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# CLINICAL CASES IN ANESTHESIA

FOURTH EDITION

ALLAN P. REED, MD
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# Clinical Cases in Anesthesia

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*To Mazie Ruth Reed, whose beautiful smile and infectious laugh bring joy wherever she goes.*

**Allan P. Reed**

*In loving memory of my parents, Herman and Lea, for their unconditional support and inspiring me to be the best that I can be.*

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# Preface to the Fourth Edition

Why a fourth edition?

Previous editions of *Clinical Cases in Anesthesia* stand out as some of the most widely available anesthesia texts worldwide. The first edition was initially conceived as a study guide for the oral board examination. Dating back to 1989, its succinct descriptions of relevant basic sciences and clinical applications of those sciences garnered praise among board candidates. As its reputation grew, the book was used by residents, fellows, and practicing anesthesiologists throughout the United States. *Clinical Cases in Anesthesia* soon became popular in other English-speaking countries and nations where medical education was conducted in English. This success was expanded by translation into Russian. Editions 2 and 3 were created as updates. They were equally well received, culminating in a Chinese translation of the third edition. English, Russian, and Chinese versions of *Clinical Cases in Anesthesia* reach anesthesia practitioners on most of the planet.

Recently, readers have asked for an updated and expanded version of the book they have relied on for so many years. *Clinical Cases in Anesthesia*, fourth edition, answers that request. New medical sciences, techniques, and concepts require a fresh look at modern anesthesia practice. Our goal is to enhance understanding of basic and clinical sciences with brief, focused, and clear explanations. Tables and boxes do more than just summarize important information. They allow for quick, easy references that can be reviewed and provide crucial facts for immediate patient care.

*Clinical Cases in Anesthesia*, fourth edition, differs from conventional anesthesia textbooks. It is not intended to replace journals or tomes. Instead, this book offers select topics that are most likely to present in the course of current practice. Many cases are repeated from previous editions, and many are new. Although some classic questions in anesthesia care remain the same over decades, approaches change based on emerging information. The new version updates these areas invoking information contained in the American Society of Anesthesiologists guidelines and practice parameters. The entire section on Intensive Care Medicine is offered in response to readers' requests. Some cases have been eliminated for lack of relevance to modern anesthetic encounters. Use of central venous catheters and pulmonary artery catheters has been de-emphasized to comport with current trends.

While expanding the text, we have attempted to maintain its relevance to oral examination board review and contemporary anesthesia practice. The practice of anesthesia is complex and relies on in-depth knowledge across multiple medical specialties. It is our hope that this new edition will further fulfill the goals of the original book, as well as convey the importance of basic anatomy, physiology, and pharmacology to safe and quality patient care.

The editors are grateful to our authors, who are dedicated practitioners and teachers. Without their contributions, this book would not be possible.

**Allan P. Reed, MD**

**Francine S. Yudkowitz, MD, FAAP**

SECTION 1

# CARDIOVASCULAR SYSTEM

CASE 1

# Coronary Artery Disease

**Amanda J. Rhee, MD • Alexander J. C. Mittnacht, MD • David L. Reich, MD**

## QUESTIONS

1. What are the determinants of myocardial oxygen supply?
2. Explain the determinants of myocardial oxygen consumption (demand).
3. What are the pharmacologic alternatives for treating myocardial ischemia in this patient?
4. Describe the considerations for performing surgery on patients with drug-eluting coronary stents.
5. Is perioperative β-adrenergic blockade indicated for this patient?
6. How should this patient be monitored intraoperatively?

A 65-year-old man with hypertension, familial hypercholesterolemia, type 2 diabetes mellitus, and angina pectoris presented for resection of a sigmoid colon tumor. Stress imaging demonstrated an anteroseptal region of ischemia. Coronary angiography showed a critical lesion of the left anterior descending coronary artery and a 50% stenosis of the proximal circumflex coronary artery. Percutaneous transluminal coronary angioplasty with drug-eluting stent (DES) implantation was performed successfully on the left anterior descending lesion 6 weeks before surgery. The patient was maintained on metoprolol, aspirin, and clopidogrel therapy. Clopidogrel was discontinued 7 days before surgery.

General anesthesia was induced with etomidate, midazolam, and fentanyl. Maintenance anesthesia consisted of oxygen, sevoflurane, and fentanyl. Muscle relaxation was provided with vecuronium. During tumor mobilization, the heart rate increased from 70 to 120 beats per minute. Blood pressure remained stable at 130/70 mm Hg. On the V5 electrocardiogram (ECG) lead, 2 mm of horizontal ST-segment depression was noted, but no abnormality was seen in lead II. An additional dose of fentanyl was associated with slowing of the heart rate to 95 beats per minute but no change in the ST-segment depression in V5.

## 1. What are the determinants of myocardial oxygen supply?

A major concern in the anesthetic management of patients with coronary artery disease (CAD) is maintaining a favorable balance between myocardial oxygen supply and demand (Figure 1-1). Myocardial oxygen supply is tenuous in patients with CAD because blockages in coronary arteries by atherosclerotic plaques, thrombi, and emboli disrupt the flow of oxygen-rich blood to heart muscle distal to the obstruction. Coronary perfusion is preserved by maintaining both coronary perfusion pressure and length of the diastolic interval. The left coronary artery is perfused during diastole. The right coronary artery is perfused during both diastole and systole. It is important to prevent shortening of the diastolic interval by preventing increases in heart rate. Coronary perfusion pressure is maintained by ensuring normal to high diastolic arterial pressure and normal to low left ventricular end-diastolic pressure (LVEDP).

## 2. Explain the determinants of myocardial oxygen consumption (demand).

Heart rate, myocardial contractility, and myocardial wall tension are the three major determinants of myocardial oxygen consumption. Heart rate is probably the most important parameter regulating myocardial oxygen supply-demand balance. Decreasing heart rate increases oxygen supply by prolonging diastole (allowing for more subendocardial perfusion) and decreases oxygen demand. The association between tachycardia and myocardial ischemia is well documented. Severe bradycardia should be avoided because it causes decreased diastolic arterial pressure and increased LVEDP. β-Adrenergic blocking drugs are commonly used to maintain mild bradycardia in patients with CAD.

Myocardial contractility refers to the ability of the heart to generate force at a given preload. Myocardial contractility is very difficult to measure and is poorly described by cardiac output or even left ventricular ejection fraction. Determination of loading conditions and measurement of velocity, force, and extent of muscle shortening facilitate description of myocardial contractility. Decreased myocardial contractility is associated with decreased myocardial oxygen demand, and decreasing myocardial contractility may be beneficial in patients with CAD. Specifically, agents that depress myocardial contractility but are not potent vasodilators may be beneficial as long as coronary perfusion pressure is maintained. Examples of such agents include midazolam and etomidate.

