken during radiofrequency ablation for a patient with a CIED?
C.13. During surgery, the patient developed frequent premature ventricular complexes and some of these resulted in rapid ventricular pacing (see Fig. 8.8). What is accounting for the pacemaker's behavior?
D. Postoperative Management
D.1. How would you monitor this patient in the postanesthesia care unit?
D.2. How would you confirm that the CIED is functioning properly after surgery?
9 Thoracic and Thoracoabdominal Aortic Aneurysms
A. Pathophysiology and Differential Diagnosis
A.1. What is a thoracic aortic aneurysm (TAA) and TAAA, and how do they typically present?
A.2. How are TAAs and TAAAs classified?
A.3. What is the pathogenesis of aortic aneurysms and what genetic conditions predispose to their formation?
A.4. What are the risk factors for TAA rupture?
A.5. What is the natural history and medical management of thoracic aneurysms?
A.6. What is a thoracic aortic dissection, and how does it typically

present?
A.7. How are thoracic aortic dissections classified?
DeBakey Classification
Stanford Classification
Penn Classification
B. Preoperative Evaluation and Preparation
B.1. What are the indications and timing of surgical intervention for TAAs?
B.2. Which patients are candidates for endovascular aortic repair, and what are the advantages to this approach?
B.3. What are the preoperative considerations for the anesthesiologist before TAA repair?
Cardiovascular
Respiratory
Renal
Neurologic
B.4. What is the preoperative management of a patient presenting with an acute aortic dissection (AAD)?
B.5. What is the spinal cord blood supply?
C. Intraoperative Management
C.1. What are the surgical approaches to thoracic aneurysm repair?
Ascending and Arch Aortic Aneurysms
Thoracoabdominal Aneurysms
C.2. How is the open repair performed?
Ascending and Arch Aortic Aneurysms
Thoracoabdominal Aneurysms
C.3. How are endovascular repairs of TAAAs performed?
C.4. What are the surgical approaches to aortic dissections?
Type A Aortic Dissection
Type B Aortic Dissection
C.5. What are the specific considerations for anesthetic management of the patient presenting for open TAAA repair?
C.6. What are the specific considerations for anesthetic management of the patient presenting for endovascular TAAA repair?
C.7. What hemodynamic monitors should be used for the patient undergoing thoracic aneurysm repair?

C.8. What strategies are used for spinal cord protection during a TAAA repair?
Left-Heart Bypass
Intraoperative Neuromonitoring
Cerebrospinal Drainage
Hypothermia
C.9. What strategies are used for mesenteric and renal preservation?
C.10. What is the pathophysiology of aortic clamping and unclamping?
Aortic Clamping
Aortic Unclamping
C.11. Why does a coagulopathy ensue and how is it prevented/treated?
D. Postoperative Anesthetic Management
D.1. What are the postoperative complications after open TAAA repair?
Respiratory Failure
Renal Failure
Spinal Cord Injury
D.2. What are the postoperative complications after endovascular TAAA repair?
Left Upper Extremity Ischemia
Stroke
Spinal Cord Ischemia
Renal Failure
Postimplantation Syndrome
Endograft Collapse
Endoleaks
10 Abdominal Aortic Aneurysm Repair
A. Medical Disease and Differential Diagnosis
A.1. What risk factors are associated with an abdominal aortic aneurysm (AAA)?
A.2. What other diseases are commonly found in patients with aortic aneurysms?
A.3. What is the incidence of morbidity and mortality in these patients if they undergo elective open surgical repair? What is the

natural history of the disease without surgical repair?
A.4. What should be done for smaller aortic aneurysms that are found in patients?
A.5. What is the risk of perioperative myocardial infarction (MI) in patients with ischemic heart disease? What can be done to reduce the risk of ischemic events in these patients?
A.6. Does the morbidity and mortality of elective repair of an aortic aneurysm differ significantly from that of an emergency repair?
B. Preoperative Evaluation and Preparation
B.1. Which preoperative laboratory tests would you require for this patient?
B.2. What is the significance of the preoperative ECG? Would you wish to pursue a preoperative cardiac workup? What tests would you request, and what would they tell you?
B.3. Is it necessary to evaluate this patient's pulmonary status?
B.4. Preoperative arterial blood gas (ABG) measurement shows pH, 7.35; $PaCO_2$, 47 mmHg; and PaO_2, 68 mmHg on room air. What is the significance of this result?
B.5. How would you measure creatinine clearance in this patient, and what is its value in this case?
B.6. Describe the blood flow to the spinal cord. What is its relevance to surgery involving the abdominal aorta?
B.7. How do you detect spinal cord ischemia?
B.8. What are the various surgical approaches to repair an AAA?
B.9. How does the choice of surgical technique affect the anesthetic management?
B.10. How would you premedicate this patient?
C. Intraoperative Management
C.1. Would you use an arterial line? What are the complications of arterial line placement?
C.2. What various monitors are available for myocardial ischemia? Is a pulmonary artery catheter (PAC) helpful in determining the occurrence of ischemia?
C.3. What additional monitors would you employ?
C.4. Is there a role for somatosensory evoked potential (SSEP) monitoring during aortic clamping?
C.5. How would you anesthetize this patient for an open repair of

the aorta? What techniques could be used for an endovascular aortic aneurysm repair? Discuss the various anesthetic techniques that can be employed for this surgery.
C.6. This patient is to be heparinized intraoperatively, and anticoagulation may be continued postoperatively. Is this a contraindication to the preoperative placement of either an epidural or intraspinal catheter? What if the patient is receiving anticoagulants in the preoperative period?
C.7. What are your plans for fluid and blood replacement during surgery?
C.8. What are the hemodynamic changes of aortic cross-clamp placement? What efforts can be made to minimize these changes both before and during cross-clamping? If the patient develops ST-segment depressions with a rising pulmonary capillary wedge pressure (PCWP) during cross-clamp, what maneuvers should be taken?
C.9. Because this case involves an infrarenal aneurysm, is renal blood flow affected with the placement of the cross-clamp? If an endovascular repair is chosen, what are the risks to the kidneys? Are there any treatment maneuvers that can be taken to minimize these risks in either repair?
C.10. What are the hemodynamic consequences of aortic cross-clamp removal? What can be done to minimize the effects of removing the aortic cross-clamp? If the systemic blood pressure remains depressed after removal of the cross-clamp, what is the differential diagnosis? How would you diagnose and correct the problem?
D. Postoperative Management
D.1. What are the parameters used to extubate this patient?
D.2. What are the anticipated changes in postoperative pulmonary function in these patients? How does the surgical technique affect postoperative pulmonary function? Are there any postoperative maneuvers that can improve respiratory parameters?
D.3. How would you control postoperative pain? What are the alternatives in the management of this patient’s postoperative pain?
11 Hypertension
A. Medical Disease and Differential Diagnosis

A.1. Define hypertension and categorize its severity.
A.2. What is the prevalence of hypertension?
A.3. What is the general classification of hypertension? Enumerate the causes of each type of hypertension.
Etiology of Hypertension
A.4. What are the clinical patterns of hypertension encountered?
A.5. What is the pathophysiology of essential hypertension?
A.6. What is the pathophysiology of isolated systolic hypertension (ISH) and of pulse pressure hypertension (PPH)?
A.7. What are the end-organ damages caused by long-standing hypertension?
Cardiac Involvement
Eye Involvement
Renal Involvement
Cerebral Involvement
A.8. Are hypertensive patients at an increased risk for perioperative cardiac morbidity?
A.9. Perioperative cerebral and renal complications are mostly associated with which subtype of hypertension?
A.10. Would you employ a controlled hypotensive technique for hypertensive patients? How much would you safely lower the BP?
A.11. What are the BP goals for patients with hypertension and when should antihypertensive drugs be initiated?
A.12. What is the mechanism of action of antihypertensive drugs?
Diuretics
Antiadrenergic Agents
Direct Vasodilators
Dopaminergic Agonists
Calcium Channel Blockers
Angiotensin-Converting Enzyme Inhibitors
Angiotensin II Receptor Blockers
Other Vasodilators
A.13. Does the choice of antihypertensive therapy influence hemodynamic responses to induction, laryngoscopy, and intubation?
A.14. Does chronic angiotensin-converting enzyme (ACE) inhibition influence anesthetic induction?

B. Preoperative Evaluation and Preparation
B.1. How would you evaluate this patient preoperatively?
B.2. Would you postpone the surgery? Why? What BP would you like the patient to achieve before surgery?
B.3. Should all or any of the chronic medications be discontinued before the operation?
B.4. Should hypokalemia be treated before anesthesia? Why?
B.5. Should hypomagnesemia be treated before anesthesia? Why?
B.6. Does an asymptomatic carotid bruit increase the risk in these patients?
B.7. The surgery was postponed for 6 weeks. The patient was on metoprolol, aspirin, atorvastatin, captopril, hydrochlorothiazide, and potassium chloride. His BP was 160/60 mmHg and potassium 4.0 mEq per L. How would you premedicate this patient?
B.8. If the patient is an untreated hypertensive patient with BP 170/70 mmHg, would you treat the patient preoperatively with an antihypertensive agent?
C. Intraoperative Management
C.1. How would you monitor this patient?
C.2. What are the anesthetic goals for hypertensive patients?
C.3. How would you induce anesthesia for the hypertensive patient?
C.4. How does tracheal intubation produce hypertension?
C.5. What happens to the left ventricular ejection fraction during and immediately following intubation?
C.6. What other measures can prevent hypertension and tachycardia at the time of intubation?
C.7. After induction and intubation, the BP decreased to 70/40 mmHg. What would you do?
C.8. What is your choice of agents for maintenance of anesthesia? Why?
C.9. How would you manage fluid therapy for hypertensive patients?
C.10. During the surgery, BP increased to 220/120 mmHg. How would you treat the hypertension?
C.11. What could you do to prevent hypertension during extubation and emergence?

C.12. Would you consider regional anesthesia for this patient?
D. Postoperative Management
D.1. The patient developed hypertension, BP 210/110 mmHg, in the postanesthesia care unit. What would you do?
12 Cardiac Tamponade
A. Medical Disease and Differential Diagnosis
A.1. What is the differential diagnosis of low CO following cardiac surgery?
A.2. Describe the pathophysiology of cardiac tamponade.
A.3. What are the common etiologies of cardiac tamponade?
A.4. What is the difference between acute and delayed cardiac tamponade?
A.5. What is regional cardiac tamponade?
A.6. Describe the ventricular interaction in cardiac tamponade.
A.7. How is coronary blood flow affected in cardiac tamponade?
A.8. What is the Beck triad? Describe the typical signs and symptoms of cardiac tamponade.
A.9. Define pulsus paradoxus and describe its pathophysiology.
A.10. What is Kussmaul sign? Is this finding consistent with tamponade physiology?
A.11. Which medical conditions mimic cardiac tamponade?
B. Preoperative Evaluation and Preparation
B.1. Interpret and explain the pathophysiologic basis for this patient's hemodynamic findings.
B.2. How would you optimize this patient's cardiovascular status prior to definitive diagnosis and treatment?
B.3. What are the radiographic findings in tamponade?
B.4. A limited bedside transthoracic echocardiogram is performed, demonstrating a layer of clotted blood anterior to the right atrium (RA) and ventricle. What echocardiographic findings support the diagnosis of tamponade?
B.5. What additional information should be obtained from a limited echocardiographic study?
B.6. Describe the procedures for treating cardiac tamponade. What are the clinical indications for each approach?
B.7. Having made the diagnosis of tamponade, what additional investigations are required prior to surgery?

B.8. Explain the technical and physiologic principles behind rotational thromboelastometry.
B.9. A rotational thromboelastometry was performed, and a 10-minute analysis reveals the following results (see Fig. 12.9 and Table 12.8). How do you interpret this information?
B.10. Given the ROTEM® findings and high clinical suspicion for occult postsurgical bleeding, what hemostatic products would you arrange to have in the operating room?
B.11. How would you organize and conduct the transport of this patient to the operating room?
C. Intraoperative Management
C.1. What are the cardiovascular effects of commonly used intravenous anesthetic and coinduction agents?
Propofol
Etomidate
Ketamine
Thiopental
Fentanyl
Midazolam
C.2. What is the effect of supine positioning and positive pressure ventilation on the hemodynamics of a patient with tamponade?
C.3. Describe the induction process for cardiac tamponade.
C.4. Following induction and intubation, the systemic blood pressure decreases to 55/30 mmHg. Describe your management.
C.5. What hemodynamic changes are frequently associated with opening the pericardial space?
C.6. Following the removal of approximately 500 mL of dark blood and clots from the mediastinum, the patient's CO remains low. What are your differential diagnoses?
C.7. What is pericardial decompression syndrome (PDS)?
D. Postoperative Management
D.1. A pericardial drain is placed following mediastinal decompression. How should this drainage tube be managed?
D.2. How would you manage hypertension in the intensive care unit?
13 Heart Transplantation and Subsequent Noncardiac Surgery
A. Medical Disease and Differential Diagnosis

A.1. What are the common diagnoses requiring adult heart transplantation?
A.2. What are the indications and relative contraindications for recipient selection?
A.3. What are the criteria for donor heart selection?
A.4. What is the role of donation after cardiac death (DCD) for heart transplantation?
A.5. What are the principles of perioperative donor management?
A.6. What are the risk factors associated with posttransplant mortality?
A.7. What is the difference between the biatrial and bicaval surgical techniques of heart transplant?
A.8. When is a combined heart/lung transplant indicated? What are the important differences?
A.9. What are the medical and surgical alternatives to cardiac transplantation?
A.10. What is the role of ventricular assist devices (VADs) in this type of patient?
A.11. What are the considerations in anesthetizing patients for LVAD insertion?
B. Preoperative Management
B.1. How would you assess this patient preoperatively?
B.2. How would you premedicate this patient? Why?
C. Intraoperative Management
C.1. What anesthetic equipment and monitors would you set up? Why?
C.2. What is the role of transesophageal echocardiography (TEE)?
C.3. Describe the induction and maintenance of anesthesia.
C.4. How would you manage this patient during cardiopulmonary bypass (CPB)?
D. Postoperative Management
D.1. What are the early postoperative complications?
D.2. What are the mechanisms of early right ventricular (RV) failure?
D.3. How would you treat RV failure following heart transplantation?
D.4. How does inhaled nitric oxide (NO) work as a selective

pulmonary vasodilator?
D.5. What is the pathophysiology of the denervated heart?
D.6. What are the common cardiac dysrhythmias following heart transplant?
D.7. What are the causes of posttransplant bleeding?
D.8. How would you treat posttransplant bleeding?
D.9. What are the causes of early graft failure?
D.10. How would you manage this patient in the intensive care unit?
E. Subsequent Noncardiac Surgery
E.1. How would you monitor this patient?
E.2. What type of anesthetic is best for the heart-transplanted patient?
E.3. What anesthetic technique would you choose for this patient?
E.4. Do you need to use a muscarinic antagonist with cholinesterase inhibitors to reverse the muscle relaxant in heart-transplanted patients?
E.5. What are the anesthetic implications for heart-transplanted patients?
E.6. What is the significant implication of the denervated heart?
E.7. What is the significance of allograft rejection?
E.8. What is the significance of infection in these patients?
E.9. What are the significant implications of drug interactions?
E.10. What is cardiac allograft vasculopathy (CAV)? Why is this important?
E.11. What is the significant implication of posttransplant hypertension?
E.12. What is the significant implication of renal dysfunction?
E.13. What types of malignancy are found in recipients?
E.14. Is ambulatory surgery appropriate for heart transplant recipients?
14 Ischemic Heart Disease and Noncardiac Surgery
A. Medical Disease and Differential Diagnosis
A.1. What are the preoperative predictors for major adverse cardiac events (MACE) perioperatively?
A.2. What are the determinants of myocardial oxygen demand? How are they measured clinically?

A.3. What factors determine myocardial oxygen supply?
A.4. What is the mechanism of perioperative myocardial ischemia and MI?
A.5. What is the incidence of perioperative reinfarction for noncardiac surgery?
A.6. State the perioperative medical therapy you would employ to reduce the incidence of myocardial ischemia.
β-Adrenergic Antagonists (Esmolol, Atenolol, Metoprolol, Bisoprolol)
α_2-Adrenergic Agonist (Clonidine)
Nitrovasodilators (Nitroglycerin, Isosorbide Dinitrate)
Calcium Channel Blockers (Verapamil, Diltiazem, Nifedipine, Nicardipine)
Aspirin
Statins
A.7. Based on his MI, would you recommend that the surgery be postponed for a certain period of time? If so, why?
A.8. Would you recommend that this elective colectomy be postponed if the patient underwent placement of a right coronary artery, second-generation DES, and is taking aspirin and clopidogrel (Plavix)?
B. Preoperative Evaluation and Preparation
B.1. How would you evaluate the patient's cardiac condition? What laboratory tests would you like to order?
B.2. Would you recommend further cardiac testing or coronary revascularization before surgery?
B.3. How would you classify the cardiac risk according to the type of surgery?
B.4. What is the role of exercise or pharmacologic stress test for this patient?
B.5. Would you discontinue any medication before surgery?
B.6. How would you premedicate this patient?
B.7. Is there a role for α_2-agonist in premedication?
C. Intraoperative Management
C.1. What are the intraoperative predictors for perioperative MACE?
Intraoperative Predictors

C.2. How would you monitor the patient in the operating room?
C.3. What electrocardiogram (ECG) leads would you monitor? Why lead V_5?
C.4. Would you use a pulmonary artery catheter (PAC)?
C.5. Would you use transesophageal echocardiography (TEE) as a monitor?
C.6. Is regional anesthesia better than general anesthesia for patients with cardiac disease?
C.7. How will you induce general anesthesia?
C.8. Would you induce anesthesia with etomidate? Why?
C.9. What is the best choice of anesthetic agents for maintenance of anesthesia? Why?
C.10. You notice a new 3-mm ST-segment depression in lead V_5. How would you treat it?
C.11. Would you give prophylactic intravenous NTG to prevent myocardial ischemia?
C.12. What is the significance of tight control of the heart rate intraoperatively?
C.13. When would you extubate the trachea in this patient? What could you do to prevent hypertension and tachycardia during extubation and emergence?
D. Postoperative Management
D.1. What are the postoperative predictors of perioperative MACE?
D.2. How would you control postoperative pain?
D.3. Is postoperative anemia associated with adverse cardiac outcome?
D.4. Is postoperative hypothermia associated with postoperative myocardial ischemia?
D.5. How would you make a diagnosis of perioperative MI (PMI)?
D.6. How would you manage the patient with a suspected PMI?
SECTION 3 The Gastrointestinal System
15 Intestinal Obstruction and Enhanced Recovery after Surgery
A. Medical Disease and Differential Diagnosis
A.1. What is the differential diagnosis of the acute abdomen?
A.2. What are the causes of intestinal obstruction of the small bowel and of the large bowel?
A.3. Differentiate between simple and strangulated bowel

obstruction.
A.4. Is it important to differentiate whether the bowel obstruction is located in the small bowel or large bowel? Why? How might the distinction be made?
A.5. What are the causes and effects of bowel distention?
A.6. Describe the fluid shifts during small bowel intestinal obstruction.
A.7. Discuss the systemic derangements that occur with intestinal obstruction.
A.8. What is an ileus? Discuss its causes and pathophysiology.
B. Preoperative Evaluation and Preparation
B.1. What is Enhanced Recovery after Surgery (ERAS)? What are the core tenants of these programs?
B.2. Can ERAS be used in this case?
B.3. What components of ERAS are applied in the preoperative phase of the care of colorectal surgery (CRS) patients?
B.4. Is it important to decompress the abdomen before induction of anesthesia? Why?
B.5. Describe the respiratory implications.
B.6. What are the implications of the tense abdominal wall?
B.7. Outline the methods of abdominal decompression.
B.8. Discuss the goals of fluid management.
B.9. What would you use as a guide to fluid volume replacement?
C. Intraoperative Management
C.1. What dangers are present during induction? How are they planned for?
C.2. Does the administration of antacids and/or histamine-2 (H_2) blockers before the induction of anesthesia have a significant value in patients with small bowel obstruction?
C.3. In what position would you intubate this patient?
C.4. What is the best muscle relaxant to use for the rapid sequence induction?
C.5. Would you remove or leave the nasogastric tube (NGT) in place before inducing anesthesia?
C.6. Would you use nitrous oxide in this patient?
C.7. Are there any benefits to using a high concentration of inspired oxygen (FIO_2)?

C.8. What components of ERAS are applied in the intraoperative phase of the care of CRS patients?
C.9. What are the strengths, weaknesses, benefits, and challenges of ERAS?
Strengths
Weakness
Benefits
Challenges
C.10. What are the indications for ERAS?
D. Postoperative Management
D.1. What are the principles of postoperative care in this patient?
D.2. Are there any postoperative respiratory problems associated with factors other than aspiration?
D.3. If the patient did aspirate gastric contents, what are the possible sequelae of this event? What is the treatment?
D.4. What is gram-negative sepsis? Describe the clinical picture and treatment.
D.5. What components of ERAS are applied in the postoperative phase of the care of CRS patients?
16 Liver Transplantation
A. Medical Disease and Differential Diagnosis
A.1. What are the potential graft options for liver transplantation?
A.2. What are the indications and contraindications for liver transplantation?
A.3. What is acute liver failure (ALF)?
A.4. What is the MELD score, and how is it used in liver transplantation evaluation?
A.5. What is portal hypertension? What are the sequelae of portal hypertension?
A.6. Describe the cardiovascular system of patients with end-stage liver disease (ESLD).
A.7. What causes acute kidney injury (AKI) in patients with cirrhosis?
A.8. What causes hyponatremia in patients with cirrhosis?
A.9. Discuss the neurologic manifestations of acute and chronic liver disease.
A.10. Why do patients with ESLD have abnormalities of

hemostasis?
A.11. What is the differential diagnosis for hypoxemia in patients with cirrhosis?
A.12. What are the risk factors and treatment guidelines for spontaneous bacterial peritonitis (SBP)?
B. Preoperative Evaluation and Preparation
B.1. What preoperative workup is desirable?
B.2. How is ascites managed preoperatively?
B.3. How is hyponatremia managed preoperatively?
B.4. What is a transjugular intrahepatic portosystemic shunt (TIPS) procedure? What is the role of TIPS in the management of patients with ESLD?
B.5. How are hepatic encephalopathy and elevated intracranial pressure (ICP) treated?
B.6. Should this patient be transfused with fresh frozen plasma prior to surgery?
C. Intraoperative Management
C.1. What monitors would you use? Why?
C.2. What are the considerations for the induction of anesthesia?
C.3. How does liver disease affect intraoperative medication management?
C.4. What happens during the first stage (preanhepatic phase) of the liver transplant operation?
C.5. What happens during the second stage (anhepatic phase) of the liver transplant operation?
C.6. What physiologic disturbances should be anticipated during the second stage (anhepatic phase) of the liver transplant operation?
C.7. What is venovenous bypass? What are the potential advantages and disadvantages of this procedure?
C.8. What surgical techniques anastomose the donor and recipient inferior vena cava (IVC)?
C.9. What are the potential advantages of the “piggyback” (vena cava preservation) technique?
C.10. What hemodynamic changes are expected after removal of vascular clamps? What is postreperfusion syndrome (PRS)?
C.11. How would you treat hyperkalemia?
C.12. Why should you anticipate hypocalcemia?

C.13. What happens during the third stage of the liver transplant operation?
C.14. What causes intraoperative bleeding during each phase of liver transplantation? How is coagulopathy monitored and treated? What are thromboelastography (TEG) and rotational thromboelastography (ROTEM)?
C.15. What are the complications of massive transfusion?
C.16. How are the complications of massive transfusion prevented?
C.17. How is hyperfibrinolysis managed?
C.18. When is intraoperative renal replacement therapy indicated?
C.19. What intraoperative signs suggest that the hepatic graft is working?
D. Postoperative Management
D.1. What are the goals of immediate postoperative care of the liver transplant patient?
D.2. What postoperative findings suggest that the hepatic graft is functioning?
D.3. What coagulation disturbances should be anticipated in the postoperative period?
D.4. Can renal function change after liver transplantation?
D.5. What vascular and biliary complications occur after liver transplantation?
D.6. What immunosuppressive agents will be given after liver transplantation? What are the major side effects?
Acknowledgment
SECTION 4 The Nervous System
17 Brain Tumor and Craniotomy
A. Medical Disease and Differential Diagnosis
A.1. What is the pathology of intracranial tumors?
A.2. What is intracranial pressure (ICP), and what are its determinants?
A.3. How does the presence of a mass alter the ICP in this patient, and what are the clinical manifestations of these alterations?
A.4. What is cerebral blood flow (CBF), and what are its determinants?
A.5. What are the cerebral steal syndromes?
A.6. Are there any issues specific to posterior cranial fossa

pathology?
A.7. What is the role of preoperative embolization therapy?
B. Preoperative Evaluation and Preparation
B.1. What are the special considerations in preoperative evaluation of the patient scheduled for posterior fossa craniotomy?
B.2. In a patient who presents with intracranial hypertension, what management might have already been initiated preoperatively, and what are the implications for anesthetic management?
B.3. What are the types of intraoperative neurophysiologic monitoring (IOM) that would likely be used for this procedure, and how will they affect the anesthetic management plan?
B.4. What are the options for patient positioning during posterior fossa surgery?
B.5. What are the principal disadvantages associated with the common posterior fossa craniotomy positions?
B.6. How does the sitting position affect your preoperative assessment and planning?
B.7. How should the patient position ultimately be determined?
B.8. Should this patient receive premedication?
C. Intraoperative Management
C.1. What are the anesthetic goals for craniotomy?
C.2. What monitors should be used during craniotomy?
C.3. Would you monitor for venous air embolism (VAE)? What are the monitoring options?
C.4. What specific risks are associated with induction of anesthesia?
C.5. How would you induce anesthesia?
C.6. What are the effects of anesthetics on cerebral metabolic rate of oxygen ($CMRO_2$), CBF, and ICP? With this in mind, how would you maintain anesthesia?
Volatile Anesthetics
Nitrous Oxide
Intravenous Anesthetics
Opioids
C.7. How would you manage ventilation and maintain arterial carbon dioxide (CO_2)?
C.8. How would you approach diuretic therapy?

C.9. How would you manage serum glucose?
C.10. How would you approach fluid management?
C.11. Once the bone plate is removed and the dura retracted, the surgeon reports that the brain is still “tight.” What would be your response?
C.12. If deliberate hypotension is indicated, how will you achieve it?
C.13. While the surgeon is resecting tumor from near the brainstem, the patient’s heart rate suddenly drops to 20 beats per minute. What is your assessment and management?
C.14. Are there any measures you can take to prevent VAE?
C.15. During the procedure, the precordial Doppler becomes loud and turbulent. The end-tidal CO_2 ($EtCO_2$) drops from 31 to 13 mmHg, and the systemic pressure from 121/63 to 64/32 mmHg. What is your assessment and management plan?
C.16. What is your approach to emergence? What if the patient does not regain consciousness?
D. Postoperative Management
D.1. What postoperative complications are of greatest concern? What level of monitoring is required?
D.2. What is your approach to postoperative pain control?
D.3. In the ICU, the patient’s neurologic status deteriorates and ICP monitoring is instituted. What are the different methods of monitoring ICP, and what are their limitations?
18 Carotid Artery Disease
A. Medical Disease and Differential Diagnosis
A.1. What are the presenting symptoms of carotid stenosis?
A.2. What is the prevalence of carotid artery disease?
A.3. What is the natural course of carotid artery disease as it relates to stroke?
A.4. What in the patient’s history puts them at higher risk for having carotid atherosclerosis?
A.5. Do we screen patients for asymptomatic carotid stenosis?
A.6. What is the risk of stroke and cardiovascular events in asymptomatic carotid atherosclerosis?
A.7. What are the current medical options that the patient has for treating carotid atherosclerosis?

A.8. What are the indications for CEA and carotid artery stenting (CAS) in asymptomatic carotid atherosclerotic disease?
A.9. What are the indications for performing a CEA in symptomatic carotid stenosis?
A.10. Is there any role for CAS in symptomatic patients?
A.11. Discuss the anatomy of the cerebral vasculature, including the carotid artery and the circle of Willis.
A.12. Discuss cerebral blood flow (CBF) in the presence of carotid artery disease.
A.13. Discuss the different surgical approaches to carotid revascularization.
A.14. Discuss the endovascular approaches to carotid stenting.
A.15. What is normal CBF?
A.16. What is critically low CBF as measured by the electroencephalogram (EEG)?
A.17. What is cerebral autoregulation?
A.18. How does $PaCO_2$ affect CBF?
A.19. What are the principal determinants of CBF?
A.20. What is meant by the term luxury perfusion?
A.21. What is meant by the term intracerebral steal?
B. Preoperative Evaluation and Preparation
B.1. What will you look for in your preoperative evaluation of this patient?
B.2. Is this patient's blood pressure too high for elective surgery?
B.3. What laboratory data are required preoperatively?
B.4. Will you treat this patients' blood glucose?
B.5. Will you premedicate this patient?
C. Intraoperative Management
C.1. How will you monitor this patient?
C.2. How will you know that the patient's cerebral perfusion is adequate during surgery?
C.3. Discuss the differences and relative advantages and disadvantages of unprocessed EEG and processed EEG monitoring.
C.4. How will you measure CBF intraoperatively? What are the relative advantages and disadvantages of each technique?
C.5. Describe the use of stump pressure and its limitations.
C.6. Describe the use of transcranial Doppler (TCD) and its

limitations.
C.7. Describe the use of jugular venous oxygen saturation ($SjvO_2$) and its limitations.
C.8. Describe the use of cerebral oximetry and its limitations.
C.9. Discuss somatosensory evoked potentials (SSEPs) as a monitor of CBF during CEA.
C.10. What type of anesthesia will you choose for this patient if she chose to have an endarterectomy?
C.11. What type of anesthesia will you choose for this patient if she chose to have a carotid stent?
C.12. How will you induce and maintain general anesthesia in this patient for CEA?
C.13. How would you proceed if the patient were to receive regional anesthesia?
C.14. Discuss the effects of anesthetics on CBF.
C.15. Discuss the protective effects of anesthetic agents on cerebral function.
C.16. How will you manage this patient's ventilation under general anesthesia?
C.17. How will you manage this patient's blood pressure intraoperatively?
C.18. Discuss reperfusion injury following CEA and CAS.
C.19. What intravenous fluids will you give this patient intraoperatively?
D. Postoperative Management
D.1. The patient does not "wake up" from general anesthesia. Why?
D.2. Postoperatively, the patient's blood pressure is 170/96 mmHg. Will you treat this?
D.3. What immediate postoperative complications might you expect after a CEA?
D.4. What postoperative complications might you expect after a CAS?
D.5. Discuss postoperative neurocognitive dysfunction following uncomplicated carotid intervention.
19 Awake Craniotomy for Mapping and Surgery in the Eloquent Cortex

A. Medical Disease and Differential Diagnosis
A.1. What is the eloquent cortex?
A.2. What is the underlying pathology?
A.3. What determines intracranial pressure (ICP)?
A.4. How does a space-occupying mass alter ICP?
A.5. What is autoregulation, and why is it important?
A.6. How is cerebral blood flow (CBF) regulated?
A.7. What drug therapies may be associated with this pathology?
B. Preoperative Evaluation and Preparation
B.1. Why is the craniotomy performed awake?
B.2. What neurologic symptoms of the patient are important?
B.3. What is the status of their other comorbid conditions?
B.4. Are there anesthetic implications from current treatment drugs?
B.5. What laboratory data are required?
B.6. What radiology data should be reviewed?
B.7. How do you prepare the patient for an awake craniotomy?
B.8. Should this patient receive premedications?
B.9. What precautions should be made for airway management?
C. Intraoperative Management
C.1. How should this patient be monitored?
C.2. Does this patient require invasive monitoring?
C.3. Can current drug therapy alter eloquent cortex mapping?
C.4. Why use hypertonic fluids during a craniotomy?
C.5. What intravenous fluids (IVFs) are recommended?
C.6. Would a lumbar drain for cerebrospinal fluid (CSF) removal benefit this patient?
C.7. Venous air embolism (VAE): Is it a concern in this case?
C.8. How is the eloquent cortex mapped?
C.9. How are intraoperative seizures treated?
C.10. How will you conduct this anesthetic?
D. Postoperative Management
D.1. What are the major concerns following craniotomy?
Acknowledgments
20 Head Injury
A. Pathophysiology and Differential Diagnosis
A.1. What types of intracranial injuries are most likely to have

occurred in this patient?
A.2. What is the difference between primary and secondary injury? What factors contribute to secondary injury?
A.3. What are the benefits and risks of administering mannitol?
Benefits
Risks
A.4. What is the effect of hyperglycemia on neurologic outcome following head trauma?
A.5. What alterations in sodium and potassium balance can occur in patients with head injury?
A.6. In addition to sodium and potassium, what other electrolyte abnormalities can be present after head trauma?
A.7. What are the neuroprotective effects of administering magnesium (Mg)?
A.8. What role do gender and female sex hormones have in the pathophysiology of traumatic brain injury (TBI)?
A.9. What is the role of decompressive craniectomy (DC) as a treatment option for ICP control after head injury?
A.10. Do genetic factors play a role in the outcome after head injury?
B. Preoperative Evaluation and Preparation
B.1. What is the GCS? What is the significance of a GCS of 7T in this patient?
B.2. In addition to the GCS, what other assessments can be done to evaluate neurologic function?
B.3. What is the role of CT scanning in the initial evaluation of the patient with head injury? What are the management options in patients whose neurologic condition is deteriorating before obtaining a CT scan?
B.4. What is the role of ICP monitoring in the management of head injury?
B.5. How can you clear this patient's cervical spine?
B.6. What are the advantages of early endotracheal intubation in this patient?
B.7. What is your plan for airway management in this patient? How would it change if the patient were combative? How would it change if the patient had facial fractures with significant swelling

of the head and neck?
B.8. What are the effects of succinylcholine on ICP? What is the significance of the effect, if any?
B.9. What coagulation abnormalities are present after TBI? What modalities can be used to provide hemostasis and reduce intracranial hematoma expansion?
C. Intraoperative Management
C.1. What is appropriate hemodynamic monitoring during CT scanning and during craniotomy for evacuation of a subdural hematoma?
C.2. Should hyperventilation be used in this patient?
C.3. What are the implications of arterial hypertension in patients with head injury? How should BP be managed?
C.4. What should be done about intravenous (IV) fluid replacement? Should corticosteroids be given empirically?
C.5. Should hypertonic saline (HTS) be administered to this patient? How is HTS administered?
C.6. The patient underwent a craniectomy for evacuation of a frontal intracerebral hematoma. Should some anesthetic agents be avoided in this situation? Which ones? What agents might be preferred in this situation?
C.7. Should hypothermia be employed in this patient?
D. Postoperative Neurointensive Care Management
D.1. What are the postoperative ventilation concerns in this patient?
D.2. What specific measure should be used to control the patient's ICP? What type of monitoring devices can be used to measure ICP?
D.3. What is neurogenic pulmonary edema? Would you avoid positive end-expiratory pressure (PEEP) in a patient with increased ICP?
D.4. What is the role of antiseizure prophylaxis in the perioperative management of head trauma?
D.5. How can cerebral oxygenation monitoring be used in the clinical management of TBI?
D.6. What methods can be used in the neurointensive care unit to prevent hyperthermia?
21 Cerebral Aneurysm
A. Medical Disease and Differential Diagnosis

A.1. What are the incidence, prevalence, and causes of subarachnoid hemorrhage (SAH), and what are the risk factors associated with rupture of intracranial aneurysms?
A.2. What are common sizes and locations of intracranial aneurysms?
A.3. What is the pathophysiology of aneurysmal rupture and SAH?
A.4. What are symptoms and signs of SAH?
A.5. How does one assess the severity of SAH?
A.6. What are the cardiovascular effects of SAH?
A.7. How is the diagnosis of SAH made?
A.8. What is the risk for rebleeding for a patient with SAH?
B. Preoperative Evaluation and Preparation
B.1. What are some concerns in going to the interventional neuroradiology suite in the midst of an angiogram to be followed immediately with coiling of an aneurysm?
B.2. What type of anesthesia is required for coiling of an aneurysm?
B.3. Should one proceed with induction of general anesthesia under these circumstances?
B.4. What types of emergencies can occur during coiling of an aneurysm, and how should they be managed?
B.5. What other modalities of endovascular therapy are available?
B.6. A craniotomy is planned for the following day to clip the middle cerebral artery aneurysm. Should surgery be postponed because of the patient's elevated troponin and CPK-MB fractions?
B.7. Would you premedicate this patient before craniotomy?
C. Intraoperative Management
C.1. What are the goals of the induction and maintenance of anesthesia for this patient?
C.2. Is placement of an arterial catheter necessary for induction of anesthesia in this patient in the interventional neuroradiology suite?
C.3. How would you assess fluid status in this patient?
C.4. Would monitoring central venous pressure (CVP) be useful for craniotomy and aneurysm clipping in this patient?
C.5. What other forms of monitoring would you consider?
C.6. What are your specific concerns during induction of anesthesia in this patient?