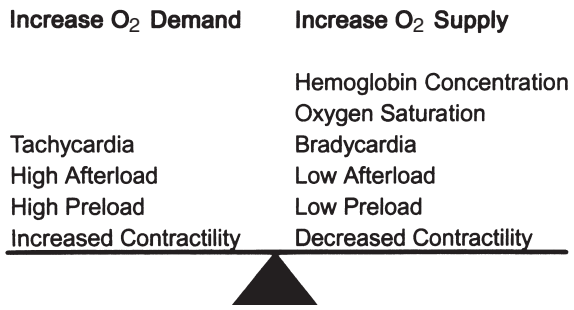


**FIGURE 1-1** ■ The balance between myocardial oxygen supply and demand.

All volatile anesthetic agents decrease systemic blood pressure by decreasing vascular resistance in a dose-dependent fashion. Although isoflurane is the most widely studied volatile anesthetic for its effect on coronary artery dilation and coronary artery steal, sevoflurane and desflurane show similar mild vaodilating effects. Intravenous anesthetic agents such as propofol, midazolam, etomidate, and ketamine have shown slight negative inotropic effects, but thiopental may have strong negative inotropic effects, which could explain the hypotension associated with its use. Dexmedetomidine is associated with decreases in heart rate and cardiac output in a dose-dependent manner but usually offers excellent hemodynamic stability. "Myocardial depressants" could be useful for patients with CAD as long as coronary perfusion pressure is maintained because they theoretically decrease myocardial oxygen demand.

Myocardial oxygen supply and demand are kept in balance by properly managing left ventricular preload, afterload, heart rate, and contractility. Major increases in preload (left ventricular end-diastolic volume) add to the volume work of the heart (increased demand) and decrease coronary perfusion pressure because of the associated increase in LVEDP (decreased supply). Nitroglycerin assists in maintaining a normal to low preload (see later). Excessive increases in afterload result in increased pressure work of the heart (wall tension) during systole (increased demand) despite the increase in coronary perfusion pressure. At the other end of the spectrum, extreme vasodilation (decreased afterload) decreases the diastolic arterial pressure and decreases myocardial oxygen supply (Table 1-1).

A decline in the blood flow supply-demand ratio can lead to myocardial ischemia, or impaired myocardial function. Ischemia results from reduced perfusion that leads to oxygen deprivation and inadequate removal of metabolites.

## 3. What are the pharmacologic alternatives for treating myocardial ischemia in this patient?

The goals of medical therapy should be to optimize coronary artery perfusion pressure (systemic diastolic pressure minus LVEDP) and control heart rate. If the patient is receiving light anesthesia, it may be beneficial to increase the depth of anesthesia to treat tachycardia and hypertension. Based on the patient's hemodynamic profile, one or more of the following therapies should be used to achieve the above-described goals.

Nitroglycerin and other nitrates exert antianginal effects by dilating epicardial coronary arteries and decreasing left ventricular preload and wall tension. This is accomplished by systemic venodilation. Nitrates also cause mild arterial vasodilation and consequently may decrease the pressure work of the myocardium. The limiting factor of nitrate therapy is hypotension, which would decrease myocardial oxygen supply and possibly cause reflex tachycardia.

β-Adrenergic blocking drugs slow the heart rate, which has two beneficial effects on myocardial ischemia. First, the duration of diastole increases and improves coronary perfusion. Second, myocardial oxygen consumption is decreased. β-Adrenergic blockers also decrease myocardial contractility, which decreases myocardial oxygen consumption. Finally, treatment of hypertension may decrease afterload, which decreases work. Metoprolol has been used for many years to achieve intraoperative β-adrenergic blockade. Esmolol, a short-acting intravenous β-adrenergic blocker, has become increasingly popular among anesthesiologists because of its relative cardiac ($\beta_1$ receptor) selectivity and favorable pharmacokinetics.

TABLE 1-1 **Hemodynamic Goals in Myocardial Ischemia to Optimize Coronary Perfusion Pressure**

| Parameter | Goal | Indicated | Contraindicated |
|---|---|---|---|
| Heart rate | Slow | β-Adrenergic blockers | Isoproterenol<br>Dobutamine<br>Ketamine<br>Pancuronium |
| Preload | Normal to low | Nitroglycerin<br>Diuretics | Volume overload |
| Afterload | Normal to high | Phenylephrine | Nitroprusside<br>High-dose isoflurane |
| Contractility | Normal to decreased | β-Adrenergic blockers<br>Volatile anesthetics | Epinephrine<br>Dopamine |

Calcium-channel entry blockers are a less common component of medical therapy for patients with CAD. Their role as intraoperative agents for the management of myocardial ischemia is less clear. There is some evidence that preoperative calcium-channel entry blocker therapy may increase the incidence of intraoperative myocardial ischemia. However, these agents may be cardioprotective against reperfusion injury and significantly improve diastolic dysfunction. Short-acting calcium-channel blockers such as nicardipine may be useful in controlling hypertension and reducing afterload during myocardial ischemia.

Phenylephrine, a "pure" α-adrenergic agonist, is the agent of choice for treatment of hypotension in myocardial ischemia because it increases diastolic pressure with no change (or a slight decrease) in heart rate. Drugs with β-adrenergic effects, such as ephedrine, dobutamine, and dopamine, increase the heart rate, increase myocardial contractility, and may have minimal to reductive effects on diastolic arterial pressure. All of these β-adrenergic actions are undesirable during myocardial ischemia.

## 4. Describe the considerations for performing surgery on patients with drug-eluting coronary stents.

Current American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend delaying elective surgery for 12 months after implantation of a DES. In patients who cannot wait that long for their surgery, such as patients undergoing cancer operations, careful assessment of the risks and benefits of withdrawing thienopyridine therapy must be undertaken. A cardiologist should be consulted to assess the degree of myocardium at risk, and the possibility of continuing antiplatelet therapy through the perioperative period should be considered. Many surgeons agree to operate with continued aspirin therapy, but few agree to continue thienopyridine. Additionally, there is no current evidence that "bridging therapy" with low-molecular-weight heparin or short-acting antiplatelet therapy is beneficial. Increased vigilance for acute perioperative myocardial infarction is required for all patients undergoing surgery within the first 12 months (and possibly longer) after DES placement.

## 5. Is perioperative β-adrenergic blockade indicated for this patient?

β-Adrenergic blockers are part of routine care for patients with unstable angina and recent myocardial infarction. β-Adrenergic blocker therapy should be initiated within the first 24 hours for ST-segment elevation myocardial infarction in patients who do not have signs of heart failure, evidence of low cardiac output, increased risk for cardiogenic shock, or other relative contraindications (i.e., P–R interval >0.24 seconds, second-degree or third-degree heart block, asthma, or reactive airway disease).