C.7. How would you accomplish a smooth and safe induction and intubation in this patient?
C.8. Would you perform a rapid sequence induction and tracheal intubation for this patient?
C.9. What are the effects of hypoxemia and hypercapnia, such as would be seen with loss of the airway on induction, on cerebral blood flow (CBF)?
C.10. What is optimal fluid management for aneurysm clipping? Would you use a dextrose-containing solution?
C.11. After the bone plate was removed and as the dura was being opened, the surgeon complained that the brain was “tight.” What could you do to achieve better brain relaxation and facilitate surgical exposure?
C.12. How might transmural pressure be decreased to allow for aneurysm clip placement?
C.13. What is the purpose of controlled hypotension, and how is it achieved?
C.14. What are some of the drawbacks of controlled hypotension?
C.15. What methods of cerebral protection might you use during this operation?
C.16. Would you induce mild hypothermia as a means of cerebral protection?
C.17. What are the indications for deep hypothermic circulatory arrest?
C.18. What steps should be taken in the case of intraoperative rupture of an intracranial aneurysm?
C.19. How would you plan the emergence from an anesthetic for aneurysm clipping?
D. Postoperative Management
D.1. Would you extubate the patient postoperatively?
D.2. What would be the differential diagnosis if the patient did not return to her preoperative neurologic condition?
D.3. On postoperative day 2, the patient became disoriented and developed hemiplegia. A CT scan was obtained, which shows no new intracranial bleeding. What other diagnostic studies should be performed?
D.4. What is cerebral vasospasm, and what causes it?

D.5. What are pathophysiologic changes seen in cerebral vasospasm?
D.6. How is the diagnosis of cerebral vasospasm made?
D.7. What steps can be taken to prevent cerebral vasospasm?
D.8. What treatments can be undertaken once a diagnosis of cerebral vasospasm is made?
D.9. What are other neurologic complications following SAH and aneurysm clipping?
D.10. What other organ systems may manifest problems postoperatively in aneurysm clipping patients?
SECTION 5 The Endocrine System
22 Pheochromocytoma
A. Medical Disease and Differential Diagnosis
A.1. What are some common differential diagnoses for arterial hypertension?
A.2. What is a pheochromocytoma?
A.3. Describe the anatomy of the adrenal gland.
A.4. What substances does the adrenal medulla secrete?
A.5. What are the mechanisms of action of epinephrine and norepinephrine?
A.6. What is the pathway for synthesis and breakdown of catecholamines?
A.7. What does the adrenal cortex secrete?
A.8. What are the metabolic actions of the glucocorticoids and the mineralocorticoids?
A.9. What are the clinical features associated with a pheochromocytoma?
A.10. What is the prevalence of pheochromocytomas and paragangliomas?
B. Preoperative Evaluation and Preparation
B.1. How can you diagnose and localize the tumor preoperatively?
B.2. How do you pharmacologically prepare the patient with a pheochromocytoma for surgery?
B.3. What other aspects of preoperative management are important?
C. Intraoperative Management
C.1. What drugs should be avoided during the operation?

C.2. How would you monitor this patient?
C.3. Describe the anesthetic management of the patient with pheochromocytoma.
C.4. What drugs are used to control the effects of catecholamine stimulation during surgery?
C.5. What are some management concerns after the tumor is removed?
C.6. What are some of the concerns with laparoscopic adrenalectomy?
D. Postoperative Management
D.1. What is the significance of postoperative hypotension? How is it treated?
D.2. What other problems can arise in the postoperative period?
23 Diabetes Mellitus
A. Medical Disease and Differential Diagnosis
A.1. What is the epidemiology of DM in the general population?
A.2. What are the factors in the etiology of the disease?
A.3. How is DM classified?
A.4. What are the complications of DM?
A.5. How are the different forms of this illness treated?
A.6. How is control of the disease adequately monitored?
A.7. What are some of the factors that alter insulin requirements?
A.8. What are the principles of management of diabetic ketoacidosis (DKA)?
A.9. What is a hyperglycemic hyperosmolar state?
B. Preoperative Evaluation and Preparation
B.1. How should this patient be evaluated?
B.2. How would the stiff joint syndrome affect her airway management?
B.3. What are the signs and implications of autonomic neuropathy in the diabetic patient?
B.4. How should this patient be prepared for anesthesia and surgery?
B.5. For elective surgery, how are insulin and glucose requirements managed on the day of surgery?
B.6. How should this patient be premedicated?
C. Intraoperative Management

C.1. What are the effects of anesthesia and surgery on insulin and glucose metabolism?
C.2. What anesthetic techniques should be considered?
C.3. How should this patient be monitored?
C.4. How is hyperglycemia treated intraoperatively?
C.5. How is hypoglycemic shock recognized and treated intraoperatively?
D. Postoperative Management
D.1. How is diabetes controlled in this patient postoperatively?
D.2. Does diabetes increase perioperative risk?
D.3. What are the common postoperative complications to be expected in a diabetic patient?
D.4. Is it necessary to achieve tight perioperative control of glucose?
SECTION 6 The Genitourinary System
24 Transurethral Resection of the Prostate and Geriatric Anesthesia
A. Medical Disease and Differential Diagnosis
A.1. What comorbidities are common in patients undergoing TURP?
A.2. What are the normal physiologic consequences of aging for the various organ systems?
A.3. How should drug dosages be adjusted for elderly patients? Should any particular medications be avoided?
A.4. Does a history of prior MI increase the patient's risk of perioperative reinfarction or stent thrombosis?
A.5. In patients with a history of recent MI, would you recommend that the surgery be postponed for a certain period?
B. Preoperative Evaluation and Preparation
B.1. How would you evaluate the patient's cardiac condition? Does he need additional testing?
B.2. Would you discontinue any antihypertensives or any medications for angina?
B.3. For a patient with a cardiac implantable electronic device (CIED), what information should you know? What precautions should be taken?
B.4. What types of coronary stents are available? What is their perioperative relevance?

B.5. What is the conventional recommendation for dual antiplatelet therapy (DAPT) in a patient with previous percutaneous coronary intervention (PCI) undergoing elective noncardiac surgery?
B.6. What risk is associated with continuing perioperative antiplatelet therapy? What risk is there with stopping it?
B.7. How should patients with coronary stents undergoing noncardiac surgery be managed?
C. Intraoperative Management
C.1. What monitors would you use for this patient?
C.2. Is there a preferred anesthetic technique for patients undergoing TURP, and why?
C.3. Does regional anesthesia result in a lower incidence of perioperative mortality than general anesthesia?
C.4. What intravenous fluid would you use during TURP?
C.5. Forty minutes after a sensory level of T10 was established with intrathecal anesthesia, and monopolar TURP (M-TURP) resection was initiated with the use of glycine as the bladder irrigating solution, the patient becomes agitated and complains of nausea. Further sedation along with an antiemetic is administered. However, shortly thereafter, the patient becomes very restless, blood pressure rises, and heart rate decreases. The patient becomes cyanotic and obtunded, blood pressure precipitously falls, and pupils are dilated and unresponsive to light. What is the most likely cause of these signs and symptoms, and would these occur during bipolar (B-TURP) or laser TURP (L-TURP) resection?
C.6. What are the important characteristics of irrigation solutions used during TURP?
C.7. What is the effect on body temperature of continuous bladder irrigation during TURP?
C.8. What is the definition of TURP syndrome? What are the signs and symptoms of the syndrome?
Cardiopulmonary
Hematologic and Renal
Central Nervous System
C.9. How does the patient absorb irrigation solution during TURP?
C.10. What factors increase the incidence of TURP syndrome?
C.11. What is the effect on cardiopulmonary, renal, and central

nervous system (CNS) functions of excessive absorption of irrigation solution during TURP?
C.12. What causes CNS dysfunction in patients who have undergone M-TURP?
C.13. How does acute hyponatremia affect the cardiovascular system?
C.14. What prophylactic measures may reduce the incidence of TURP syndrome?
C.15. What therapeutic measures are recommended for patients with TURP syndrome?
C.16. Is hypertonic saline administration necessary to correct hyponatremia? Explain. What are the risks of rapidly correcting hyponatremia?
C.17. What are the toxic effects of glycine? Is there an antidote to glycine toxicity? What are the metabolic by-products of glycine?
C.18. What are the symptoms and clinical course of TURP-induced hyperammonemia?
C.19. What are the clinical characteristics, causes, and prognosis of TURP-related blindness?
C.20. What are the causes of excessive bleeding during TURP?
C.21. What are the causes, signs, symptoms, and treatment of bladder perforation during TURP?
C.22. What are the causes of hypotension during TURP?
D. Postoperative Management
D.1. What is the source of postoperative bacteremia in patients who have undergone TURP? What factors increase the incidence of bacteremia?
D.2. What are the signs of post-TURP septicemia? What preventive measures are generally recommended?
D.3. Is postoperative hypothermia a risk factor for myocardial ischemia?
D.4. What is postoperative cognitive dysfunction (POCD)? How does this differ from delirium, and what is the time course to resolution?
D.5. What are the mechanisms and risk factors for POCD? How would you mitigate the risk of POCD? Does anesthesia type influence development of POCD?

E. Comparing M-TURP, B-TURP, and L-TURP
E.1. What differentiates M-TURP from B-TURP?
E.2. Are decreased morbidity and mortality associated more closely with M-TURP or with B-TURP?
E.3. What differentiates the technologies for L-TURP?
25 Kidney Transplant
A. Medical Disease and Differential Diagnosis
A.1. What are the causes of chronic renal disease that can progress to renal failure?
A.2. How is chronic kidney disease (CKD) diagnosed?
A.3. What are the indications for dialysis?
A.4. What are the common clinical manifestations of ESRD?
A.5. What electrolyte imbalances occur in patients with impaired renal function, and how are they treated?
A.6. How is metabolic acidosis managed in chronic renal failure?
A.7. Are patients with renal disease at increased risk of cardiovascular disease?
A.8. When is the best time to receive a kidney transplant?
A.9. How are immunosuppressive drugs managed in kidney transplant recipients?
A.10. How are kidneys allocated to recipients on the waiting list in the United States?
A.11. What is donation after cardiac death (DCD)?
A.12. What is a living donor transplant program?
A.13. What is a paired donor exchange transplant program?
A.14. What are some barriers to receiving a kidney transplant?
A.15. What surgical techniques are available for donor nephrectomy (DN)?
A.16. How is a donor kidney preserved?
A.17. Describe the operative procedure of kidney transplantation.
B. Preoperative Evaluation and Preparation
B.1. What preoperative workup would you order for a recipient?
B.2. How does the presence of obesity affect the outcome of a transplanted kidney?
B.3. How are routine medications and immunosuppressive medications managed in the perioperative period?
C. Intraoperative Management

C.1. Are a central venous pressure (CVP) monitoring line, an arterial line, and a pulmonary artery catheter required for the transplant procedure?
C.2. What type of intravenous fluid should be used during surgery?
C.3. How would you conduct the anesthesia induction?
C.4. Is succinylcholine contraindicated in renal failure patients?
C.5. How are the nondepolarizing muscle relaxants affected by renal failure?
C.6. How would you maintain anesthesia during the case?
C.7. What are the effects of inhalation anesthetics on renal blood flow (RBF), glomerular filtration (GFR), and urine output?
C.8. What are the potential nephrotoxic effects of inhalation anesthetics? What are the nephrotoxic metabolites of inhalation anesthetics?
C.9. How does renal failure affect the pharmacology of opioids?
D. Postoperative Management
D.1. How is the diagnosis of transplant rejection made?
D.2. What are immunosuppressive agents, and how do they affect anesthetic care?
26 Robotic-Assisted Laparoscopic Surgery
A. Medical Disease and Differential Diagnosis
A.1. What is the incidence of carcinoma of the prostate?
A.2. How is prostate cancer diagnosed?
A.3. How is prostate cancer treated?
A.4. Define laparoscopy.
A.5. Describe the development of robotic-assisted laparoscopy.
A.6. What are the advantages and disadvantages of minimally invasive surgery over open surgery?
A.7. What are the contraindications to laparoscopic or robotic-assisted laparoscopic surgery? Is pregnancy a contraindication to robotic surgery?
A.8. What other specialties commonly perform robotic surgery?
A.9. Why is carbon dioxide (CO_2) the gas of choice for robotic laparoscopy? What are its disadvantages?
A.10. How much endogenous CO_2 is produced at basal level and at maximal exercise?
A.11. How much CO_2 is stored in the body? Where is it stored? Of

what significance is this to laparoscopy?
A.12. Describe the diffusion and solubility properties of CO_2 and their significance in laparoscopy.
A.13. Is CO_2 soluble in water or plasma? Is it soluble in blood? Why?
B. Preoperative Evaluation and Preparation
B.1. What do you want to know about this patient's history and physical condition that may affect whether or not you clear him for robotic surgery?
B.2. What factors increase this patient's risk of pulmonary complications?
B.3. What laboratory tests should be performed preoperatively?
B.4. What specific information should the patient be given about robotic surgery before obtaining informed consent?
B.5. What additional procedures should be done before surgery?
B.6. What are the three major forces that uniquely alter the patient's physiology during robotic laparoscopy?
C. Intraoperative Management
C.1. What is the anesthetic technique of choice for robotic-assisted laparoscopy? Why?
C.2. Can a laryngeal mask airway (LMA) be used?
C.3. What anesthetic agents or adjuvant drugs are recommended for laparoscopy? Are any anesthetic agents contraindicated?
C.4. Should nitrous oxide (N_2O) be used during laparoscopy? What are the pros and cons? Does N_2O cause bowel distention during laparoscopy? Does N_2O cause nausea and vomiting after laparoscopy?
C.5. Can laparoscopy be performed under local or regional anesthesia?
C.6. What monitors and devices would you apply to the patient? Why?
C.7. How is the patient to be positioned? What special precautions are required for robotic laparoscopy?
C.8. How will you ventilate the patient? What are the respiratory and circulatory effects of the Trendelenburg position during laparoscopy?

Respiratory
Circulatory
C.9. What techniques are available for initial access to the peritoneal cavity? What anesthetic problems can arise during insufflation?
C.10. What intravenous (IV) solution and how much fluid volume do you plan to infuse?
C.11. Under what circumstances should laparoscopy be converted to laparotomy?
C.12. What is the arterial to end-tidal CO_2 gradient ($PaCO_2$–$EtCO_2$) in the normal awake patient? What is the cause of the gradient? Does the gradient change during laparoscopy? Why?
C.13. Is an arterial line necessary? Why? Does end-tidal CO_2 tension accurately reflect arterial CO_2 tension? Under what circumstances may the $EtCO_2$ exceed the $PaCO_2$? Why?
C.14. What are the possible causes of hypercarbia?
C.15. What factors play a role in the unusually rapid and marked elevation of CO_2 that is sometimes seen in laparoscopy?
C.16. How rapidly does the $PaCO_2$ rise in the apneic patient (endogenous CO_2)? How rapidly does the $PaCO_2$ rise if 5% CO_2 gas is inhaled (exogenous)? How rapidly can the CO_2 rise during laparoscopy? What factors explain the differences?
C.17. What is the net effect of pneumoperitoneum, hypercarbia, and steep Trendelenburg on the cardiovascular system?
C.18. What is the net effect of pneumoperitoneum, hypercarbia, and steep Trendelenburg on the respiratory system?
C.19. What is the net effect of pneumoperitoneum, hypercarbia, and steep Trendelenburg on the central nervous system?
C.20. What are the neuroendocrine changes that occur during laparoscopy?
C.21. What is the net effect of pneumoperitoneum, hypercarbia, and steep Trendelenburg on the renal system?
C.22. What is the net effect of pneumoperitoneum, hypercarbia, and steep Trendelenburg on the bowel and gastrointestinal system?
C.23. How would you recognize a CO_2 embolism during

laparoscopy? How does this differ from an air embolism? Why should N_2O be discontinued during suspected embolization? Will N_2O increase the size of CO_2 emboli?
C.24. What is the mechanism of increase in shunting resulting from embolization?
C.25. How is a gas embolism (CO_2 or air) treated?
C.26. What are the causes of pneumothorax or pneumomediastinum during laparoscopy? How would you diagnose it? How would you treat it?
C.27. How would you decide when to extubate?
D. Postoperative Management
D.1. What are some of the unique complications of laparoscopy?
Injuries from Instruments
Complications of Pneumoperitoneum
Systemic Effects of CO_2 Absorption
Trendelenburg Position
Late Complications
D.2. In the postanesthesia care unit (PACU), our patient complains of numbness and weakness of the lower extremities after 6 hours of anesthesia for robotic prostatectomy. What tests will you order?
When would you remove the Foley catheter and arterial line?
Under what circumstances would you order a chest x-ray film?
D.3. What is the incidence of postoperative nausea and vomiting?
SECTION 7 The Reproductive System
27 Placenta Previa/Placenta Accreta Spectrum
A. Medical Disease and Differential Diagnosis
A.1. What are the leading causes of maternal mortality, and what role does anesthesia play in this mortality?
A.2. What is the differential diagnosis for an antepartum hemorrhage?
A.3. How would you diagnose the etiology of antepartum bleeding after midpregnancy?
A.4. What is the incidence of placenta previa, and what are the associated conditions?
A.5. What are the different types of placenta previa?
A.6. What is the usual obstetric management for placenta previa?