The 2009 ACC/AHA focused update on perioperative β blockade recommends the following:

- In patients undergoing surgery, β-adrenergic blockers should be continued for patients already receiving them.
- In patients who have CAD, have evidence of cardiac ischemia, or are at high cardiac risk, β-adrenergic blockers should probably be initiated preoperatively and considered intraoperatively to titrate heart rate and blood pressure during vascular or intermediate-risk surgery.
- β-Adrenergic blockers should not be given to patients undergoing surgery who have an absolute contraindication to receiving them.
- In patients undergoing noncardiac surgery, it is not advisable to give high doses of β blockers to patients not currently taking them.

Continuation of preoperative β-adrenergic blockade during the 48-hour perioperative period is a current Surgical Care Improvement Program quality measure.

## 6. How should this patient be monitored intraoperatively?

The most important modality for monitoring this patient intraoperatively is a multiple-lead ECG system. Of the ECG changes of myocardial ischemia that are present on a standard 12-lead ECG, 89% can be detected by a V5 precordial ECG lead alone. Since the late 1970s, the recommendation has been to follow limb lead II and precordial lead V5 simultaneously for detection of intraoperative myocardial ischemia. This combination reflects the distribution of both the right and the left coronary arteries and should enable >90% of ischemic episodes to be detected.

Current operating room ECG systems are usually capable of continuous ST-segment monitoring. Generally, this monitoring determines the relationship of the ST segment 60–80 msec after the J-point (junction between the QRS complex and the ST segment) to the baseline (during the PQ interval). Ischemia may be defined as >0.1 mV of horizontal or downsloping ST-segment depression or >0.2 mV of ST-segment elevation. These systems are rendered less effective by left ventricular hypertrophy and frequent electrocautery and are not useful in left bundle-branch block or ventricular pacing.

Transesophageal echocardiography (TEE), if available, is an extremely sensitive method of detecting myocardial ischemia. TEE is performed by continuously imaging the transgastric short-axis view of the left ventricle. The images represent distributions of the three major coronary vessels. The attention of busy practitioners is frequently diverted from continuous TEE observation by other important tasks. Changes in regional wall motion are not specific for myocardial ischemia, even if they are highly sensitive. Additionally, equipment cost and need for specialized training limit the use of TEE.

## SUGGESTED READINGS

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CASE 2

# Recent Myocardial Infarction

**Amanda J. Rhee, MD • Alexander J. C. Mittnacht, MD • David L. Reich, MD**

## QUESTIONS

1. How do you evaluate cardiac risk in a patient scheduled for noncardiac surgery?
2. How is cardiac status evaluated before elective noncardiac surgery?
3. What is the cardiac risk in this patient, and what additional investigations should be performed?
4. What are the implications for anesthetic management when coronary revascularization is performed before noncardiac surgery?
5. Which intraoperative monitors would you use?
6. What additional drugs would you have prepared?
7. What anesthetic technique would you use?
8. How would you manage this patient postoperatively?

A 68-year-old woman with multiple cardiac risk factors experienced sudden onset of crushing substernal chest pain. Despite aggressive thrombolytic therapy, the patient had electrocardiogram (ECG) evidence of a transmural anterolateral myocardial infarction (MI). She developed acute cholecystitis 3 weeks later and was scheduled for cholecystectomy.

### 1. How do you evaluate cardiac risk in a patient scheduled for noncardiac surgery?

#### *Initial Approach*

Preoperative cardiac evaluation and assessment include a review of the history, physical examination, and laboratory results. Knowledge of the planned surgical procedure is also important. The history should assess the following:

- Severity and reversibility of coronary artery disease (CAD) (e.g., risk factors, anginal patterns, history of MI)
- Left ventricular (LV) and right ventricular function (e.g., exercise capacity, pulmonary edema, pulmonary hypertension)
- Presence of symptomatic arrhythmias (e.g., palpitations, syncopal or presyncopal episodes)
- Coexisting valvular disease
- Presence of a pacemaker or implantable cardioverter defibrillator

Comorbidities that commonly occur in patients with CAD include peripheral vascular disease, cerebrovascular disease, diabetes mellitus, renal insufficiency, and chronic pulmonary disease. A calculation of the patient's metabolic equivalents (METs) of tasks helps to determine cardiac risk (Figure 2-1).

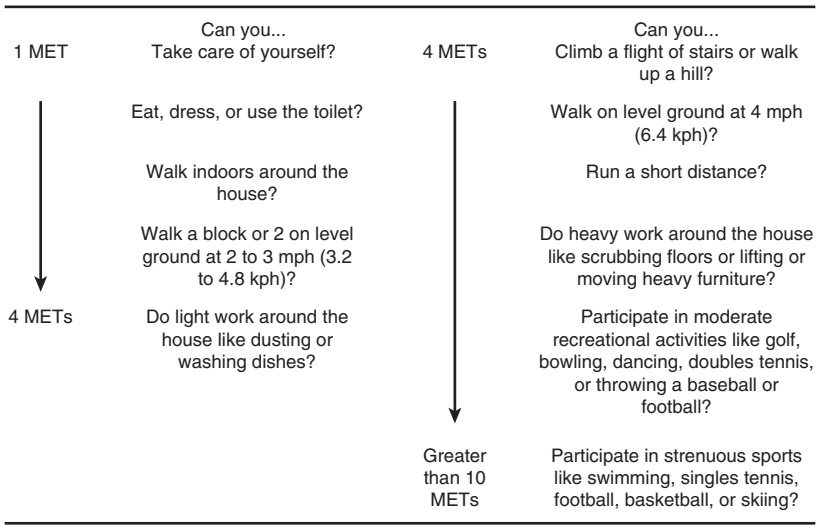
On physical examination, particular attention should be paid to the vital signs, specifically heart rate, blood pressure, and pulse pressure. These parameters provide information about the balance of myocardial oxygen consumption and delivery. Additionally, the presence of left-sided or right-sided failure (jugular venous distention, peripheral edema, pulmonary edema, or $S_3$) and the presence of murmurs should be assessed.