A.7. What is vasa previa? How is it diagnosed and managed?
A.8. What are the risk factors for the development of a placental abruption?
A.9. How is placental abruption diagnosed and managed?
A.10. What complications are associated with placental abruption?
A.11. Who is at risk for uterine rupture, and how is uterine rupture diagnosed?
A.12. What is the treatment for uterine rupture?
A.13. Is this patient at risk for postpartum bleeding?
A.14. What is the placenta accreta spectrum (PAS)?
A.15. How is the PAS diagnosed?
A.16. How is the PAS managed obstetrically?
A.17. What tests and/or interventions can improve neonatal outcome of a preterm birth?
B. Preoperative Evaluation and Preparation
B.1. How does pregnancy change respiratory function, and what impact does this have on anesthetic care?
B.2. What are the maternal cardiovascular changes of pregnancy?
B.3. What are the maternal gastrointestinal changes of pregnancy?
B.4. What hematologic changes occur during pregnancy?
B.5. What laboratory data do you need before taking this patient to the operating room?
B.6. What preoperative medications would you administer to this patient?
C. Intraoperative Management
C.1. What monitors would you use for this patient?
C.2. What anesthetic could be used in this patient?
C.3. What are the absolute and relative contraindications for neuraxial anesthesia?
C.4. How is postpartum hemorrhage (PPH) defined, and what are the etiologies of this bleeding?
C.5. After delivery of the fetus, the placenta is removed with some difficulty in one small area and generalized oozing from the placental implantation site is noted. What is the most likely cause of this patient’s bleeding?
C.6. After delivery of the placenta in a cesarean section, what maneuvers and drugs can enhance myometrial contractility and

therefore decrease blood loss?
C.7. When should this patient receive tranexamic acid (TXA)?
C.8. If this patient had ongoing bleeding intraoperatively, what guidelines help determine when red blood cell (RBC) transfusions should be given?
C.9. What laboratory tests should be ordered during the resuscitation of this patient?
C.10. If this patient had a massive blood loss, what blood replacement therapy would be indicated?
C.11. What is the role of recombinant activated factor VII (rFVIIa) in the hemorrhaging obstetric patient?
C.12. What is the role of type O Rh-negative (universal donor) uncrossmatched blood in emergency transfusions, and how does this change your future management?
C.13. What complications can occur from the transfusion of blood products?
C.14. What is the role of autologous transfusion in obstetric patients?
C.15. Significant intraoperative blood loss required the transfusion of 8 units of type-specific, crossmatched packed RBCs (pRBCs). This patient had generalized oozing in the surgical field and hematuria. What is your differential diagnosis?
C.16. What is disseminated intravascular coagulation (DIC)?
C.17. Define amniotic fluid embolism (AFE) syndrome and discuss treatment.
D. Postoperative Management
D.1. If the patient received epidural anesthesia and subsequently developed DIC, when should the epidural catheter be removed?
D.2. You have successfully treated the patient's massive hemorrhage. Her laboratory values have returned to normal. The patient, however, is still hypotensive despite appropriate intravascular volume replacement and support with vasopressors. What is your concern in this case?
28 Hypertensive Disorders of Pregnancy
A. Medical Disease and Differential Diagnosis
A.1. What is the classification of hypertension disorders in pregnancy as defined by the American College of Obstetricians and

Gynecologists?
A.2. What is preeclampsia?
A.3. What is preeclampsia with severe features?
A.4. What is eclampsia?
A.5. What is HELLP syndrome?
A.6. What are the risk factors for developing preeclampsia?
A.7. What is the mortality associated with preeclampsia?
A.8. Discuss the pathogenesis of preeclampsia.
Immunologic Factors
Genetic Factors
Endothelial Factors
Platelet Factors
Calcium
Coagulation Factors
Fatty Acid Metabolism
Markers of Angiogenesis
A.9. Discuss the pathologic alterations of preeclampsia.
Cardiovascular Changes
Hemodynamic Changes
Hematologic Changes
Renal Changes
Endocrine Changes
Respiratory Changes
Hepatic Changes
Neurologic Changes
Uteroplacental Perfusion
A.10. What are some of the complications associated with preeclampsia?
B. Preoperative Evaluation and Preparation
B.1. What initial laboratory studies are recommended for patients with preeclampsia?
B.2. Discuss bleeding time and platelet count evaluation during preoperative assessment of a patient with preeclampsia requesting epidural analgesia/anesthesia for labor and delivery.
B.3. What types of monitoring are important for patients with preeclampsia? When is a central venous pressure (CVP) monitor indicated?

B.4. Discuss the obstetric management of preeclampsia with severe features.
B.5. What are the antihypertensive agents of choice for preeclampsia?
B.6. What drug therapy is the treatment of choice for seizure prophylaxis?
B.7. Discuss the mechanism of action of magnesium sulfate.
B.8. What are the fetal effects of magnesium sulfate therapy?
B.9. Discuss the treatment of magnesium sulfate toxicity.
B.10. What conditions mandate immediate delivery, regardless of the gestational age?
B.11. Discuss the management of eclampsia.
C. Intraoperative Management
C.1. What is your choice of labor analgesia for patients with preeclampsia?
C.2. What is the advantage of prehydration prior to initiation of neuraxial analgesia?
C.3. What sensory level of analgesia is required for labor and delivery?
C.4. Discuss the commonly used local anesthetics for labor analgesia.
C.5. Is the addition of epinephrine to local anesthetics advisable in preeclamptic patients?
C.6. What is the treatment for the abnormal fetal heart rate pattern seen with maternal hypotension after neuraxial analgesia is instituted?
C.7. What would you do after an accidental dural puncture? How do you treat postdural puncture headache?
C.8. How would you manage total spinal anesthesia?
C.9. Should methylergonovine be given to preeclamptic patients?
C.10. When and how would you give spinal anesthesia?
C.11. Discuss a general anesthesia technique for the patient with preeclampsia presenting for cesarean delivery.
C.12. What agents can you use to prevent hypertension during the induction of general anesthesia for cesarean delivery?
D. Postoperative Management
D.1. Discuss the postpartum management of preeclamptic patients.

D.2. Can nonsteroidal anti-inflammatory drugs (NSAIDs) be used to treat postpartum pain in preeclamptic patients?
29 Breech Presentation, Fetal Distress, and Mitral Stenosis
A. Medical Disease and Differential Diagnosis
A.1. How are fetal lie, presentation, and position defined and determined?
A.2. What is the approximate frequency of the various lies and presentations at or near term?
A.3. What are the different types of breech presentation, and what is their incidence?
A.4. What is the cause of breech presentation?
A.5. What are the delivery problems associated with breech presentation?
A.6. What is the usual obstetrical management for patients with breech presentation?
A.7. What is the incidence of heart disease in pregnancy and the mortality rate associated with maternal cardiac disease?
A.8. How is peripartum cardiomyopathy defined?
A.9. What classifications help predict an individual pregnant woman’s cardiac risk?
A.10. What are the cardiovascular changes of pregnancy?
A.11. What changes normally occur in heart sounds during pregnancy?
A.12. What are the normal electrocardiographic and echocardiographic changes seen during pregnancy?
A.13. What causes rheumatic heart disease?
A.14. What are the physiologic consequences of mitral stenosis?
A.15. What are the auscultatory findings associated with mitral stenosis?
A.16. What may be seen on the electrocardiogram (ECG) in patients with mitral stenosis?
A.17. What are the echocardiographic findings associated with mitral stenosis?
A.18. What is the effect of the physiologic changes of pregnancy on patients with mitral stenosis?
A.19. If mitral stenosis is first recognized during pregnancy and symptoms develop, how would you treat the patient?

A.20. What are the determinants of fetal oxygenation?
A.21. What are the determinants of uterine blood flow?
B. Preoperative Evaluation and Preparation
B.1. How is fetal well-being assessed during labor?
B.2. How are FHR and maternal contractions monitored?
B.3. What is the normal FHR with beat-to-beat variability?
B.4. What are FHR decelerations?
B.5. How accurate is FHR monitoring in predicting fetal well-being?
B.6. In a fetus with minimal FHR variability, what other modalities can be used to assess fetal well-being?
B.7. What is the significance of meconium-stained amniotic fluid?
B.8. What is meconium aspiration syndrome?
B.9. What are the usual noninvasive tests used to evaluate the pregnant cardiac patient?
B.10. What preoperative medications, if any, would you give this patient?
C. Intraoperative Management
C.1. What monitors would you use in this functional New York Heart Association (NYHA) class II patient during her cesarean section?
C.2. When would you use invasive monitoring in a pregnant patient with cardiac disease?
C.3. What are the hemodynamic goals of intraoperative management of the pregnant patient with mitral stenosis?
C.4. What anesthetic technique would you use for this emergency cesarean section?
C.5. How would you manage local anesthetic systemic toxicity (LAST) in this patient?
C.6. If cardiac arrest were to occur prior to delivery, how would you proceed?
C.7. What technique could you use for general anesthesia in this patient?
C.8. If you are unexpectedly unable to intubate this patient, how would you manage the airway?
C.9. Would this patient benefit from the use of β-blockers?
C.10. What is the effect of the inhalation agents on uterine

contractility?
C.11. What is the Apgar scoring system?
C.12. What is the significance of Apgar scores?
C.13. At birth, what should be done to minimize an infant's risk of meconium aspiration syndrome?
C.14. If the Apgar score of the newborn is 3 at 1 minute, how would you treat the newborn?
C.15. Blood gases are sent immediately after delivery. What are the normal values for umbilical vein and artery blood gases?
D. Postoperative Management
D.1. Immediately after the baby is delivered, the mother's oxygen saturation decreases. What is the differential diagnosis?
D.2. Additional bleeding occurs in the postanesthesia care unit, and the obstetrician diagnoses retained placenta. What, if any, antibiotics are indicated to prevent endometritis after manual extraction of retained placenta?
30 Appendectomy for a Pregnant Patient 648
A. Medical Disease and Differential Diagnosis
A.1. What is the differential diagnosis for acute abdomen in the pregnant patient?
Medical Conditions
Obstetric Conditions
Gynecologic Conditions
Surgical Conditions
A.2. How would you make the clinical diagnosis of acute appendicitis?
A.3. What is the incidence of surgery during pregnancy? What is the incidence of appendicitis during pregnancy?
A.4. What is the incidence of gangrenous appendix/peritonitis during pregnancy, and is this incidence higher in pregnant than in nonpregnant women?
A.5. What are the main concerns associated with nonobstetric surgery in the pregnant patient?
A.6. What are the factors influencing teratogenicity from anesthetic agents in humans?
A.7. Are there any specific concerns regarding neurotoxicity and cognitive development in the developing fetus?

A.8. What factors influence fetal oxygenation, and how would you prevent intrauterine fetal asphyxia?
A.9. What is the incidence of trauma during pregnancy, and what are the risks to the mother and the fetus secondary to trauma?
A.10. What are other common surgeries performed during pregnancy?
B. Preoperative Evaluation and Preparation
B.1. Preoperatively, what would you discuss with this patient? Are any additional medical consultations warranted?
B.2. Is there a difference in the goal of anesthesia for delivery and for nonobstetric surgery in a pregnant patient?
B.3. How would you premedicate this patient?
C. Intraoperative Management
C.1. What factors would alter your anesthetic technique from that used for a nonpregnant patient?
Cardiovascular System
Respiratory System
Gastrointestinal System
Central Nervous System
Airway, Skin, and Mucous Membranes
C.2. If you choose epidural anesthesia, describe your technique and dosage.
C.3. If the patient needs supplemental analgesia, what would be your choice?
C.4. What vasopressor would you choose to improve uteroplacental perfusion?
C.5. When this patient arrived in the operating room, she desired a general anesthetic. Describe your technique.
C.6. Does any controversy exist surrounding the use of nitrous oxide?
C.7. Does any controversy exist surrounding operating room personnel, anesthetic exposure, and pregnancy outcomes?
C.8. What is the impact of nonobstetric surgery on maternal mortality, birth defects, and fetal loss? What factors influence it?
C.9. Should intraoperative fetal heart rate (FHR) monitoring be used? What would you expect to see on the electronic fetal monitor during anesthesia?

C.10. How would your anesthetic management differ if the patient were having upper extremity surgery?
C.11. The surgeon schedules the procedure to be performed laparoscopically. Does this pose any additional problems?
D. Postoperative Management
D.1. When would you extubate this patient?
D.2. Postoperatively, what monitors would you use?
D.3. What other postoperative precautions would you take? What is the incidence of preterm delivery following nonobstetric surgery during pregnancy?
D.4. The next day, the patient went into premature labor and now needs a cesarean section for prematurity and breech presentation. She requires another general anesthetic. In what way would your technique differ from your previous anesthetic technique?

SECTION 8 The Hematologic System

31 Hemophilia and Disorders of Coagulation
A. Medical Disease and Differential Diagnosis
A.1. Describe the various laboratory tests that evaluate the coagulation cascade and the specific components measured by each.
A.2. What is the difference between platelet adhesion, activation, and aggregation at sites of vascular injury?
A.3. Describe the physiologic events that occur following endothelial interruption in the blood vessel.
A.4. What factors prevent the extension of a clot beyond the site of injury?
A.5. Describe the factors involved in the extrinsic, intrinsic, and common coagulation cascade.
A.6. Describe the typical presentation history and pathophysiology associated with von Willebrand disease (vWD).
A.7. Explain the pathophysiology, frequency, and treatment of significant rare disorders of coagulation (factor VII [FVII], factor XII [FXII], and fibrinogen).
A.8. Differentiate between hemophilia A, B, and C.
A.9. What are the differences in factor replacement therapy between patients with hemophilia A and hemophilia B?
A.10. What is acquired hemophilia?

A.11. Which plasma protein is important in maintaining normal levels of factor VIII (FVIII)?
A.12. How are patients with severe hemophilia managed in the outpatient setting?
A.13. Describe the levels of FVIII necessary to maintain hemostasis in patients with spontaneous or surgical bleeding.
B. Preoperative Evaluation and Preparation
B.1. What steps would you take to normalize this patient's coagulation status before surgery?
B.2. What is meant by 1 unit of FVIII clotting activity, and how much does 1 unit of FVIII clotting activity per kilogram of body weight increase FVIII concentrations?
Approach 1
Approach 2
Plasma Volume Calculation
B.3. Would you administer FVIII using a bolus or infusion technique?
B.4. Can hemophiliac patients fail to mount an appropriate coagulation response following FVIII infusion?
B.5. If a patient with hemophilia does not respond to a bolus injection of FVIII, can an infusion technique be effective?
B.6. How much FVIII activity is present in plasma? What are the risks associated with plasma administration?
B.7. What are the indications for the administration of plasma?
B.8. What is cryoprecipitate, and how is it prepared? How much FVIII activity is present in cryoprecipitate? When is cryoprecipitate indicated?
B.9. Describe the advantages and disadvantages of the products that are available for repletion of FVIII activity.
B.10. What is the role of desmopressin (D-amino D-arginine vasopressin [DDAVP]) for hemostatic management in this patient?
B.11. What is the role of antifibrinolytic therapy in the perioperative period for the patient with hemophilia? What are examples of antifibrinolytics used in the treatment of hemophilia?
B.12. What are the options for operative treatment of patients with acquired hemophilia? Describe the mechanism of action and dosing considerations for each of these therapies.

C. Intraoperative Management
C.1. Is it safe to administer an intramuscular injection to this patient before surgery?
C.2. Would an axillary block be appropriate for this patient?
C.3. If general anesthesia is used, would it be safe to intubate the patient's trachea?
C.4. Would you use any special precautions for this patient who is positive for HIV?
C.5. What special considerations should be taken in choosing anesthetic drugs for this patient?
C.6. During an operative procedure, if the surgeon indicates that significant blood loss is occurring, would you transfuse this patient with packed red blood cells (RBCs) or whole blood?
C.7. During the transfusion of the first unit of whole blood, the patient's temperature rose from 36.8°C to 37.9°C (98.2°F to 100.2°F). What immediate steps should be taken by the anesthesiologist at this time?
C.8. Does giving blood intraoperatively increase the potential for the development of FVIII inhibitors?
C.9. Can FVIII be safely administered to patients who have developed circulating inhibitors?
C.10. The surgeon has requested the use of a tourniquet to minimize surgical bleeding. What are the physiologic and hemodynamic responses to tourniquet use?
C.11. Is it appropriate to suction the endotracheal tube and oropharynx of this patient before extubation?
D. Postoperative Management
D.1. What special consideration should be given to postoperative pain management for this patient?
D.2. What steps should be taken to enhance the coagulation status of this patient in the postoperative period while at home?
D.3. Can this patient be treated with FVIII supplements using home infusion?
Acknowledgment
32 Sickle Cell Disease
A. Medical Disease and Differential Diagnosis
A.1. What was the most likely underlying medical condition in this

patient? How would you confirm the diagnosis of sickle cell anemia (SCA)?
A.2. What is sickle cell disease (SCD)?
A.3. What is sickle cell trait (SCT)?
A.4. What are some of the other common hemoglobinopathies and what are their clinical features?
A.5. What are the clinical features of SCD?
A.6. Describe the different types of sickle cell crises.
A.7. Discuss the pathophysiologic effects of SCD.
A.8. What is acute chest syndrome?
B. Preoperative Evaluation and Preparation
B.1. What preoperative evaluation and testing would you perform on this patient prior to anesthesia? Would you ask for a hematology consult, and what question(s) would you ask?
B.2. What preoperative instructions would you give this patient prior to being admitted to the hospital? How would you prepare this patient for general anesthesia and regional anesthesia?
B.3. Discuss the indications for perioperative exchange transfusion in this patient.
B.4. What are the indications for blood transfusion in SCD?
Acute conditions
Chronic conditions
C. Intraoperative Management
C.1. Discuss the anesthetic management for this patient. Discuss both regional and general anesthesia considerations.
C.2. Discuss how the comorbidities associated with SCD can affect your anesthetic management.
C.3. What precautions should one take to prevent sickling in this patient?
C.4. Discuss what issues or concerns should be brought up by the team during the debrief at the conclusion of the case. What would you sign-out to the postanesthesia care unit (PACU) staff?
D. Postoperative Management
D.1. Discuss the postoperative management of this patient. What opioid sparing techniques can you use and discuss a multimodal analgesic plan?
D.2. What complications might occur in this patient in the

immediate postoperative period?
D.3. What is the treatment of sickle cell crisis?
D.4. What is the role of hyperbaric oxygen therapy in treatment of sickle cell crisis?
SECTION 9 Eye, Ear, Nose, and Throat
33 Airway Trauma
A. Medical Disease and Differential Diagnosis
A.1. What variables mitigate injury from motorcycle collisions?
A.2. What other significant trauma may be present?
A.3. How is the initial assessment of a trauma patient organized?
A.4. How would you evaluate airway and breathing?
A.5. How would you evaluate the circulation?
A.6. How would you evaluate mental status and neurologic condition?
A.7. What diagnostic tests are indicated for this patient based on the mechanism of injury?
A.8. What are the zones of the neck, and what is their clinical significance?
A.9. What immediate treatment is necessary before diagnostic studies?
A.10. When and where should the impaling object be removed?
B. Preoperative Evaluation and Preparation
B.1. What laboratory tests would you want?
B.2. What x-ray studies are most important to the anesthesiologist?
B.3. Is an electrocardiogram (ECG) necessary?
B.4. Should this patient be intubated before going for computed tomography (CT) scanning?
B.5. When and where should this patient’s airway be managed?
B.6. Are any prophylactic medications indicated?
C. Intraoperative Management
C.1. What monitors would you use? Is invasive monitoring necessary before definitive airway control?
C.2. What is the surgical approach to a zone I neck injury?
C.3. Is the patient likely to require tube thoracostomy? Should this be placed before managing the airway?
C.4. What are the options for managing this patient’s airway?
C.5. What are the risks of rapid sequence induction in this patient?