Routine laboratory tests, electrolytes, blood urea nitrogen, creatinine, and complete blood counts may have some predictive value of cardiac risk. These tests may reveal the presence of anemia, hypokalemia from diuretic therapy, and increasing creatinine levels heralding renal insufficiency. Also, specific cardiac drug levels such as digoxin should be considered. Point-of-care testing for the efficacy of medications such as clopidogrel and aspirin may be useful as well. Chest radiograph aids in assessing heart size and shape. An ECG should be obtained; however, a normal ECG may be present in 50% of patients with CAD. The most common ECG findings in patients with CAD are ST-T wave abnormalities (65%–90%), LV hypertrophy (10%–20%), and pathologic Q waves (0.5%–8%). ECGs are indicated for patients with at least one clinical risk factor who are undergoing vascular surgical procedures or for patients with known congestive heart failure (CHF), peripheral arterial disease, or cerebrovascular disease who are undergoing intermediate-risk surgical procedures. ECGs are not indicated for asymptomatic patients undergoing low-risk surgical procedures.

Further evaluation depends on the results of the aforementioned preliminary investigations and the planned surgical procedure.

#### *Assigning Clinical Risk*

The standard of care, as of this writing, is defined by the American College of Cardiology/American Heart Association (ACC/AHA) 2007 Guidelines for Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery. The general paradigm is that patients are




kph indicates kilometers per hour; MET, metabolic equivalent; and mph, miles per hour.

**FIGURE 2-1 ■ Metabolic equivalent of tasks (METs).** Modified from Fleisher LA, et al. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll of Cardiol 50: e159-e242, 2007. Based on Hlatky MA, et al. A brief self-administered questionnaire to determine functional capacity (the Duke Activity Status Index). Am J Cardiol 64: 651–4, 1989; and Fletcher GF, et al. Exercise standards: statement for healthcare professionals from the American Heart Association. Circulation 86: 340–4, 1992.

risk-stratified based on clinical risk factors (Box 2-1), surgical procedures (Table 2-1), and noninvasive testing. In elective procedures, this algorithmic approach should be used by internists, surgeons, and anesthesiologists as a cardiovascular evaluation strategy.

In the past, numerous classification systems (e.g., Goldman, Detsky, and Eagle) were designed to predict the risk of cardiac morbidity. These classification systems did not include patients with high-risk conditions that are considered to be major predictors of perioperative cardiac events (PCE). The ACC/AHA 2007 Guidelines reflect Lee's Revised Cardiac Risk Index, which is the most commonly used system today. Another commonly employed system is the National Surgical Quality Improvement Program risk model. Both of these models assess patients with high-risk characteristics and are more applicable today.

Unstable angina is a major clinical predictor of PCE in the ACC/AHA Guidelines, whereas chronic stable angina is an intermediate clinical predictor of PCE. Fleisher and Barash (1992) suggested that patients should be classified in a more functional way. They contended that not all patients with stable angina have the same disease process (i.e., coronary anatomy, frequency of ischemia, and LV function). The number of ischemic

**BOX 2-1 Clinical Risk Factors**

**Major Clinical Risk Factors**

- Unstable coronary syndromes
  - Unstable or severe angina
  - Recent myocardial infarction
- Decompensated heart failure
- Significant arrhythmias
- Severe valvular disease

**Intermediate Clinical Risk Factors**

- History of ischemic heart disease
- History of compensated or prior heart failure
- History of cerebrovascular disease
- Renal insufficiency

**Minor Clinical Risk Factors**

- Advanced age (>70 years old)
- Abnormal eletrocardiogram
  - Left ventricular hypertrophy
  - Left bundle-branch block
  - ST-T abnormalities
- Rhythm other than sinus rhythm
- Uncontrolled systemic hypertension

**TABLE 2-1 Risk Stratification for Surgical Procedures**

| Cardiac Risk Stratification | Procedure Example |
|---|---|
| High | Aortic and other major vascular surgery<br>Peripheral vascular surgery |
| Intermediate | Intraperitoneal and intrathoracic surgery<br>Carotid endarterectomy<br>Head and neck surgery<br>Orthopedic surgery<br>Prostate surgery |
| Low | Endoscopic procedures<br>Superficial procedures<br>Cataract surgery<br>Breast surgery<br>Ambulatory surgery |

episodes is especially difficult to quantitate without some sort of continuous monitoring (i.e., ambulatory ECG). This information is probably important because >75% of ischemic episodes are silent, and >50% of patients with CAD (not just diabetics) have silent ischemia. It is unclear what the role of silent ischemia is in myocardial injury, although it seems to portend a worse prognosis if present in patients with unstable angina or patients after MI.

The relationship between history of MI and PCE varies significantly based on the age of the infarction. Recent infarctions are defined by cardiologists as infarctions within the last 7–30 days and are acknowledged as a major clinical predictor of PCE. Prior MI by history or pathologic Q waves on ECG is an intermediate clinical predictor. Interpretation of history of MI and PCE is complicated in anesthesia practice because anesthesiologists traditionally refer to recent infarctions as occurring within the preceding 6 weeks to 6 months. Classic "reinfarction" studies from data collected 20–40 years ago found that patients with an infarct within 3 months had a 5.7%–30% incidence of reinfarction. Between 3 and 6 months, the risks range from 2.3%–15%, and an infarct >6 months before surgery is associated with a 1.9%–6% incidence. The mortality rate of repeat MI was about 50%, and this figure varies very little among the various studies. The lower numbers in each group are from the study of Rao et al. (1983), in which aggressive hemodynamic monitoring was used and patients recovered in the intensive care unit postoperatively. The problem with applying these data to modern care is that they precede the widespread use of β blockers, coronary interventions, and enzyme-based diagnosis of infarctions. Nevertheless, there is no doubt that more recent MIs represent a significant risk factor for PCE. The severity of the infarction must also be considered.

Medical literature distinguishes mortality rates in Q wave versus non–Q wave MIs, infarctions involving the right versus the left coronary artery distribution, uncomplicated versus complicated infarctions (i.e., recurrent pain, CHF, or arrhythmias), and negative versus positive post-MI exercise stress test results. It seems reasonable to assume that mortality rates from all recent MIs should not be classified together based solely on the time since the infarction.

CHF in the general population has a poor prognosis. The 5-year survival rate is approximately 50%, although this may be improving with modern afterload-reduction and antiarrhythmic therapies. The 1-year mortality rate is approximately 30% in patients with LV ejection fractions <30%. The ACC/AHA guidelines include uncompensated CHF as a major clinical predictor and compensated or prior CHF as an intermediate clinical predictor.

Arrhythmias are a common problem, especially in elderly patients. Arrhythmias are usually benign except in patients with underlying heart disease, in whom they serve as markers for increased morbidity and mortality. Many patients with LV dysfunction and arrhythmias die as a result of LV failure and not an arrhythmia. Acknowledged major clinical predictors include high-degree atrioventricular block, symptomatic ventricular arrhythmias in the presence of underlying heart disease, and supraventricular arrhythmias with uncontrolled ventricular rate. Minor predictors include abnormal ECG (i.e., LV hypertrophy, left bundle-branch block, and ST-T wave abnormalities). Rhythm other than sinus (e.g., atrial fibrillation) is also a minor clinical predictor.