C.6. What anesthetic agents would you use for a rapid sequence induction?
C.7. How can you minimize the risk of exacerbating cervical spine trauma?
C.8. How can you minimize the risks of aspiration?
C.9. How would you anesthetize the airway for an awake intubation?
C.10. What are the risks of awake fiberoptic intubation?
C.11. If the patient cannot be ventilated, what options are available?
C.12. Would a laryngeal mask airway (LMA) or other pharyngeal airway be of assistance?
C.13. What surgical airway options are available in this case?
C.14. What maintenance anesthetics are indicated or contraindicated in this patient?
C.15. What complications will the surgical plan introduce?
D. Postoperative Management
D.1. What are the criteria for extubation?
D.2. What techniques may be used during extubation?
D.3. How does alcohol abuse affect postoperative management?
D.4. What pain medication should be used?
34 Open-Eye Injury and Cataract Surgery
A. Medical Disease and Differential Diagnosis
A.1. Why is this patient a particular challenge to the anesthesiologist?
A.2. What are the determinants of intraocular pressure (IOP) under normal circumstances? What is the normal range? What was the expected IOP in this patient's injured eye?
A.3. How is aqueous humor formed and eliminated?
A.4. How is IOP affected by arterial PCO_2, systemic blood pressure, coughing and vomiting, deep inspiration, and hypoxemia?
A.5. What is the role of the central nervous system (CNS) on IOP?
A.6. What is glaucoma?
A.7. Is atropine contraindicated in patients with glaucoma?
A.8. How do carbonic anhydrase inhibitors work to decrease IOP? By what mechanism may osmotic agents decrease IOP?
A.9. Are carbonic anhydrase inhibitors or osmotic diuretics

indicated in open-globe injuries?
A.10. Are topically applied ophthalmic medications absorbed systemically? How can this absorption be reduced? Which eyedrops may have effects that are of concern to the anesthesiologist?
Atropine
Scopolamine
Cyclopentolate (Cyclogyl)
Tropicamide (Mydriacyl)
Phenylephrine Hydrochloride (Neo-Synephrine)
Epinephrine
Timolol Maleate (Timoptic)
Betaxolol Hydrochloride (Betoptic)
Acetylcholine
Echothiophate Iodide (Phospholine Iodide)
Cocaine
B. Preoperative Evaluation and Preparation
B.1. Is an open-globe injury always a surgical emergency?
B.2. What preoperative evaluation would you require?
B.3. The patient ate shortly before the accident. Would you attempt to pass a nasogastric tube or to administer emetics to empty the stomach?
B.4. Could this case be done with topical anesthesia or a retrobulbar block?
B.5. How would you premedicate this patient?
C. Intraoperative Management
C.1. What are some factors that may increase the risk of vitreous herniation during induction and maintenance of anesthesia?
C.2. Will you intubate this patient? Would you consider a laryngeal mask airway? How does intubation affect IOP? How can this effect be minimized?
C.3. Would you consider an awake intubation?
C.4. Is succinylcholine contraindicated in open-globe injuries? How does succinylcholine affect IOP?
C.5. Does pretreatment with nondepolarizing muscle relaxants prevent the succinylcholine-induced elevation in IOP?
C.6. How do nondepolarizing muscle relaxants affect IOP?

C.7. How will you perform a rapid sequence induction and intubation without using succinylcholine?
C.8. What are the effects of ketamine on the eye?
C.9. Would you consider the use of etomidate as an induction agent? What about propofol?
C.10. How do inhalation agents affect IOP and by what mechanism?
C.11. During the procedure, the patient's pulse suddenly dropped to 40 beats per minute. What do you think was happening? What is the oculocardiac reflex (OCR)?
C.12. What are the afferent and efferent pathways of the OCR?
C.13. What factors contribute to the incidence of the OCR?
C.14. How do you diagnose and treat the OCR?
C.15. Is atropine useful for the OCR?
C.16. Can a retrobulbar block prevent the OCR? Is it appropriate in this patient?
D. Postoperative Management
D.1. Would you reverse the neuromuscular blockade in this patient?
D.2. Do reversal doses of atropine affect IOP?
D.3. What would you do before extubating this patient?
D.4. When would you extubate this patient?
D.5. The patient awakened in the recovery room and complained of pain and tearing in the opposite eye. The conjunctiva was inflamed. What was the likely cause?
D.6. Will taping the eyes shut or applying ointment prevent corneal abrasions? Are there any contributing factors?
D.7. What should you do when you suspect your patient might have a corneal abrasion?
D.7. A month after the surgical repair, the patient complained of impaired vision in the operative eye. He was examined and found to have a detached retina. As part of the surgical treatment, the ophthalmologist injected a gas bubble into the patient's posterior chamber. Why is this important to an anesthesiologist?
E. Anesthesia for Cataract Surgery
E.1. What is a cataract?
E.2. What are the causes and risk factors of cataract formation?

E.3. How would you conduct the preoperative medical evaluation for a patient having cataract surgery?
E.4. What is the cardiac risk for this patient? If this patient is on anticoagulation and/or antiplatelet medications, should he stop or continue these medications?
E.5. What are the anesthetic options for cataract surgery?
E.6. What is the postoperative course after cataract surgery?
35 Laser Treatment for Laryngeal Lesions
A. Medical Disease and Differential Diagnosis
A.1. What is the cause of RRP?
A.2. What is the usual presentation of RRP?
A.3. How do you diagnose RRP?
A.4. What are the available treatment options for RRP?
A.5. What are common adverse effects of α-interferon therapy?
A.6. What is the differential diagnosis of hoarseness in this child?
B. Preoperative Evaluation and Preparation
B.1. What are the key points of the preanesthetic history and physical examination in this patient?
B.2. What preoperative laboratory tests are necessary?
B.3. How should this child be premedicated before coming to the operating room?
B.4. What are the special anesthetic considerations prior to inducing anesthesia in this patient?
C. Intraoperative Management
C.1. What is a laser, and how does it work?
C.2. What are the characteristics of laser radiation?
C.3. Discuss some advantages associated with the use of lasers for laryngeal surgery.
C.4. What are some disadvantages of lasers compared with microdebriders?
C.5. How would you protect the external surface of a conventional endotracheal tube (ETT) for use during laser microlaryngoscopy?
C.6. What special ETTs are available for laser surgery?
C.7. How would you manage an airway fire?
C.8. What is the Venturi effect?
C.9. What is Venturi jet ventilation?
C.10. How would you institute and maintain manual jet ventilation?

C.11. How is anesthesia maintained during jet ventilation?
C.12. What are the complications of jet ventilation?
C.13. Are there contraindications for the use of jet ventilation?
C.14. Discuss airway management options during laryngeal papilloma resection.
C.15. How would you plan to monitor this patient?
C.16. How would you induce anesthesia for an intermittent apnea technique?
D. Postoperative Management
D.1. What are the common postoperative complications?
SECTION 10 Pediatrics
36 Tracheoesophageal Fistula
A. Pathophysiology and Differential Diagnosis
A.1. What is the diagnosis? What are the clinical features of this disease?
A.2. What is the pathophysiology of this disease?
A.3. Describe the normal development of the trachea and esophagus.
A.4. How are tracheoesophageal fistula (TEF) and esophageal atresia (EA) inherited?
A.5. How are the different types of TEF/EA classified?
A.6. What other problems may this child have, and when should these be investigated?
A.7. What should the parents be told regarding perioperative risk? Risk of recurrence?
B. Preoperative Evaluation and Preparation
B.1. What laboratory workup should be obtained before surgery?
B.2. Describe management in the NICU before surgery.
B.3. How is severe lung disease managed before repair?
B.4. Should this patient be intubated preoperatively for airway protection?
C. Intraoperative Management
C.1. What invasive lines and monitoring are appropriate before induction? After induction?
C.2. Discuss fluid and temperature management for this baby.
C.3. What are the options regarding induction and intubation?
C.4. What is the role of rigid and fiberoptic bronchoscopy in this

patient prior to incision?
C.5. Describe the steps of an open repair of EA/TEF.
C.6. What are common intraoperative problems, and how can they be managed?
C.7. If the surgeon decides to proceed thoracoscopically, how will you perform your anesthetic? Is one-lung ventilation required? What are some complications unique to thoracoscopy in the newborn?
D. Postoperative Management
D.1. When should the baby be extubated?
D.2. What options are available for postoperative analgesia?
D.3. What are early and late complications of TEF repair?
37 Congenital Diaphragmatic Hernia
A. Medical Disease and Differential Diagnosis
A.1. What differential diagnoses are compatible with these signs and symptoms?
A.2. Describe the incidence and classification of congenital diaphragmatic hernia (CDH).
A.3. What are the causes of hypoxemia in patients with CDH?
A.4. How do you assess the severity of pulmonary hypoplasia?
A.5. How do you make a diagnosis of right-to-left shunting through the patent ductus arteriosus?
A.6. What other congenital anomalies are usually associated with CDH?
B. Preoperative Evaluation and Preparation
B.1. How would you interpret the following arterial blood gas analyses: pH, 7.20; $PaCO_2$, 55 mmHg; PaO_2, 35 mmHg; and CO_2 content, 19 mEq per L? How would you correct them?
B.2. What immediate treatment should be given to improve the newborn's respiratory status preoperatively?
B.3. Should CDH be repaired urgently once the diagnosis is made and confirmed?
B.4. What are the effects of nitric oxide (NO) on pulmonary and systemic circulation?
B.5. What is the current role of extracorporeal membrane oxygenation (ECMO) in the management of CDH?
C. Intraoperative Management

C.1. What monitors would you use for this neonate during surgery?
Respiratory
Cardiovascular
Thermoregulatory
C.2. How would you induce and maintain anesthesia?
C.3. Would you use nitrous oxide for anesthesia? Why?
C.4. How would you ventilate the patient?
C.5. Is the infant with CDH more at risk from hypothermia?
C.6. The surgeon returned the intrathoracic stomach and intestine to the peritoneal cavity and the ipsilateral lung was found to be hypoplastic and collapsed. The resident anesthesiologist tried to expand the collapsed lung manually with positive airway pressure. Five minutes after the abdomen was closed, the blood pressure suddenly dropped from 70/40 to 30/20 mmHg, the heart rate from 150 to 80 beats per minute, and the pulse oximeter from 95% down to 60% saturation. What would you immediately do?
C.7. Discuss fluid therapy in this patient.
C.8. At the conclusion of surgery, would you extubate the patient in the operating room?
D. Postoperative Management
D.1. What is the mortality rate in patients with CDH? What postoperative problems would you expect in this patient?
38 Tetralogy of Fallot
A. Medical Disease and Differential Diagnosis
A.1. What is TOF?
Tetralogy of Fallot with Pulmonary Stenosis
Tetralogy of Fallot with Pulmonary Atresia
Tetralogy of Fallot with Absent Pulmonary Valve
A.2. What is the pathophysiology of TOF/PS?
A.3. What is shunting, and how is Q_P:Q_S calculated?
A.4. What is the pathophysiology of TOF with pulmonary atresia?
A.5. How is SaO_2 determined in single ventricle physiology?
A.6. What is a “pink Tet”?
A.7. What are hypercyanotic spells? How are they treated?
A.8. What palliative surgical procedures are available for treating patients with TOF/PS?
A.9. What palliative catheter-based procedures are available for

patients with TOF?
A.10. What definitive surgical procedures are available for treating patients with TOF/PS?
A.11. What palliative and definitive surgical procedures are available for patients with TOF with pulmonary atresia?
A.12. What are the long-term outcomes of patients with TOF?
B. Preoperative Evaluation and Preparation
B.1. What preoperative history and physical examination information do you want?
B.2. Which other abnormalities need to be considered in this patient?
B.3. What premedication will you give to a child with congenital heart disease?
C. Intraoperative Management
C.1. How will you induce anesthesia in this patient if intravenous (IV) access cannot be obtained?
C.2. Why would end-tidal carbon dioxide ($EtCO_2$) monitoring be of particular use in a patient with TOF/PS?
C.3. What is near-infrared spectroscopy (NIRS) and what does it measure?
C.4. What are the important management issues during creation of a palliative shunt?
C.5. What is the effect of inhalation anesthetics on airway reflexes, myocardial contractility, systemic vascular resistance (SVR), and pulmonary vascular resistance (PVR) in children?
C.6. What are the pre-cardiopulmonary bypass (pre-CPB) anesthetic goals for a patient undergoing definitive surgical correction of TOF/PS?
C.7. What interventions will reliably reduce PVR?
C.8. How does heparin administration and activated coagulation time (ACT) monitoring for CPB differ in children as compared with adults?
C.9. How is heparin reversed?
C.10. What is the incidence of protamine reactions in children?
C.11. What is the role of transesophageal echocardiography (TEE) in this patient?
C.12. What effect would a residual ventricular septal defect (VSD)

have in this patient following separation from CPB?
D. Postoperative Management
D.1. How should postoperative ventilation be managed in this patient following placement of a transannular patch for TOF/PS?
D.2. Following complete repair of TOF/PS in an infant, what SaO_2 is acceptable?
D.3. Following placement of a modified Blalock-Taussig shunt (MBTS) for TOF/PS in an infant, what SaO_2 is acceptable?
D.4. What is junctional ectopic tachycardia (JET)?
39 Transposition of the Great Arteries
A. Medical Disease and Differential Diagnosis
A.1. What defines the cardiac situs?
A.2. What is transposition of the great arteries (D-TGA)?
A.3. What additional cardiac lesions are associated with D-TGA?
A.4. What is the natural history of D-TGA?
A.5. What is the pathophysiology of D-TGA?
A.6. What determines the oxygen saturation in patients with D-TGA?
A.7. Why did this infant have reverse differential cyanosis?
A.8. What are the preoperative issues pertaining to the coronary arteries in D-TGA?
A.9. What are the clinical subsets of D-TGA?
A.10. What is the differential diagnosis of D-TGA and how is the diagnosis made?
A.11. What preoperative interventions can help stabilize a patient with D-TGA?
Intact Ventricular Septum
Ventricular Septal Defect
Ventricular Septal Defect and Left Ventricular Outflow Tract Obstruction
Pulmonary Artery Hypertension
A.12. What are the surgical options for repair? Why is one chosen over the others?
Arterial Anatomic Repair: Arterial Switch (Jatene) Operation
Intra-atrial Physiologic Repairs: Mustard and Senning Procedures
Rastelli, LeCompte, and Nikaidoh Procedures
B. Preoperative Evaluation and Preparation

B.1. What information is important to prepare for this case?
B.2. What are the anesthetic goals before cardiopulmonary bypass (CPB)?
B.3. What is the plan for glucose management in this patient?
C. Intraoperative Management
C.1. How would you monitor this infant?
C.2. What would be the best method of induction for this patient?
C.3. Is CPB in infants and children different from adults?
C.4. What is modified ultrafiltration (MUF)?
C.5. Briefly describe the surgical techniques of the Mustard/Senning, ASO, and Rastelli procedures.
Intra-atrial Physiologic Repairs: Mustard and Senning Procedures
Arterial Anatomic Repair: Arterial Switch (Jatene) Operation
Rastelli Procedure
C.6. What is hypothermia, and how is it classified? What is low-flow cardiopulmonary bypass (LFCPB)? What is deep hypothermic circulatory arrest (DHCA)?
C.7. Why is hypothermia beneficial to the brain during LFCPB and DHCA?
C.8. Explain the difference between α-stat and pH-stat blood gas management.
C.9. What are the immediate post-CPB issues following ASO?
D. Postoperative Management
D.1. How is myocardial ischemia addressed in the intensive care unit (ICU) following the ASO?
D.2. What immediate postoperative problems would be anticipated following the Rastelli procedure?
D.3. What intermediate and long-term surgical problems are seen after ASO?
D.4. What are the long-term outcomes after ASO?
D.5. What are the long-term outcomes after Rastelli repair for patients with D-TGA with left ventricular outflow tract (LVOT) obstruction?
D.6. What is long-term neurologic outcome like after ASO?
40 Pyloric Stenosis
A. Medical Disease and Differential Diagnosis
A.1. What is the diagnosis in this patient?

A.2. What is the differential diagnosis of pyloric stenosis?
A.3. What are the metabolic problems in this newborn secondary to his disease?
A.4. What are the adverse effects of metabolic alkalosis?
A.5. How would you treat this infant?
Supportive Therapy
Fluids
Electrolytes
Prevention of Aspiration
Diagnostic Tests
Surgery
A.6. How would you determine fluid replacement in a newborn, and what fluids would you use?
Maintenance Fluids
Electrolytes
Correction of Deficits
Replacement of Losses
A.7. How would you correct the metabolic alkalosis in this patient?
A.8. What causes a cardiac murmur?
B. Preoperative Evaluation and Preparation
B.1. How would you evaluate this patient preoperatively?
History
Physical Examination
Laboratory Findings
B.2. How would you evaluate a heart murmur?
B.3. How would you differentiate between functional versus organic murmur?
B.4. What are the types of VSD? What type of shunt do they cause?
B.5. What are the risks of surgery and anesthesia in a patient with VSD?
B.6. How would you prepare this patient rapidly for emergency surgery? Is surgical intervention an acute emergency in this case?
B.7. How would you prepare this patient for anesthesia?
C. Intraoperative Management
C.1. What induction–intubation sequence would you use?
C.2. What are the anatomic characteristics of the airway in the newborn and how do they differ from those in the adult?

C.3. How do you determine the size of an endotracheal tube in a pediatric patient?
C.4. What anesthesia system would you use and why?
C.5. What are the advantages and the disadvantages of commonly employed nonrebreathing systems?
C.6. How would you monitor this patient intraoperatively?
C.7. How does the pulse oximeter function?
C.8. What factors affect the measurement of oxygen saturation by the pulse oximeter?
D. Postoperative Management
D.1. What are the complications that can occur in the postanesthesia recovery period?
D.2. How would you treat postextubation “croup” in this infant?
41 Inflammatory Airway Disease in Childhood: Laryngotracheobronchitis
A. Medical Disease and Differential Diagnosis
A.1. What portion of the airway is affected in the croup syndrome and why?
A.2. What is stridor?
A.3. How does stridor correlate with anatomic location?
A.4. Define croup. What is the clinical presentation of laryngotracheitis?
A.5. What is the differential diagnosis of acute upper airway obstruction in children?
A.6. What is bacterial tracheitis?
A.7. What congenital problems can mimic features of croup?
A.8. How is the severity of croup assessed?
A.9. What is the medical management of croup? Does this have implications for the anesthesiologist?
A.10. What is epiglottitis? What are its common causes? What is the incidence?
A.11. What are the clinical manifestations of epiglottitis?
A.12. How is the diagnosis of epiglottitis made?
A.13. What is postextubation croup? How is it managed?
A.14. What are the nonacute causes of partial airway obstruction in children?
Extrinsic Pathologies

Intrinsic Pathologies
B. Preoperative Evaluation and Preparation
B.1. Is intubation always required in children with epiglottitis?
B.2. Why is general anesthesia administered to a child with epiglottitis?
B.3. How would you prepare the patient for anesthesia?
C. Intraoperative Management
C.1. How is the airway of the child with epiglottitis best secured?
C.2. How would you induce anesthesia?
C.3. Should a child with epiglottitis undergo a rapid sequence induction?
C.4. Is awake intubation a practical alternative to secure the patient's airway?
C.5. What would you do if the airway cannot be secured with intubation?
C.6. Should this patient have a nasotracheal or orotracheal tube placed?
C.7. Shortly after intubation, frothy secretions were obtained on suctioning the endotracheal tube. What is the reason for this? How can this be treated?
D. Postoperative Management
D.1. How long should this patient remain intubated? What criteria determine extubation time?
D.2. How would you make this patient comfortable during the course of intubation?
D.3. What outcome can one expect for the child with acute epiglottitis?
42 Cleft Palate
A. Medical Disease and Differential Diagnosis
A.1. Describe the anatomic concept of a cleft palate and a cleft lip.
A.2. What is the cause of a cleft lip or a cleft palate?
A.3. What is the incidence of a cleft lip and a cleft palate?
A.4. Discuss the pathophysiology of a cleft lip and palate in the neonate and the older child (e.g., age >5 years).
A.5. What other conditions are associated with a cleft lip and a cleft palate?
A.6. What is Pierre Robin syndrome?