Patients with valvular heart disease are difficult to evaluate because the lesions cause changes that are independently associated with increased risk (i.e., CHF, rhythm changes). However, severe valvular disease is considered a major clinical predictor. If aortic stenosis is symptomatic, the surgery generally should be postponed or canceled for possible aortic valve replacement or other intervention before elective surgery. Patients with severe aortic stenosis undergoing noncardiac surgery have a mortality rate of approximately 10%.

### *Assigning Surgical Risk*

In addition to patient characteristics, risk is determined by the surgical procedure (see Table 2-1). Higher risk surgeries include procedures with greater potential for hemodynamic cardiac stress. Such stressors could be alterations in heart rate, blood pressure, intravascular volume, clotting, oxygenation, neurohumoral activation, blood loss, and pain.

It is generally agreed that patients with a "combined" risk of PCE (i.e., based on patient and surgical factors) of >10% warrant further evaluation. Noncardiac surgical procedures associated with the highest PCE rate are mostly vascular surgical procedures. Peripheral vascular and aortic surgeries have high PCE rates, whereas carotid artery surgery has PCE rates of about 5%. Although the data are still emerging, it appears that endovascular repairs have low associated risk. The high PCE rate of vascular surgical procedures is usually attributed to the high incidence of CAD in patients undergoing vascular surgery (estimated to be 90%) and to the stress imposed on the myocardium by hemodynamic changes.

The metabolic changes induced by surgery, such as increased levels of stress hormones and increases in platelet adhesiveness, are also implicated as factors that increase PCE. Nonvascular surgical procedures associated with higher morbidity and mortality include intrathoracic and intraabdominal surgeries. Presumably, the increased risk is because of the greater hemodynamic changes associated with large fluid shifts, compression of the great veins, and aberrations in cardiopulmonary function during thoracic surgery. Emergency surgery is also associated with increased risk. Procedures associated with a lower risk of PCE include extremity surgery, transurethral prostate resections, and cataract surgery. The risk of surgery must always be included in the estimation of patient risk, and this is constantly changing owing to the emergence of less invasive techniques that cause less physiologic disturbance.

The assignment of "cardiac risk" to a particular patient for a particular surgical procedure is difficult, but there are guidelines and an algorithm that should be followed (Figure 2-2). The need for further evaluation depends on whether the information gained would change the planned surgical or anesthetic management. These changes in

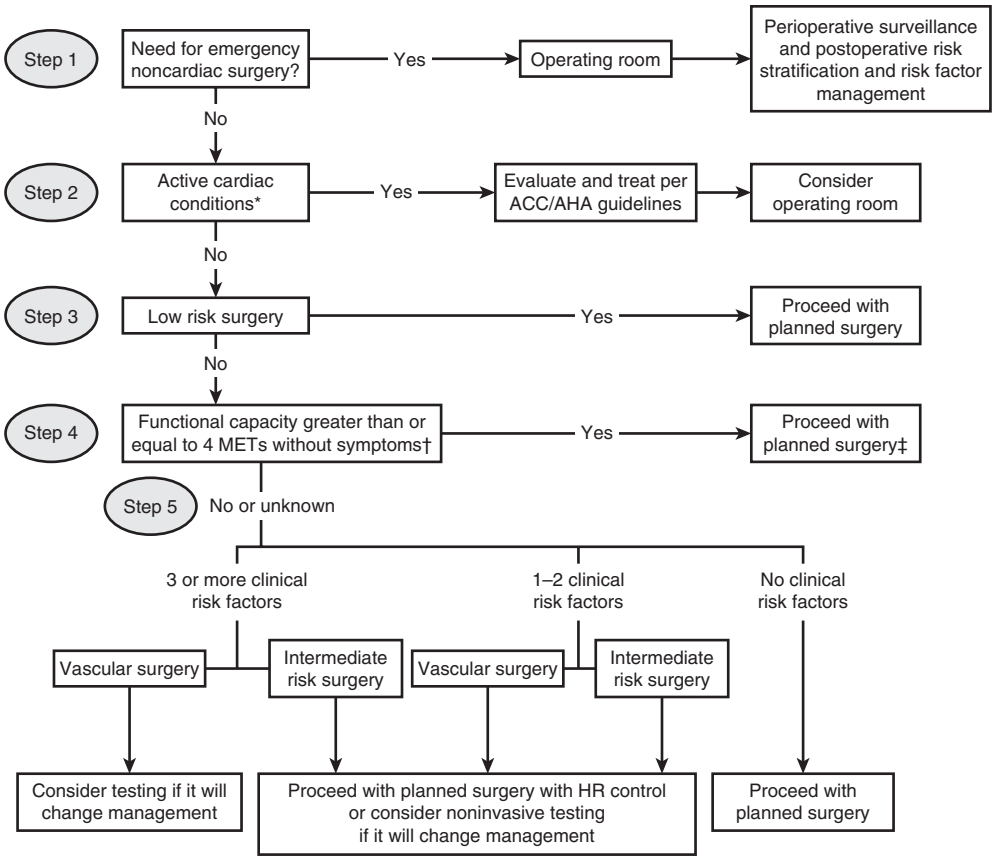



**FIGURE 2-2** ■ Algorithm for managing a patient with cardiac disease undergoing noncardiac surgery. *ACC/AHA,* American College of Cardiology/American Heart Association; *HR,* heart rate; *METs,* metabolic equivalents. Modified from Fleisher LA, et al. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll of Cardiology 50: e159-e242, 2007.
* Refer to Box 2-2
† Refer to Figure 2-1
‡ Noninvasive testing may be considered before surgery in specific patients with risk factors if it will change management.

management might include altering the surgical procedure to one associated with lower risk, medical or surgical treatment of CAD, perioperative anticoagulation, or perhaps more aggressive intraoperative and postoperative monitoring. Although many of these strategies sound logical, there is relatively weak evidence of outcome improvements with interventions.

## 2. How is cardiac status evaluated before elective noncardiac surgery?

Based on the evaluation described in Question 1, further investigation of the patient's cardiac status before elective noncardiac surgery may be warranted. Indications for preoperative ECGs are discussed in Question 1. Patients with active cardiac conditions (Box 2-2) should undergo noninvasive stress testing, which includes exercise stress testing, dobutamine stress echocardiogram, and intravenous dipyridamole/adenosine myocardial perfusion imaging with both thallium 201 and technetium 99m.

Myocardial revascularization by percutaneous coronary angioplasty and stent placement or coronary artery bypass grafting (CABG) before elective noncardiac surgery for PCE risk reduction is not recommended in patients with stable CAD. However, coronary revascularization before

**BOX 2-2 Active Cardiac Conditions Requiring Noninvasive Testing**

- Unstable coronary syndromes
  - Unstable angina
  - Recent myocardial infarction
- Decompensated heart failure
- Significant arrhythmias
  - High-grade atrioventricular block
  - Mobitz II atrioventricular block
  - Third-degree atrioventricular block
  - Symptomatic ventricular arrhythmias
  - Supraventricular arrhythmias (including atrial fibrillation) with uncontrolled ventricular rate (heart rate >100 beats per minute at rest)
  - Symptomatic bradycardia
  - Newly recognized ventricular tachycardia
- Severe valvular disease
  - Severe aortic stenosis
    - Mean pressure gradient >40 mm Hg
    - Aortic valve area <1.0 $cm^2$
    - Symptomatic
  - Symptomatic mitral stenosis
    - Progressive dyspnea on exertion
    - Exertional presyncope
    - Heart failure

noncardiac surgery is useful in patients with the following conditions:

- Stable angina with left main coronary artery stenosis
- Stable angina with three-vessel disease
- Stable angina with two-vessel disease and significant proximal left anterior descending artery stenosis and either ejection fraction <50% or ischemia on noninvasive testing
- High-risk unstable angina or non–ST-segment elevation MI
- Acute ST-segment elevation MI

Elective noncardiac surgery is not recommended within 4–6 weeks of placement of a bare metal coronary stent (BMS) or within 12 months of placement of a drug-eluting coronary stent (DES) in patients in whom discontinuing thienopyridine or aspirin/thienopyridine therapy is required. Elective noncardiac surgery is also not recommended within 4 weeks of coronary artery balloon angioplasty.

### 3. What is the cardiac risk in this patient, and what additional investigations should be performed?

This patient is an elderly woman with known CAD and a recent MI who is undergoing emergency surgery. Several important factors require consideration. The first of these is the patient's course after MI. If she has recurrent pain, CHF, or late ventricular arrhythmias (>48 hours after MI) she has a 15%–30% risk of death or reinfarction in the first year after MI even without surgery.

Another issue is whether there was evidence of reperfusion after thrombolytic therapy. Evidence of reperfusion includes pain relief, reperfusion arrhythmias, large increases in creatine phosphokinase enzyme levels, and an improvement in the ECG without evidence of MI. Anticoagulant therapy is important. Heparin therapy used for patients with recurrent chest pain would need to be stopped before surgery. More recent studies suggest that the timing may be very important. Patients in whom heparin was stopped for >9.5 hours were more likely to develop recurrent ischemia requiring urgent intervention.

Most patients who have received thrombolytic therapy have significant residual stenosis in vessels that have been reperfused, and they often undergo early cardiac catheterization, especially if they had a complicated infarction. Some centers treat patients who are doing well the same as any patient with a recent uncomplicated MI—a modified symptom-limited stress test is performed before discharge (on post-MI days 5–7), and a symptom-limited stress test is performed 6 weeks later.

The presence of sepsis is an important consideration. Hemodynamic changes associated with sepsis may increase demands on the myocardium, including increased cardiac output because of endotoxin-induced vasodilation and myocardial depression from myocardial depressant factor. Also, hypotension from septic shock may decrease coronary artery perfusion pressure leading to myocardial ischemia.

If the patient must have an urgent surgical procedure and no additional cardiac studies have been performed (e.g., stress test or coronary angiogram), one should assume the patient has significant CAD. If time permits, transesophageal echocardiography (TEE), specifically assessing wall motion, LV ejection fraction, and mitral valve function, provides useful information.

See Question 2 for indications for myocardial revascularization prior to elective noncardiac surgery for PCE risk reduction.

### 4. What are the implications for anesthetic management when coronary revascularization is performed before noncardiac surgery?

Increasingly, patients who have received a percutaneous coronary artery intervention (PCI) are scheduled for elective noncardiac surgery. The type of intervention—balloon angioplasty, BMS, or DES—determines how long the patient must remain on antiplatelet therapy and when elective surgery should be performed. The 2007 ACC/AHA guidelines do not specify a timing recommendation for noncardiac surgery after CABG, but they present data in which patients received vascular surgery a median of 29 days (Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echo-V [DECREASE-V] study) and 48 days (Coronary Artery Revascularization Prophylaxis [CARP] study) after CABG. The 2004 and 2011 Guidelines for Coronary Artery Bypass Graft Surgery do not recommend a specific time to wait after CABG. It seems reasonable to wait 4–6 weeks after CABG before performing noncardiac surgery, if possible; the decision to proceed should be directed by the same algorithm presented in the 2007 ACC/AHA guidelines.

The 2007 ACC/AHA guidelines regarding type of stent placement, antiplatelet therapy, and timing of elective surgery are summarized in Table 2-2. Briefly, dual antiplatelet therapy is recommended for 1 month for patients with a BMS and for 1 year for patients with a DES. Thereafter, aspirin should be continued indefinitely. Prolongation of dual antiplatelet therapy in patients with a DES should be considered in the following circumstances:

- Previous stent thrombosis
- Left main stent placement
- Multivessel stent placement
- Stent placed in the only remaining coronary artery or graft

Elective surgery should be postponed until after dual antiplatelet therapy is no longer warranted (i.e., 1 month for patients with BMS, 1 year for patients with DES). Aspirin should be continued into the perioperative period, unless the benefit of decreasing surgical bleeding outweighs the risk of stent thrombosis.

In the case of emergent or urgent surgery, dual antiplatelet therapy should be continued into the perioperative period if possible. If continuing dual antiplatelet therapy is impossible, aspirin should be continued, and the thienopyridine should be restarted as soon as possible to avoid a PCE.

A difficult situation arises when patients require PCI before urgent surgery. The type of PCI is determined by when the surgery needs to be performed (i.e., 2 weeks vs. 1 month) and whether antiplatelet therapy can continue into the perioperative period. If dual antiplatelet therapy

TABLE 2-2 **Percutaneous Coronary Artery Intervention and Timing of Elective Surgery**

| Intervention | Antiplatelet Therapy | Timing of Elective Surgery |
|---|---|---|
| Balloon angioplasty | Aspirin | Delay 2–4 weeks<br>To OR on aspirin* |
| BMS | Thienopyridine/aspirin for 1 month<br>Continue aspirin after 1 month | Delay 1 month to 1 year<br>To OR on aspirin*† |
| DES | Thienopyridine/aspirin for 1 year<br>Continue aspirin after 1 year | Delay at least 1 year<br>To OR on aspirin*† |

*BMS*, Bare metal stent; *DES*, drug-eluting stent; *OR*, operating room.
*Aspirin should be continued throughout the perioperative period. If stopping aspirin is considered, the risk of stent thrombosis should be weighed against the risk of surgical bleeding.
†If patient is still on thienopyridine, it should be continued as soon as possible after surgery.

is contraindicated for the planned surgical procedure and it must be performed within the next month, balloon angioplasty would be indicated. If the surgery can be delayed for 1 month, a BMS can be placed. In this situation, a DES would not be indicated, especially if dual antiplatelet therapy needs to be discontinued. Each situation involves weighing the risk of bleeding during surgery and urgency of the surgery versus the possibility of a catastrophic cardiac event.