A.7. What is Treacher Collins syndrome?
A.8. What kind of specialized team care would these patients need?
A.9. Discuss indications and timing of closure of cleft lip and palate.
A.10. What is velopharyngeal incompetence, and how can it be diagnosed?
A.11. What is the relation of tonsillectomy and adenoidectomy to velopharyngeal incompetence?
B. Preoperative Evaluation and Preparation
B.1. What information do you need before closure of a cleft lip and palate?
B.2. What preoperative orders are needed?
C. Intraoperative Management
C.1. What monitors will you need for cheiloplasty and palatoplasty?
C.2. Discuss the induction and the anesthetic management for cleft lip and palate.
C.3. What positioning is recommended for cleft palate repair surgery?
C.4. What are the reported complications of this type of surgery and anesthesia?
C.5. Briefly describe the surgical techniques used to repair cleft defects.
C.6. How does a pharyngeal flap affect anesthetic management or any subsequent anesthetic administered to this patient?
C.7. What is an Abbe flap? What are its anesthetic implications?
C.8. What is the crucial problem of anesthesia for cleft palate? What are the unique considerations of this surgical repair?
C.9. What is laryngospasm? How would you make a diagnosis of laryngospasm?
C.10. How would you manage the patient with laryngospasm?
D. Postoperative Management
D.1. What complications of cleft lip and cleft palate surgery may be seen in the recovery room?
D.2. How do you protect the airway postoperatively?
D.3. How would you control postoperative pain in patients following a cleft lip and cleft palate repair?

43 Congenital Heart Disease with a Cervical Mass in Infancy
A. Medical Disease and Differential Diagnosis
A.1. What is 22q11 deletion syndrome?
A.2. What are the associated cardiovascular defects in 22q11 deletion syndrome?
A.3. What are the metabolic and endocrine abnormalities in patients with 22q11 deletion syndrome and the attendant manifestations?
A.4. What are the immunologic findings in 22q11 deletion syndrome?
A.5. What is the differential diagnosis of cervical masses in infancy?
A.6. What is a cystic hygroma? What are the complications? What is the treatment?
A.7. What is the IAA anomaly?
A.8. What is the pathophysiology of the IAA syndrome?
A.9. How is ductal patency maintained?
A.10. What are the side effects of prostaglandin infusion?
A.11. What is the hyperoxia test?
B. Preoperative Evaluation and Preparation
B.1. What preoperative studies should be obtained to evaluate the neck mass?
B.2. How would you categorize the difficult airway in children?
B.3. What features of the difficult airway can be noted on physical examination?
B.4. How would you preoperatively optimize the ability to secure the airway in the operating room?
B.5. What laboratory studies are necessary before surgery?
B.6. What are the causes of heart failure (HF) in the infant? How would you assess this infant in your preoperative evaluation for signs of HF?
B.7. How would you optimize the preoperative treatment of HF?
B.8. How would you premedicate this infant?
B.9. When is premedication useful in infants and children?
B.10. Before the planned surgery, the infant is scheduled for a magnetic resonance imaging (MRI) scan. You are asked to ensure that the baby remains immobile for 20 minutes to perform the scan

adequately. How would you accomplish this?
C. Intraoperative Management
C.1. What anesthesia equipment, circuit, and monitors would you use?
C.2. Describe techniques other than direct laryngoscopy that would be useful for securing the airway in this baby.
Infant Video Laryngoscope
Intubation through a Laryngeal Mask Airway
Retrograde Cricothyroid Wire
Blind Nasal Intubation
Nasal Intubation with Laryngoscope and Magill Forceps
Fiberoptic Intubation
C.3. How would you monitor blood loss in this patient?
C.4. What anesthetic technique should be used in a patient who may experience severe loss of blood intraoperatively?
C.5. How would you induce and maintain anesthesia in this neonate?
C.6. Intraoperatively, the surgeon must dissect the tumor in the anterior mediastinum and needs to have a quiet surgical field. How would you accomplish this in the infant?
D. Postoperative Management
D.1. How would you manage this patient postoperatively?
44 Patent Ductus Arteriosus and Prematurity
A. Medical Disease and Differential Diagnosis
A.1. How would you classify prematurity? What are the common problems associated with prematurity?
A.2. What are the survival rates of preterm infants?
A.3. What are the incidence and survival rates of respiratory distress syndrome (RDS)? Discuss its pathophysiology.
A.4. What is bronchopulmonary dysplasia (BPD)? How would you treat it?
A.5. What are apnea spells? What are the possible causes of apneic spells?
A.6. Discuss the incidence and pathophysiology of PDA in preterm infants.
A.7. How would you make a diagnosis of PDA? Describe its treatment.

A.8. Would you give digitalis to treat congestive heart failure in preterm infants? Why?
A.9. How does indomethacin close the ductus? What are the adverse effects of indomethacin?
A.10. When is surgical closure indicated? What are the complications associated with surgical ligation?
A.11. What is retinopathy of prematurity (ROP) (retrolental fibroplasia [RLF])? Discuss its etiology, pathophysiology, prognosis, prevention, and treatment.
A.12. Define neutral and critical temperatures. What are these values in the preterm neonate, in the term neonate, and in the adult? Discuss temperature regulation in the neonate.
B. Preoperative Evaluation and Preparation
B.1. How would you evaluate this patient preoperatively?
B.2. What are the normal values of arterial blood gases and pH in neonates and infants?
B.3. Interpret the arterial blood gases: pH, 7.30; $PaCO_2$, 60 mmHg; PaO_2, 49 mmHg; HCO_3^-, 20 mEq per L on 50% oxygen; and 6 cm H_2O of positive end-expiratory pressure (PEEP). How would you improve them?
B.4. What are the normal values of arterial blood pressure, heart rate, and respiratory rate for preterm infants?
B.5. What are the normal values of WBC, red blood cells (RBCs), hemoglobin, glucose, electrolytes, calcium, blood urea nitrogen, and creatinine for preterm infants?
B.6. Would you transfuse blood to this patient preoperatively?
B.7. How would you interpret the urinalysis: specific gravity, 1.005; sugar, 1+; and protein, 1+?
B.8. Would you correct a serum calcium level of 6.0 mg per dL? What other information would you like to have? Which contains more calcium, 10 mL of 10% calcium chloride or 10 mL of 10% calcium gluconate? Could you hyperventilate this child safely?
B.9. How would you premedicate this patient?
C. Intraoperative Management
C.1. Where should the procedure take place? In the neonatal intensive care unit (NICU) or the operating room?

C.2. What monitors would you use for this child during surgery?
C.3. How does the oxygen analyzer work?
C.4. What is the Doppler effect? How does the Doppler transducer measure blood pressure?
C.5. What is the mechanism of pulse oximetry? Why is it important to monitor arterial oxygen saturation? What levels of arterial oxygen saturation would you like to keep during surgery?
C.6. How would you maintain the patient's body temperature?
C.7. How do the anesthetic requirements of the preterm infant differ from those of the adult?
C.8. What size endotracheal tube would you have used if the patient had not been intubated?
C.9. How would you have induced anesthesia if the patient had not been intubated?
C.10. How would you maintain anesthesia?
C.11. How would you ventilate the patient? What tidal volume, respiratory rates, and FIO_2 would you set for the infant?
C.12. Discuss blood and fluid therapy in this preterm infant.
C.13. During dissection of the ductus arteriosus, the arterial oxygen saturation dropped from 92% to 80% and the heart rate decreased from 140 beats per minute to 80 beats per minute. What were the causes? How would you correct this situation?
D. Postoperative Management
D.1. Would you reverse the muscle relaxants and extubate the patient at the end of surgery?
D.2. How can one minimize the risk of transporting the patient to the NICU after surgery?
D.3. The patient's condition deteriorated postoperatively in the intensive care unit (ICU). Physical examination revealed persistent cardiac murmur. What was the possible diagnosis?
45 Post-tonsillectomy Hemorrhage
A. Medical Disease and Differential Diagnosis
A.1. Approximately how many pediatric tonsillectomies are performed in the United States each year? What are the indications for tonsillectomy?
A.2. What is the differential diagnosis for this patient?
A.3. What is the treatment for a patient with von Willebrand

disease?
A.4. Describe the vascular anatomy of the tonsils. What is the incidence of post-tonsillectomy hemorrhage?
A.5. What are the risk factors for post-tonsillectomy hemorrhage? Does age matter?
A.6. Describe the morbidity and mortality of post-tonsillectomy hemorrhage.
B. Preoperative Evaluation and Preparation
B.1. What is your approach to assessing this patient?
B.2. What will you set up in the operating room for this patient? How will your preparation be different from a routine general anesthetic set up?
B.3. Should you plan to use vasopressors?
B.4. The patient seems anxious. Will you administer a sedative to calm the patient down?
B.5. How do you plan on interpreting this patient's laboratory results?
B.6. What are your expectations of the surgeon, specifically as it relates to induction of anesthesia?
C. Intraoperative Management
C.1. What is your plan for induction of anesthesia? During the initial procedure, this patient underwent an uneventful inhalational induction, with postinduction intravenous (IV) placement. Would you perform an inhalational induction again? Why or why not?
C.2. What is your plan for management of blood in the oropharynx?
C.3. What is your plan for airway management?
C.4. Laryngoscopy and intubation prove challenging due to blood in the airway. What options do you have now?
C.5. What is your plan for maintenance of the anesthetic? What other medications might you want to give?
C.6. Assuming the surgical intervention is successful, what is your plan for emergence and extubation?
D. Postoperative Management
D.1. Is postoperative management in the pediatric intensive care unit (PICU) indicated?
D.2. What would you require for safe transport from the operating

room to the PICU?
D.3. Discuss potential postoperative complications for this patient.
D.4. What discharge instructions should be given post-tonsillectomy?
SECTION 11 Pain Management and Neuraxial Blocks
46 Brachial Plexus Block
A. Medical Disease and Differential Diagnosis
A.1. What are the presenting problems in this patient?
A.2. What additional medical history would you want to obtain?
A.3. What implications does the use of atenolol have on the patient's coexisting medical condition?
A.4. Why is immobilization of the arm important following humeral fracture?
A.5. What nerve is at particular risk for injury from humeral fracture?
B. Preoperative Evaluation and Preparation
B.1. What testing would be helpful to elucidate the cause of this patient's fainting spells?
B.2. What premedication would you order?
B.3. What are the respiratory effects of benzodiazepines?
C. Intraoperative Management
C.1. What anesthetic technique would you use?
C.2. Describe the relevant anatomy of the brachial plexus.
C.3. What relevant anatomic structures in the neck and below the neck can be injured or injected accidentally during brachial plexus block?
C.4. What regional technique would you choose to block the brachial plexus in this patient?
C.5. What are the advantages and disadvantages of the following blocks?
Interscalene Block
Supraclavicular Block
Infraclavicular Block
Axillary Block
C.6. Describe the landmarks and procedures for nerve stimulator and ultrasound-guided interscalene block.
C.7. Describe the landmarks and procedures for supraclavicular

block.
C.8. Describe the landmarks and procedures for infraclavicular block.
C.9. Describe the landmarks and procedures for axillary block.
C.10. The patient requests to have the brachial plexus block performed after you administer general anesthesia. Would you agree to this request?
C.11. What relevant respiratory complications or side effects are you concerned about in this patient?
C.12. What is the incidence of hemidiaphragmatic paresis following interscalene brachial plexus block? Can this complication be avoided by decreasing the volume or concentration of local anesthetic injected or by using ultrasound-guided supraclavicular block?
C.13. Describe the pulmonary function changes that occur after interscalene brachial plexus block.
C.14. What would you do if the patient complained of dyspnea after you performed an interscalene or supraclavicular block?
C.15. The surgeon prefers to perform the surgical procedure in the sitting position. What are the advantages and disadvantages of this position compared to the lateral position in this patient?
C.16. Which nerves are most commonly missed with axillary brachial plexus block? With interscalene block? With all brachial plexus blocks?
C.17. What is the expected duration of brachial plexus block with 30 mL of 1.5% mepivacaine with 5 μg per mL epinephrine?
C.18. What is the maximum safe dose of local anesthetic for brachial plexus block?
D. Postoperative Management
D.1. What regimen would you suggest for postoperative pain management?
D.2. In the postanesthesia care unit, the patient complains of dyspnea. How would you evaluate and manage this?
D.3. On the third postoperative day after removal of the brachial plexus catheter, the patient complains of persistent numbness and paresthesia in the ulnar nerve distribution. What would you tell the patient? How would you manage neurologic dysfunction after

brachial plexus block that persists for 1 week?
47 Nerve Blocks of the Lower Extremity
A. Preoperative Evaluation
A.1. What is the Glasgow Coma Scale and its significance in this patient?
A.2. Should surgery be allowed to proceed in this patient who has a subdural bleed?
A.3. Does the patient's atrial fibrillation need to be addressed prior to surgery, and if so, how?
B. Preoperative Preparation
B.1. What is dabigatran (Pradaxa)? How is its effect measured? How far in advance of elective surgery should it be stopped? Can its effect be reversed?
B.2. What concerns do you have regarding neuraxial anesthesia in this patient who has a subdural hematoma?
B.3. What concerns do you have regarding neuraxial anesthesia in this patient who has prior back surgery?
B.4. The surgeon is willing to wait a few days prior to surgery while the swelling around the injury decreases. When would you feel comfortable proceeding with surgery in this patient?
C. Intraoperative Management
C.1. What two nerve plexuses need to be blocked in this case? What nerve roots contribute to each plexus? Name the major nerves that come from each plexus.
C.2. What is the innervation to the medial and lateral aspects of the ankle? What nerves need to be blocked for his surgery?
C.3. What nerves are blocked with an ankle block? Would you do an ankle block in this case?
C.4. Explain the posterior landmark technique to blocking the lumbar plexus. What motor response would be elicited with a nerve stimulator? At what stimulation level would you feel safe injecting the patient? Why not at a lower level of stimulation? Can ultrasound guidance be utilized for this injection?
C.5. What is a fascia iliaca block (three-in-one block)?
C.6. Describe the different ultrasound approaches to blocking the saphenous nerve above the knee.
C.7. What benefits might a saphenous nerve block above the knee

provide compared to a femoral nerve block?
C.8. How would pain from a midthigh tourniquet dictate which peripheral nerve blocks to use in this patient? Describe the landmark technique of sciatic nerve block in the gluteal region. What is seen while performing an ultrasound technique to block the sciatic nerve?
C.9. Why does a popliteal nerve block have a high failure rate if performed too proximate to the popliteal fossa when using a landmark/nerve stimulator technique? Describe how this can be avoided when using ultrasound-based popliteal block.
C.10. What is the IPACK block? In what situations would this block be useful?
D. Postoperative Pain Management
D.1. Describe compartment syndrome and how that risk would influence your postoperative plan for peripheral regional analgesia.
D.2. How would the addition of dexamethasone to your local anesthetic influence the duration of the blocks placed in the OR?
D.3. What is liposomal bupivacaine?
D.4. What benefit would a peripheral nerve catheter provide over a long-acting local anesthetic? Are there any downsides?
D.5. You were able to perform a continuous spinal epidural (CSE) at L3–L4 and used 0.125% bupivacaine via epidural route for postoperative pain control. The patient reports that he is comfortable regarding both his back pain and his ankle pain. What benefit would continuing the patient's methadone confer in this case?
D.6. How can regional analgesia aid in fast-track postoperative care?
48 Complex Regional Pain Syndromes
A. Medical Disease and Differential Diagnosis
A.1. What is the differential diagnosis of pain in this patient?
A.2. What is complex regional pain syndrome (CRPS)?
A.3. What are the two types of CRPS?
A.4. What are the diagnostic criteria for CRPS? What is the incidence of this disease?
A.5. Define allodynia, hyperalgesia, hyperesthesia, and dysesthesia.
A.6. What are the stages of CRPS?

Stage I
Stage II
Stage III
A.7. What are the possible etiologies of CRPS?
A.8. Explain the pathophysiology of the development of CRPS.
A.9. Define sympathetically maintained pain (SMP) and sympathetically independent pain (SIP).
A.10. How does CRPS differ from neuralgia?
A.11. What is central pain? How will you differentiate central pain from CRPS?
A.12. Is the social history of this patient relevant to the development of chronic pain syndrome?
B. Pain Management
B.1. How will you work up CRPS types I and II?
B.2. Describe the sympathetic nerve supply to the arm?
B.3. Where is the stellate ganglion located?
B.4. What are the anatomic landmarks used in the stellate ganglion block?
B.5. What are the clinical signs of stellate ganglion block?
B.6. What is Horner syndrome?
B.7. After a stellate ganglion block, this patient reports no significant change in the degree of pain despite developing Horner syndrome. Is the pain psychogenic in this patient?
B.8. What types of nerve fibers are interrupted in stellate ganglion block?
B.9. What is a differential block?
B.10. What are the two major classes of local anesthetics? Describe the major differences in their clinical pharmacology.
B.11. What factors determine the onset, potency, and duration of a local anesthetic block?
B.12. How does the addition of epinephrine to commercially available premixed solutions affect the efficacy of local anesthetics?
B.13. How will you treat this patient?
B.14. What is the pharmacologic management of CRPS?
B.15. What is the role of intravenous regional block (Bier method) in diagnosis and treatment of CRPS?

B.16. Compare and contrast the mechanism of actions of ketamine and methadone.
B.17. What roles does ketamine infusion play in the treatment of CRPS? Is there a guideline for ketamine infusion in treating CRPS?
B.18. What is neuromodulation? What is the role of spinal cord stimulation (SCS) in treating CRPS?
B.19. What is the role of surgical sympathectomy?
B.20. What role does intrathecal (IT) therapy play in managing CRPS?
B.21. If opioids are prescribed as treatment for CRPS patients, what is the Centers for Disease Control and Prevention (CDC) guideline of chronic opioid therapy?
C. Complications
C.1 What are the complications of stellate ganglion block?
C.2 What is the systemic toxicity of local anesthetics?
Central Nervous System Effects
Cardiovascular Effects
C.3 How do you treat the systemic toxicity of local anesthetic drugs?
C.4 What are the possible complications of SCS?
C.5. What are the possible complications of IT therapy?
49 Cancer Pain
A. Medical Disease and Differential Diagnosis
A.1. What is the definition of pain?
A.2. How significant is the problem of pain in patients with cancer?
A.3. What are the components of cancer pain?
A.4. How does the pain contribute to the suffering of patients with cancer?
A.5. How do psychological factors affect pain in patients with cancer?
A.6. What are the causes of pain in patients with cancer?
A.7. How do you classify pin in patients with cancer?
A.8. What are the characteristics of pancreatic cancer pain?
A.9. How do you assess pain in patients with cancer?
A.10. What is the differential diagnosis of abdominal pain?
B. Pharmacologic Treatment of Pain
B.1. What is the World Health Organization stepladder approach

for cancer pain management?
B.2. What class of drugs does morphine sulfate belongs to?
B.3. What is the difference between morphine and synthetic opioids?
B.4. How does mixed opioid agonist/antagonist differ from opioid agonist?
B.5. Describe the role of methadone in the management of cancer pain.
B.6. What are the advantages and disadvantages of methadone?
B.7. What is the mechanism of action of opioids?
B.8. What are the side effects of opioid therapy?
B.9. Define tolerance and physical dependence.
B.10. How would you treat the side effects of opioid therapy?
B.11. What is tramadol? Is it an opioid?
B.12. When would you consider adjuvant analgesics as part of the treatment plan?
B.13. The patient and his family are worried about addiction. How would you approach this problem?
B.14. Describe different routes of opioid administration.
B.15. Describe advantages and complications of patient-controlled analgesia (PCA). What is minimum effective analgesic concentration (MEAC)?
B.16. What is meperidine? How is it different from other opioids?
B.17. What is rotation of opioids? When would you consider rotation of opioids?
C. Invasive Therapy
C.1. Describe the role of peripheral nerve blocks in cancer pain management.
C.2. Describe the role of celiac plexus block in cancer pain management.
C.3. What are the complications of celiac plexus block?
C.4. Would you consider neuraxial opioid infusion in this patient? Discuss complications of this procedure.
C.5. Which medications can be used intrathecally? What is ziconotide?
C.6. What is a Personal Therapy Manager (PTM), and what role does it play in neuraxial pain relief?

C.7. Would you consider neuraxial neurolysis in this patient to manage his pain? Discuss advantages and disadvantages of these blocks.
C.8. Which neuroablative procedures can be considered in the terminal stage of pancreatic cancer?
C.9. Describe the role of radiation therapy in cancer pain.
D. Nonpharmacologic Management
D.1. What are the various nonpharmacologic techniques of cancer pain management?
D.2. What physical modalities have been successfully tried in cancer pain management?
D.3. Describe the role of neuromodulation in cancer pain management.
D.4. What psychological techniques have been promoted for comfort care and pain relief?
D.5. What are distraction and reframing techniques? What is the role of hypnosis in cancer pain?
50 Low Back Pain and Sciatica
A. Medical Disease and Differential Diagnosis
A.1. How great an issue is low back pain in the general population?
A.2. What is the prevalence of low back pain?
A.3. What is the societal cost of low back pain?
A.4. What causes low back pain?
A.5. What are the risk factors for low back pain?
A.6. What are the potential sources of pain in the spine?
A.7. What is the anatomy of the intervertebral discs? What is the mechanism of pain from herniated discs?
A.8. What is the anatomy of the spinal facets? How do the facet joints cause pain?
A.9. What are the important findings through history and physical examination?
A.10. What are the appropriate diagnostic studies for low back pain?
A.11. What is the differential diagnosis of low back pain?
A.12. What are the causes of persistent back pain after multiple spine surgeries?
B. Management of Low Back Pain and Sciatica

B.1. What are the noninterventional treatments available?
B.2. What traditional interventional treatments are available and how should they be used?
B.3. What are some of the recent safety improvements recommended for lumbar epidural steroid injection?
B.4. What are some of other approaches in minimally invasive interventions?
B.5. What are the concerns about magnetic resonance imaging (MRI) safety in patients with a spinal cord stimulator (SCS)?
B.6. When should surgery be considered?
B.7. What surgical options are available for the treatment of disc disease?
51 Perioperative Pain Management
A. Perioperative Pain Management for Thoracotomy
A.1. What would be your advice to the patient about the planned thoracotomy and postoperative pain relief?
A.2. How will you decide about the choice of anesthetic technique?
A.3. What is chronic postsurgical pain (CPSP)? Does video-assisted thoracic surgery reduce the risk of chronic pain after thoracotomy?
A.4. What would be your perioperative analgesic strategy?
A.5. Does the choice of analgesic technique influence postoperative outcome?
A.6. Does it matter if the epidural catheter is at the thoracic or lumbar level?
A.7. Does the choice of drugs influence the efficacy or safety of thoracic epidural analgesia (TEA)?
A.8. What are the usual doses and concentrations of the anesthetic combinations commonly employed in epidural analgesia?
A.9. If accidental dural puncture occurs during placement of the epidural needle, what steps should be taken?
A.10. What are the alternatives to TEA?
A.11. What is the usual clinical regimen for intravenous patient-controlled analgesia (IV-PCA) and is special patient monitoring required during its use?
A.12. What are the side effects and complications of epidural technique?

A.13. What recommendations for placement and removal of epidural catheter will you make if this patient is on antiplatelet or anticoagulant therapy or thromboprophylaxis is planned?
Prophylactic Unfractionated Heparin
Therapeutic Intravenous Unfractionated Heparin
Preoperative Low Molecular Weight Heparin (Enoxaparin)
Postoperative Low Molecular Weight Heparin
Oral Anticoagulants
Newer Agents
B. Chronic Opioid Therapy and Perioperative Pain Management
B.1. How does chronic opioid therapy influence postoperative pain management?
B.2. What are the causes for increased postoperative pain and opioid consumption in patients chronically using opioids?
B.3. What are the main differences between a chronic opioid-consuming patient and a patient who abuses or is addicted to opioids?
B.4. What issues need to be considered in the opioid-tolerant patient who is scheduled for surgery?
B.5. What would be your strategy regarding preoperative information and choice of anesthesia technique?
B.6. What are the choices for perioperative pain management in opioid-tolerant patients?
B.7. What issues need to be considered before discharging an opioid-tolerant patient?
C. Perioperative Pain Management for Ambulatory Surgery
C.1. What would be your preoperative considerations and advice to the patient?
C.2. What are the consequences of inadequate pain management after ambulatory surgery?
C.3. What is the role of premedication or preoperative analgesic?
C.4. Does the choice of anesthetic technique influence postoperative pain?
C.5. Are nonsteroidal anti-inflammatory drugs (NSAIDs) effective? If so, does the choice of drug matter?
C.6. What is the role of surgical technique in influencing postoperative pain after a laparoscopic cholecystectomy?

C.7. What would be your strategy for pain control after discharge home?
D. The Role of an Acute Pain Service (APS)
D.1. What is the extent of the problem, and which patients are at greatest risk of undertreatment?
D.2. What are the consequences of inadequate postoperative pain relief?
D.3. What is the role of an APS in improving postoperative pain management?
D.4. Does an APS improve postoperative outcome?
52 Acupuncture
A. Acupuncture as a Complementary Medical Therapy
A.1. What is acupuncture?
A.2. How is acupuncture practiced? (Video 52.1)
A.3. What are the mechanisms of acupuncture analgesia?
A.4. What were the conclusions of the National Institutes of Health Consensus Conference about acupuncture?
A.5. Can acupuncture be a novel nonopioid alternative pain therapy?
B. Acupuncture for the Treatment of Chronic Conditions
B.1. What are the rationales in integrating acupuncture for the treatment of postoperative nausea and vomiting?
B.2. Can acupuncture be used for the treatment of chemotherapy-induced nausea and vomiting?
B.3. How effective is acupuncture for the management of chronic headache?
B.4. Can acupuncture be used for the treatment of chronic neck and back pain?
B.5. Can acupuncture be used for the treatment of osteoarthritis?
B.6. What role can acupuncture play in the care of patients with cancer?
B.7. Can acupuncture/acupressure be used to decrease anxiety?
B.8. What is ear acupuncture/acupressure? Can it be useful for alleviating anxiety and pain? (Video 52.2)
C. Complications
C.1. What are the possible complications of acupuncture treatment?
SECTION 12 Miscellaneous

53 Myasthenia Gravis
A. Medical Disease and Differential Diagnosis
A.1. What is MG?
A.2. What is the etiology and pathophysiology of MG?
A.3. Describe the clinical classification of MG.
A.4. How is the diagnosis of MG made?
A.5. What should be considered in the differential diagnosis?
A.6. How does myasthenic syndrome (Lambert-Eaton syndrome) differ from MG?
A.7. What treatments are available for a patient with MG?
Medical Therapy
Surgical Therapy
B. Preoperative Evaluation and Preparation
B.1. Describe the preoperative evaluation of this patient.
B.2. What preoperative laboratory data are required?
B.3. How should the patient's medications be managed preoperatively?
C. Intraoperative Management
C.1. What are your considerations in the choice of anesthetic technique?
C.2. How should this patient be monitored intraoperatively?
C.3. What anesthetic regimen would you choose for this patient?
C.4. Can neuromuscular blocking drugs be used safely in a patient with MG?
C.5. Should the MG patient who is in remission (i.e., symptom free without treatment) be managed differently?
D. Postoperative Management
D.1. What factors will help you predict this patient's need for continued intubation or other postoperative ventilatory support?
D.2. How will you determine if this patient's trachea can be safely extubated?
D.3. How will you manage postoperative analgesia?
D.4. How will you define and manage postextubation ventilatory failure in this patient?
54 Malignant Hyperthermia
A. Medical Disease and Differential Diagnosis
A.1. What was the problem of concern in this case?

A.2. What is malignant hyperthermia (MH)?
A.3. What are the clinical features of a susceptible patient?
A.4. Does the history of previous uneventful sevoflurane anesthesia reasonably exclude the patient's susceptibility to MH?
A.5. What are the clinical features of the syndrome?
Hyperkalemic Cardiac Arrest
A.6. What are the laboratory findings during an acute crisis of MH?
A.7. What is the incidence of this syndrome?
A.8. What is the mode of inheritance of the disease? Does MH "skip" generations?
A.9. What genetic disorder results in MH susceptibility?
A.10. What is the pathophysiology of the syndrome?
A.11. What laboratory tests can further substantiate the susceptibility of the patient to MH?
Molecular Genetic Testing for MH Susceptibility
A.12. What is neuroleptic malignant syndrome (NMS)?
B. Preoperative Evaluation and Preparation
B.1. How would you prepare this patient for anesthesia and surgery?
B.2. Is dantrolene prophylaxis indicated?
B.3. What laboratory tests would you obtain before surgery?
B.4. Is outpatient surgery appropriate for this patient?
B.5. In anticipation of general anesthesia, what preparations would you make?
C. Intraoperative Management
C.1. What anesthetic techniques and agents would you employ?
C.2. Should body (core) temperature be monitored during general anesthesia lasting more than a short time?
C.3. What anesthetic agents are contraindicated?
C.4. If the surgeon wants to use local anesthesia for a procedure, what agents will you recommend?
C.5. What is the significance of masseter muscle spasm occurring after succinylcholine administration?
C.6. Twenty minutes into the procedure with sevoflurane anesthesia, the patient developed increasing tachycardia with ventricular premature beats and mottled skin. What emergency measures would you take?

C.7. What modalities would you monitor closely during management of the crisis?
C.8. What steps should be taken to avoid major morbidity from MH?
C.9. How does the new formulation of dantrolene (Ryanodex) compare with the existing formulation of dantrolene (Dantrium or Revonto)?
D. Postoperative Management
D.1. What complications may follow this syndrome?
D.2. What would be your follow-up in this case?
D.3. What would you advise the patient and the family?
D.4. What precautions should an MH-susceptible patient take outside of the operating room (OR)?
55 Postoperative Residual Neuromuscular Weakness and Prolonged Apnea
A. Medical Diseases and Differential Diagnosis
A.1. What is the differential diagnosis for postoperative hypoventilation?
A.2. How is residual neuromuscular blockade (NMB) diagnosed?
A.3. What is the order of recovery of voluntary muscle groups from nondepolarizing muscle relaxants?
A.4. What is the mechanism of action of succinylcholine, and how is it metabolized? What are the side effects of succinylcholine?
A.5. If succinylcholine were the only muscle relaxant used during the case and the patient did not exhibit a response to train-of-four (TOF) stimulation, what is the likely diagnosis? How would you confirm it?
A.6. What are acetylcholinesterase and serum cholinesterase? What is the clinical significance of heterozygosity for atypical pseudocholinesterase (PChE)?
A.7. What is the incidence of atypical cholinesterase activity?
A.8. What are some factors that can lower PChE levels?
B. Intraoperative Management
B.1. How is the choice among muscle relaxants made?
B.2. What factors can alter sensitivity to nondepolarizing neuromuscular blockers?
B.3. What are the characteristics of nondepolarizing block?

B.4. What is a TOF stimulus?
B.5. Why is the TOF ratio of clinical importance?
B.6. How do we define adequate recovery of neuromuscular function?
B.7. Are there useful and/or trustworthy clinical tests of neuromuscular recovery?
B.8. How accurate are subjective estimates of the TOF ratio, and what purpose do peripheral nerve stimulator (PNS) monitors serve?
B.9. What is double burst stimulation (DBS)?
B.10. What is the posttetanic count (PTC)?
B.11. How can the TOF ratio be measured quantitatively?
B.12. What are the limitations of acetylcholinesterase antagonists?
B.13. Is there anything wrong with administering neostigmine when the TOFC is less than 3?
B.14. Is reversal of blockade always necessary?
B.15. Is there any way to rapidly antagonize a profound nondepolarizing block?
C. Postoperative Management
C.1. What is the incidence of residual NMB in the PACU?
C.2. Does undetected postoperative residual neuromuscular block (PORB) have clinical consequences?
56 Burns
A. Medical Disease and Differential Diagnosis
A.1. How do you classify the burn injury?
A.2. How do you express the extent of the burn injury?
A.3. Should the “rule of nines” be used in children?
A.4. What functions does the skin perform?
A.5. What pathophysiologic changes accompany major thermal injury?
A.6. What is the prognosis for this patient? What major factors affect his prognosis?
A.7. What are the common causes of death in burn patients?
A.8. Does this patient have a smoke inhalation burn? How do you make the diagnosis?
A.9. What is carbon monoxide poisoning? How do you diagnose and treat carbon monoxide poisoning?
A.10. What resuscitative measure would you institute immediately

in this patient with 40% burns?
A.11. What fluid formula would you use?
Parkland Formula
A.12. What cardiovascular changes typify the burn injury?
A.13. What changes occur in hepatic function? What are the anesthetic implications of such changes?
A.14. What are Curling ulcers? How can they be prevented?
A.15. What complications are associated with electrical burns?
B. Preoperative Evaluation and Preparation
B.1. What preoperative preparations would you order? What are particular concerns in this patient?
B.2. What are the various operative and management options available for severely burned patients?
B.3. What are the advantages and disadvantages of early tangential excision split-thickness skin grafting (TE/STSG)?
B.4. What is this patient's mean arterial blood pressure? How do you calculate it?
B.5. Are you concerned about this patient's blood pressure? What treatment would you institute?
B.6. This patient was ventilated with respirator settings of tidal volume, 800 mL; respiratory rate, 20 breaths per minute; fraction of inspired oxygen (FIO_2), 60%; and positive end-expiratory pressure, 10 cm H_2O. Arterial blood gas analyses showed the following: pH, 7.24; PO_2, 56 mmHg; PCO_2, 60 mmHg; and oxygen saturation, 80%. How would you interpret these arterial blood gas analysis results? What are the possible causes of high PCO_2 and low PO_2?
B.7. How do you calculate oxygen content and oxygen delivery? What factors govern the oxygen delivery to the tissues?
C. Intraoperative Management
C.1. What monitors would you use in the operating room?
C.2. What information can be obtained from an arterial line and a pulmonary artery catheter? How are these calculations performed?
C.3. If the patient had not been intubated, how would you proceed with the anesthetic induction?
C.4. Why is awake intubation considered the safest?
C.5. What anesthetic agents would you use? Discuss inhalation

versus intravenous agents.
C.6. Why are you concerned about the patient's body temperature? What is normothermia for a burned patient?
C.7. How is temperature best maintained?
C.8. What derangements occur with hypothermia?
C.9. What muscle relaxant would you use?
C.10. Why is succinylcholine contraindicated in burned patients? For how long should it be avoided?
C.11. What other adverse effects are associated with succinylcholine?
C.12. How are the doses of nondepolarizing muscle relaxants affected by burn injury?
C.13. How are the muscle relaxants such as succinylcholine, atracurium, cisatracurium, vecuronium, pancuronium, rocuronium, and curare metabolized and eliminated? Which of them has significant histamine release?
D. Postoperative Management
D.1. How would you monitor this patient during transport?
D.2. What is meant by diffusion hypoxia? How do you prevent it?
D.3. Why do patients often shiver in the recovery room on emergence from anesthesia?
D.4. Discuss the causes of oliguria in the recovery room.
57 Trauma
A. Medical Disease and Differential Diagnosis
A.1. How is trauma classified?
A.2. What are the injuries associated with thoracic trauma?
A.3. What are the injuries associated with cardiac trauma?
A.4. What is the pathophysiology of acute pericardial tamponade?
A.5. What are the anesthetic implications for treating cardiac tamponade?
A.6. How is the initial assessment and management of the trauma patient performed?
A.7. What constitutes a primary survey, and what is its objective?
A.8. What constitutes a secondary survey, and what is its objective?
A.9. What is the definition of massive hemothorax? What are the signs and symptoms of a hemothorax?
A.10. What are the indications for a thoracotomy to treat a

hemothorax?
A.11. How are pneumothoraces categorized?
A.12. What is an occult pneumothorax?
A.13. If the patient has a widened mediastinum on chest radiograph, what are your concerns?
A.14. What are the most commonly injured organs in blunt abdominal trauma?
A.15. What is a focused abdominal sonography for trauma (FAST) examination?
A.16. What is diagnostic peritoneal lavage (DPL)?
A.17. Why was DPL not performed for this patient?
A.18. Define shock.
A.19. What are the four types of shock?
A.20. List the signs and symptoms of shock.
A.21. What is the pathophysiology of hypovolemic shock?
Cardiovascular Derangement
Acid–Base Disturbance
A.22. How would you classify hemorrhage?
A.23. What is the initial treatment of hemorrhagic shock?
A.24. Would you choose crystalloid, colloid, or blood products to treat hemorrhagic shock?
A.25. Is there a place for dextran or hetastarch (Hespan) in treating hypovolemic shock?
B. Preoperative Evaluation and Preparation
B.1. What premedication would you order?
B.2. What preoperative testing would you order?
C. Intraoperative Management
C.1. How would you monitor this patient?
C.2. How would you induce anesthesia?
C.3. What technique could you use if single-lung ventilation was indicated?
C.4. What agents would you choose to maintain anesthesia?
C.5. What muscle relaxant would you choose?
C.6. What can be done to decrease the incidence of intraoperative awareness?
C.7. Five minutes after intubation, the peak airway pressure increased from 20 to 40 cm H_2O. What are the possible causes?