## 5. Which intraoperative monitors would you use?

A general goal is to maintain intraoperative hemodynamics within 20% of preoperative values. In addition to the standard intraoperative monitors, other monitors that should be considered include invasive continuous intraarterial catheters, pulmonary artery catheters (PACs), and TEEs. An intraarterial catheter allows for beat-to-beat blood pressure monitoring. Although 40% of intraoperative ischemic episodes are not related to aberrations in hemodynamics, some studies demonstrate that inadequate management of hemodynamic abnormalities may increase risk. Hypotension (blood pressure <30% baseline for >10 minutes) was shown to be a strong predictor of PCE in one study. There are no studies showing conclusively that hypertension is associated with adverse outcome.

An intraarterial catheter also offers the ability to perform laboratory testing throughout the intraoperative period; this would facilitate optimizing metabolic and respiratory derangements. Glucose management is important because hyperglycemia is an independent predictor of cardiovascular risk and is directly related to mortality during MI. Finally, point-of-care testing is necessary for rapid determination of anticoagulation levels and adequate reversal.

Tachycardia has not been definitively shown to be associated with PCE, although studies suggest a relationship. Also, hypothermia may increase myocardial oxygen demand and has been shown to be an independent predictor of morbid cardiac events. Temperature should be monitored, and normothermia should be maintained.

An effective tool for monitoring myocardial ischemia in anesthetized patients is a multiple-lead ECG. Monitoring precordial chest leads V4 and V5 detects >90% of ischemic events that would be seen on a 12-lead ECG, although it has been reported to have only 9% sensitivity compared with the "gold standard" (myocardial lactate extraction). ST-segment depressions and T-wave morphology changes are most commonly seen. However, in some patients, the ECG is not an effective intraoperative monitor of myocardial ischemia, including patients with LV hypertrophy, conduction abnormalities, and ventricular pacemaker dependence. Computerized ST-segment continuous analysis can be useful to monitor patients with known CAD or patients undergoing vascular surgery to detect myocardial ischemia.

The use of PACs may be reasonable in patients at risk for major hemodynamic disturbances that are easily detected with PACs. Routine use is not recommended and can cause harm. Although PACs may be useful in selected groups of patients, there are no recent conclusive data showing benefit over risk. Potential complications include vessel or cardiac perforation, arrhythmia, pulmonary embolism, and incorrect management based on data misinterpretation. The development of V waves on the pulmonary artery wedge pressure waveform may be an indication of myocardial ischemia, but it is neither sensitive nor specific enough to be regarded as a reliable monitor for this purpose (Figure 2-3). However, the usefulness of the PAC extends beyond its questionable ability to detect ischemia. The PAC provides information about the patient's intravascular volume status; provides a quantitative estimate of myocardial compliance; and allows for calculation of cardiac output and other hemodynamic measurements, such as systemic vascular resistance and stroke volume.

TEE is the most sensitive detector of intraoperative ischemia by demonstrating regional wall motion abnormalities and is capable of detecting ischemia earlier than any other modality. Use of TEE requires specialized skills and training as defined by the American Society of Echocardiography. Although its usefulness in detecting ischemia is well established, it is unclear what TEE changes are predictive of PCE. Several older studies did not find LV wall motion abnormalities were predictive of cardiac morbidity. Also, regional wall motion abnormalities during ischemia sometimes do not resolve when ischemia has dissipated. Finally, TEE provides additional physiologic information, such as estimates of LV ejection fraction and intravascular volume status, which may help with intraoperative management in patients with ventricular dysfunction.

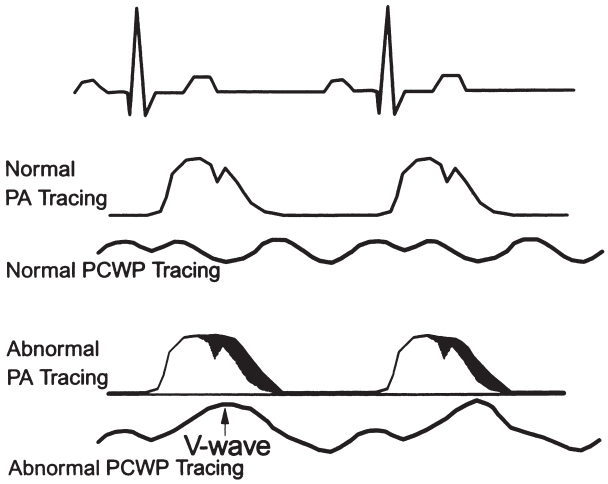



**FIGURE 2-3** ■ Relationship between the ECG, pulmonary artery (PA) waveform, and pulmonary capillary wedge pressure (PCWP) waveform is illustrated in normal circumstances and in the presence of V waves. There is widening of the PA waveform and loss of the dicrotic notch in the presence of V waves. The peak of the V wave occurs about the same time as the T wave on the ECG.

### 6. What additional drugs would you have prepared?

Intravenous nitroglycerin, esmolol, and vasopressors should be immediately available to treat ischemia and hemodynamic aberrations. Phenylephrine is particularly useful in restoring myocardial blood flow in hypotensive patients without causing major increases in myocardial oxygen consumption owing to tachycardia. β Adrenergic blockers should be managed as per the 2009 ACC/AHA guidelines on perioperative β adrenergic blocker management (see Chapter 1 for further elaboration).

### 7. What anesthetic technique would you use?

Anesthetic technique has not been shown to be a predictor of PCE. There are several trials involving different subsets of patients, including patients who underwent vascular or abdominal surgery that showed no difference in outcome between patients who received epidural versus general anesthesia. A trial by Cohen et al. in 1988 showed a possible increase in 30-day mortality in patients who received monitored anesthesia care; however, this may have been the result of selection bias. The anesthetic technique used should be based on patient assessment, maintenance of stable intraoperative hemodynamics, and adequate postoperative analgesia. Tachycardia should be avoided in patients with CAD. Agents such as ketamine and pancuronium are probably best avoided.