C.8. How would you make a diagnosis of tension pneumothorax?
C.9. What is the treatment of tension pneumothorax?
C.10. The patient's blood loss was continuing, and the hematocrit was 18%. What type of blood would you give if the type and crossmatch are not completed?
C.11. What precautions should be taken if more than 2 units of low titer type O uncrossmatched whole blood are given?
C.12. What are the complications associated with any blood transfusion?
Transfusion Reactions
Transmission of Disease
Microembolization
What is considered a massive transfusion (MT)? What is the Assessment of Blood Consumption (ABC) score?
C.14. What are the complications associated with an MT?
C.15. Can the shift of the oxygen–hemoglobin dissociation curve be quantified?
C.16. How is hypothermia defined?
C.17. What are the adverse effects of hypothermia?
C.18. What is the treatment of hypothermia?
C.19. What are the effects of blood transfusion on the immune system?
C.20. What are the guidelines for transfusion of blood products?
Red Blood Cell Transfusion Criteria
Platelet Transfusion Criteria
Fresh Frozen Plasma Transfusion Criteria
Cryoprecipitate Transfusion Criteria
What are the guidelines for the ratio of plasma/platelet transfusion to packed red blood cells in an MT?
C.22. If a patient were a member of the Jehovah's Witness religious sect, would you give a blood transfusion?
C.23. If a child is a Jehovah's Witness and suffered from hemorrhagic shock, what would you do?
C.24. What are the concentrated factors and hemostatic agents available for bleeding patients?
Recombinant Activated Factor VII (rFVIIa, NovoSeven)
Four-Factor Prothrombin Complex Concentrate

Fibrinogen Concentrates
Tranexamic Acid
What is thromboelastography (TEG) and thromboelastometry? How can they guide transfusion?
Rotation Thromboelastometry
Thromboelastography
D. Postoperative Management
D.1. What is acute respiratory distress syndrome (ARDS)? What is acute lung injury?
D.2. How is ARDS treated?
D.3. In the recovery room, you are called to see this patient because of oliguria. How would you evaluate and treat this patient?
Prerenal
Renal
Postrenal
D.4. If this patient had a crush injury and low urine output, what other concerns might you have? What if the patient has dark or "tea-colored" urine?
58 Scoliosis
A. Medical Disease and Differential Diagnosis
A.1. What is scoliosis?
A.2. What is the most common type of scoliosis?
A.3. What are the other types of scoliosis?
Idiopathic
Neuromuscular
Myopathic
Congenital
Neurofibromatosis
Mesenchymal Disorders
Trauma
A.4. How is the severity of scoliosis assessed, and why is the severity important?
A.5. What are the nonoperative treatment options of scoliosis?
A.6. What abnormalities in pulmonary function tests (PFTs) are most commonly seen in scoliosis? What is the cause of these abnormalities?
A.7. What is the most common arterial blood gas abnormality seen

in scoliosis? What are possible causes for this abnormality?
A.8. What abnormalities of ventilatory drive may be associated with scoliosis?
A.9. How may the cardiovascular system be affected in patients with scoliosis?
A.10. What is the relationship between scoliosis and malignant hyperthermia?
B. Preoperative Evaluation and Preparation
B.1. What should the anesthesiologist know about the nature of the spinal curve?
B.2. What aspects of the history are most important?
B.3. What aspects of the physical examination are most important?
B.4. Why is a preoperative neurologic assessment important?
B.5. What tests would you order preoperatively?
B.6. What is an enhanced recovery after surgery (ERAS) pathway? How has it been applied to the recovery for pediatric patients undergoing posterior spinal instrumentation and fusion?
B.7. How will the surgical procedure influence the anesthetic management?
C. Intraoperative Management
C.1. What monitoring would you use?
C.2. What is the incidence of neurologic complications in scoliosis surgery, and which patients are at highest risk?
C.3. What monitoring techniques are used to minimize neurologic complication?
C.4. What are somatosensory evoked potentials (SSEPs), and how are they used?
C.5. How reliable are SSEPs for predicting spinal injury?
C.6. What are motor evoked potentials (MEPs), and how are they used?
C.7. How is spinal cord monitoring affected by anesthetic agents? What other factors affect spinal cord monitoring?
C.8. What is the optimal anesthetic technique for scoliosis surgery?
C.9. What should be done if the SSEPs or MEPs become abnormal during surgery?
C.10. How is the “wake-up” test performed? What complications can occur during this test?

C.11. Four hours into the surgical procedure, the surgeon reports some bubbling in the thoracic portion of the wound. Shortly thereafter, end-tidal carbon dioxide decreases abruptly from 35 to 18 mmHg, heart rate increases from 80 to 120 beats per minute, blood pressure begins to fall, and arterial saturation decreases to 90%. On auscultation through esophageal stethoscope, you hear a loud gurgling murmur. What is your diagnosis?
C.12. How common is significant air embolism during scoliosis surgery?
C.13. What should be done if an air embolus is suspected?
C.14. What complications occur related to positioning the patient?
C.15. What is transfusion-related acute lung injury (TRALI)? How do you distinguish it from transfusion-associated circulatory overload (TACO)?
C.16. What techniques can be used to minimize transfusion requirements?
D. Postoperative Management
D.1. When would you extubate the patient?
D.2. What should be done to optimize pulmonary status?
D.3. What laboratory tests should be ordered postoperatively?
D.4. What fluid therapy would you use postoperatively?
D.5. What complications may occur following scoliosis surgery?
D.6. Upon arrival to the recovery room, you notice that the urine appears to be tea colored. What is your diagnosis, and how should this be managed?
D.7. How would you manage this patient's pain, nausea, and vomiting postoperatively?
59 Hypoxia and Equipment Failure
A. Medical Disease and Differential Diagnosis
A.1. What is hypoxia, and what is hypoxemia?
A.2. Is the partial pressure of oxygen in arterial blood (PaO_2) related to age?
A.3. Was this patient hypoxemic?
A.4. What is a pulse oximeter, and what is a hemoximeter?
A.5. How does a pulse oximeter work?
A.6. How is a two-wavelength pulse oximeter calibrated by the manufacturer?

A.7. What may affect the accuracy of a two-wavelength pulse oximeter?
A.8. How do the dyshemoglobins, methemoglobin (metHb), and carboxyhemoglobin (HbCO) affect SpO_2 readings?
A.9. What is a capnometer, and what is capnography? Of what value are they in patient monitoring?
A.10. What is meant by the term end-tidal carbon dioxide ($EtCO_2$)?
A.11. What is the appearance of a normal capnogram, and what is its significance?
A.12. What are mainstream and sidestream capnometers?
A.13. Show some common capnograms and provide a differential diagnosis of each event.
A.14. What is the arterial–alveolar difference in carbon dioxide (CO_2)?
A.15. What are some of the important safety features of the contemporary anesthesia workstation?
Features Intended to Prevent Human Error
Features to Correct for Use Error
Monitoring Systems
Alarm Systems
A.16. What are the common sites for gas leakage?
A.17. How is the anesthesia machine checked for leaks?
B. Preoperative Evaluation and Preparation
B.1. What should be included in the equipment checkout in preparation for anesthesia?
Emergency ventilation equipment
High-pressure system
Low-pressure systems
Scavenging system
Breathing system
Manual and automatic ventilation systems
Monitors
Final position
B.2. What emergency equipment should be easily available to the anesthesiologist?
B.3. How should this patient be premedicated?
C. Intraoperative Management

C.1. How should this patient be monitored?
Oxygenation
Ventilation
Circulation
Body temperature
C.2. Following uncomplicated induction of anesthesia and endotracheal intubation, the procedure begins. Upon insufflation of the abdomen with CO_2, the SpO_2 decreases to 78%. What acute diagnostic and therapeutic interventions would you perform?
C.3. The endotracheal tube was withdrawn 2 cm. Squeezing the reservoir bag in the circle breathing system failed to generate positive pressure in the circuit. What are the common sites for gas leaks in the circle breathing system?
C.4. The patient was taken out of Trendelenburg position. Direct laryngoscopy revealed the endotracheal tube to be supraglottic. Additionally, green secretions were noted to be pooled in the posterior pharynx. What should be done next?
D. Postoperative Management
D.1. What criteria would you use for tracheal extubation?
D.2. What are the causes of postoperative hypoxemia?
D.3. What is the difference between shunt, ventilation/perfusion mismatch, and dead space?
D.4. Postoperatively, the patient developed hypoxia and pulmonary edema. What is the differential diagnosis of pulmonary edema? What is the most likely cause of pulmonary edema in this patient?
D.5. How should the ventilator be set if mechanical ventilation is required postoperatively?
D.6. If this patient had acute respiratory distress syndrome (ARDS) secondary to aspiration, besides low-tidal volume ventilation, what other changes in routine therapy should be considered?
D.7. What therapies routinely administered by the anesthesiologist may cause acute lung injury?
D.8. What methods of oxygen administration may be used postoperatively?
60 Electroconvulsive Therapy
A. Medical Disease and Differential Diagnosis
A.1. What are the indications for ECT?

A.2. Are there any contraindications to ECT?
A.3. What is the mechanism of action of ECT?
B. Preoperative Evaluation and Preparation
B.1. How would you assess the cardiac status of this patient?
B.2. How should his anticoagulation be managed during ECT?
B.3. What implications do his history of sleep apnea have on management of ECT?
B.4. How does his history of TIA and carotid endarterectomy impact your preoperative evaluation?
B.5. Is ECT contraindicated in a patient with a permanent pacemaker or implantable cardioverter-defibrillator?
B.6. Are there any psychiatric medications he is taking that would impact your anesthetic care?
C. Intraoperative Management
C.1. Describe the hemodynamic and cardiac response to ECT in a typical patient.
C.2. Is an arterial line warranted in this patient?
C.3. By what means would you attempt to maximize hemodynamic stability?
C.4. Describe the cerebral hemodynamic effects of ECT.
C.5. How would you proceed with an anesthetic induction for this procedure?
C.6. How do you intend to manage his airway during each treatment?
D. Postoperative Management
D.1. The patient is extremely agitated upon emergence. Discuss the risk factors for postictal agitation (PIA) as well as the therapeutic options.
D.2. After three consecutive uneventful inpatient treatments, the psychiatrist asks if the patient may undergo ECT as an outpatient. Would you agree to this plan?
61 Ambulatory Surgery
A. Medical Disease and Differential Diagnosis
A.1. Is this patient morbidly obese?
A.2. What medical conditions may be associated with obesity and morbid obesity?
A.3. Is there a link to a decline in memory and thinking with

anesthesia and surgery?
B. Preoperative Evaluation and Preparation
B.1. What advantages does outpatient surgery offer?
B.2. What are the goals of the preoperative evaluation of the surgical outpatient?
B.3. In order to thoroughly screen for disease, should one put all outpatients through a full battery of laboratory testing?
B.4. What preoperative laboratory testing is necessary for surgical outpatients?
B.5. Which outpatients should receive a preoperative chest roentgenogram?
B.6. In which patients is an electrocardiogram (ECG) necessary before outpatient anesthesia and surgery?
B.7. Would age or physical status influence the decision to perform outpatient surgery?
B.8. What patients are considered inappropriate for ambulatory surgery?
B.9. What questions are critically important to ask this patient when obtaining her history?
B.10. What instructions should the patient be given with regard to continuing or discontinuing lisinopril in the perioperative period?
B.11. What is an enhanced recovery after surgery (ERAS) protocol, and how would you apply it in the outpatient setting?
B.12. How would you premedicate this patient?
B.13. Should every outpatient receive prophylaxis against aspiration pneumonitis?
B.14. Is an overnight fast justified for all outpatients?
C. Intraoperative Management
C.1. What are the important considerations in choosing an anesthetic technique for outpatient surgery?
C.2. How would you monitor this patient?
C.3. What is the bispectral index (BIS) monitor, and what information does it convey?
C.4. What benefits might be derived from using a BIS monitor?
C.5. Is BIS monitoring applicable to children?
C.6. What are the major limitations of BIS monitoring?
C.7. What does a BIS reading of 56 mean?

C.8. What anesthetic agents would you use to induce and maintain general anesthesia in this patient?
C.9. Under what circumstances might spinal anesthesia be appropriate for outpatient surgery?
D. Postoperative Management
D.1. What are the common causes of nausea and vomiting in outpatients?
D.2. How would you pharmacologically prevent PONV in the susceptible ambulatory patient?
D.3. How is postoperative pain treated?
D.4. What criteria would you use to establish that a patient can be safely discharged after ambulatory surgery?
D.5. How would you decide when to discharge a patient after regional anesthesia?
D.6. What instructions should be given to an ambulatory surgical patients upon discharge?
62 Magnetic Resonance Imaging
A. Medical Disease and Differential Diagnosis
A.1. What is MRI, and how does it work?
A.2. What are some advantages of MRI?
A.3. What are some disadvantages associated with MRI? What are some safety concerns?
A.4. How do you manage patients with implanted devices?
A.5. What are the biologic effects of clinical MRI?
A.6. What are the anesthetic considerations for this procedure?
A.7. What is intraoperative MRI (iMRI)? What is real-time MRI, and in what setting can this be used?
B. Preoperative Evaluation and Preparation
B.1. What type of patients may require sedation or general anesthesia for MRI?
B.2. Do all children require sedation for MRI?
B.3. What preoperative laboratory testing would you require for this patient?
B.4. How would you premedicate this patient? What are some options that can be used to premedicate other patients for MRI?
C. Intraoperative Management
C.1. What are some of the anesthetic options for this patient?

C.2. How is an MRI conducted?
C.3. How would you monitor this patient?
C.4. What special considerations apply to monitoring equipment used during MRI?
C.5. How would you induce and maintain general anesthesia in this patient?
C.6. What are ways to maintain the airway during an MRI scan?
C.7. During the scan, you notice loss of end-tidal carbon dioxide. You immediately go into the scanner, remove the patient from the MRI scanner and initiate bag ventilation. However, you are still unable to ventilate the patient, and asystole follows. What do you do next?
C.8. What is the risk to the patient of gadolinium administration in the presence of acute renal insufficiency?
D. Postoperative Management
D.1. How will you recover the patient from anesthesia?
63 Morbid Obesity, Obstructive Sleep Apnea, and Bariatric Anesthesia
A. Medical Disease and Differential Diagnosis
A.1. What problems exist with this patient? The patient asks you if he is high risk. What is the evidence? Is surgical therapy a safe and viable alternative for this patient?
A.2. Define the terms overweight, obesity, MO, super obesity (SO), super-SO (SSO), normal weight, ideal body weight (IBW), and lean body weight (LBW). What is the impact of obesity on society?
A.3. What is OSA? What are the risk factors for OSA?
A.4. How is OSA diagnosed? What is a sleep study, or PSG? How are results obtained from a PSG used to grade the severity of OSA? What are the subtypes of OSA? Are there genetic disorders with a predisposition to OSA? What is the role of OSA screening tests in the preoperative setting?
A.5. How does OSA differ in the pediatric population in clinical presentation and pathogenesis?
A.6. What is the Pickwickian syndrome (PS)? What is obesity hypoventilation syndrome (OHS)? Describe the pathogenesis of severe OSA.
A.7. What is the association between obesity and OSA? What is the

etiology of OSA in severe obesity?
A.8. What are the anesthetic implications of OSA?
A.9. What type of metabolic problems would you expect to find in morbidly obese patients? What are the roles of leptin and ghrelin in obesity?
A.10. Describe the changes that occur in the following respiratory parameters in morbidly obese patients:
A.11. What changes occur in PaO_2 and $PaCO_2$ in morbidly obese patients?
A.12. What changes occur in intrapulmonary shunt (Q_S/Q_T) and dead space (V_D/V_T) in MO? Describe the Shunt equation and the physiologic dead space, or Bohr equation.
A.13. What changes occur in the cardiovascular system of the obese patient? Discuss cardiac output, blood volume, blood pressure, and pulmonary arterial pressure.
A.14. Are there any other disease entities commonly associated with obesity? What is their relationship?
A.15. What anatomic changes that affect the airway are associated with MO and OSA?
A.16. What derangements of the gastrointestinal system are associated with MO?
B. Preoperative Evaluation and Preparation
B.1. How would this patient be optimized for surgery preoperatively? Would you use preoperative screening questionnaires to diagnose OSA? Summarize the workup for this patient.
B.2. One of the recent developments in bariatric surgery is that many patients are receiving prebariatric screening procedures performed in the endoscopy suite. Describe the anesthetic considerations.
B.3. Summarize the evidence-based workup, risk, chance of various adverse outcome, and expected length of stay for this patient.
B.4. What is the role of enhanced recovery after surgery (ERAS) in bariatric surgery? How does the public find a quality bariatric surgery team and surgical facility? What is the role of robotics in bariatric surgery?

B.5. Would you premedicate the patient?
B.6. Describe the mechanism of action of each premedication in the ENERGY protocol.
B.7. How would you adjust doses of anesthetics in the morbidly obese?
C. Intraoperative Management
C.1. How would you monitor this patient?
C.2. The American Society of Anesthesiologists' (ASA) Difficult Airway Algorithm (DAA) provides a guideline for management of the difficult airway. How do the comorbidities of MO and OSA modify implementation of the algorithm?
C.3. Why is it important to preoxygenate the obese patient? How would you do it? Compare the effectiveness of the four-maximum-breath and 3-minute techniques. What is the importance of continuous positive airway pressure (CPAP) during the induction of general anesthesia? Describe use of the nasal CPAP mask in the induction of general anesthesia.
C.4. There are many new airway devices on the marketplace. Which of these devices have been particularly successful on the morbidly obese or OSA patient?
C.5. How would you induce anesthesia? Describe the intubation technique.
C.6. How would you maintain general anesthesia? What agents would you choose? How would you prepare for emergence?
C.7. Which muscle relaxants would you use?
C.8. Is postoperative pain severe after bariatric surgery? What are the pain generators? What is the role of regional anesthesia to decrease opioid requirements for bariatric surgery? What are the advantages and disadvantages of regional anesthesia? What are some of the newer techniques available?
C.9. What is the pathophysiology of pneumoperitoneum (PNP)? What is the effect on the cardiopulmonary system? How does it change perioperative care? What are the optimal ventilator strategies for morbidly obese patients undergoing bariatric surgery?
C.10. What are the devices that anesthesiologists place in the upper gastrointestinal canal during laparoscopic bariatric surgery? Are there risks associated with placement and management of these

devices?
C.11. When will you extubate this patient? Describe weight-based extubation criteria.
C.12. What is apneic oxygenation?
C.13. What is diffusion hypoxia (DH)? How do you prevent it?
D. Postoperative Management
D.1. What are the early postoperative complications of bariatric surgical procedures?
D.2. What are the late complications of bariatric surgical procedures?
D.3. What is the effect of position on respiratory function in the obese patient?
D.4. How would you prevent postoperative atelectasis?
D.5. How long would you prescribe supplementary oxygen postoperatively?
D.6. How would you control postoperative pain?
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