### 8. How would you manage this patient postoperatively?

Ideally, the patient should be monitored in an intensive care setting postoperatively for hemodynamic alterations, hypothermia, and ischemia. The most common time for a PCE is within 48 hours after surgery. Postoperative troponin measurement is recommended in patients with chest pain or ECG changes. Pain management is important because pain is associated with an increase in myocardial oxygen demand.

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CASE 3

# Congestive Heart Failure

**Amanda J. Rhee, MD • Alexander J. C. Mittnacht, MD • David L. Reich, MD**

## QUESTIONS

1. Name possible etiologies for dilated cardiomyopathy.
2. Explain the pathophysiology of dilated cardiomyopathy.
3. Which monitors would you use for this patient in the perioperative period?
4. How would you anesthetize this patient?

A 55-year-old man with dilated cardiomyopathy (DCM) presented for open reduction and internal fixation of a tibial fracture. He had been in a motor vehicle accident. Past medical history included alcohol abuse, orthopnea, dyspnea on exertion, and several episodes of pulmonary edema. The patient's medications included digoxin, furosemide, and captopril. Physical examination revealed bibasilar rales and $S_3$ gallop. A gated blood pool scan showed a left ventricular ejection fraction of 15%. Cardiac catheterization indicated a left ventricular end-diastolic pressure of 25 mm Hg, a cardiac index of 1.8 L/min/$m^2$, $2^+$ mitral regurgitation, and no coronary artery disease.

### 1. Name possible etiologies for dilated cardiomyopathy.

DCM can be genetically derived or acquired and can exist in both inflammatory and noninflammatory forms. The genetic form comprises 20%–35% of DCM and is usually inherited in an autosomal dominant pattern, although there are also X-linked recessive and mitochondrial patterns of inheritance. DCM is a common cause of heart failure with a prevalence of 36 per 100,000 people. DCM is characterized by ventricular chamber enlargement and systolic dysfunction with normal left ventricular wall thickness.

The inflammatory variety, or myocarditis, is usually the result of infection or parasitic infestation. Myocarditis manifests with a clinical picture of fatigue, dyspnea, and palpitations that usually occur in the first weeks of infection. Palpitations progress to overt congestive heart failure (CHF) with cardiac dilation, tachycardia, pulsus alternans (i.e., regular alternation of pressure pulse amplitude with a regular rhythm), and pulmonary edema. Complete recovery from infectious myocarditis is usually the case, but there are exceptions, such as myocarditis associated with diphtheria or Chagas disease. Diphtheria can produce either right or left bundle-branch block. The combination of diphtheria and bundle-branch block has a mortality rate of approximately 50%. If complete heart block ensues, the mortality rate is 80%–100%. Chagas disease can lead to right bundle-branch block and other arrhythmias in 80% of patients. Viral infections, mycotic infections, and helminthic myocardial involvement have varying clinical profiles that include arrhythmias, CHF, pericarditis, or valvular or vessel obstruction. The noninflammatory variety of DCM also manifests with the clinical picture of myocardial failure but in this case secondary to toxic, degenerative, or infiltrative processes in the myocardium. In some cases, the exact etiology is unknown (idiopathic DCM).

Alcoholic cardiomyopathy is a typical hypokinetic, noninflammatory cardiomyopathy associated with tachycardia and premature ventricular contractions that progresses to left ventricular failure with incompetent mitral and tricuspid valves. This cardiomyopathy is probably due to direct toxic effects of ethanol or its metabolite, acetaldehyde, which releases and depletes cardiac norepinephrine. In chronic alcoholics, acute ingestion of ethanol produces decreases in contractility, elevations in ventricular end-diastolic pressure, and increases in systemic vascular resistance. Alcoholic cardiomyopathy is classified into three hemodynamic stages (Table 3-1).

TABLE 3-1 **Stages of Alcoholic Cardiomyopathy**

| Stage | Cardiac Output | Ventricular Pressures | LVEDV | Ejection Fraction |
|---|---|---|---|---|
| I | Normal | Normal | Normal | Decreased |
| II | Normal | Increased | Increased | Decreased |
| III | Decreased | Increased | Increased | Severely decreased |

*LVEDV,* Left ventricular end-diastolic volume.

Doxorubicin (Adriamycin) is an antibiotic medication with chemotherapeutic effects. It can disrupt myocardial mitochondrial calcium homeostasis and can produce a dose-dependent DCM. Amyloidosis can also cause DCM by myocardial infiltration, although it is also associated with restrictive and obstructive forms of cardiomyopathy, valvular lesions, conduction abnormalities, and infiltration of amyloid in the coronary arteries causing obstruction.

## 2. Explain the pathophysiology of dilated cardiomyopathy.

DCM is characterized by elevated filling pressures, failure of myocardial contractile strength, and a marked inverse relationship between arterial impedance and stroke volume. DCM manifests with a clinical picture very similar to CHF produced by severe coronary artery disease (CAD).

Pathophysiologically, as ventricular muscle weakens, the ventricle dilates to take advantage of the increased force of contraction that results from increased myocardial fiber length. However, as the ventricular radius increases, there is elevation of ventricular wall tension, increasing both oxygen consumption of the myocardium and total internal work of the muscle. As the myocardium deteriorates further, cardiac output decreases, and compensatory increase in sympathetic activity occurs to maintain cardiac output and organ perfusion.

One feature of the failing myocardium is inability to maintain stroke volume against elevated arterial impedance to ejection. As left ventricular dysfunction worsens, stroke volume becomes more dependent on arterial impedance (afterload). In the failing ventricle, stroke volume decreases almost linearly with increases in afterload. The increased sympathetic outflow that accompanies left ventricular failure initiates a vicious cycle of increased resistance to forward flow, decreased stroke volume, reduced cardiac output, and further sympathetic stimulation in an effort to maintain circulatory homeostasis (Figure 3-1).

There is often a degree of mitral regurgitation in severe DCM as a result of stretching of the mitral anulus and distortion of the geometry of the chordae tendineae. Forward stroke volume improves with afterload reduction, even though there is no increase in ejection fraction; this suggests that reduction of mitral regurgitation is the mechanism of improvement. Afterload reduction also decreases left ventricular filling pressure, which relieves pulmonary congestion and should preserve coronary perfusion pressure.

The clinical picture of DCM falls into the two familiar categories of "forward" failure and "backward" failure (Box 3-1). The features of "forward" failure, including fatigue, hypotension, and oliguria, are due to diminished cardiac output and organ perfusion. Decreased renal perfusion results in activation of the renin-angiotensin-aldosterone system, which increases the effective circulating blood volume through sodium and water retention. "Backward" failure is related to elevated filling pressures required by the failing ventricle or ventricles. As the left ventricle dilates,

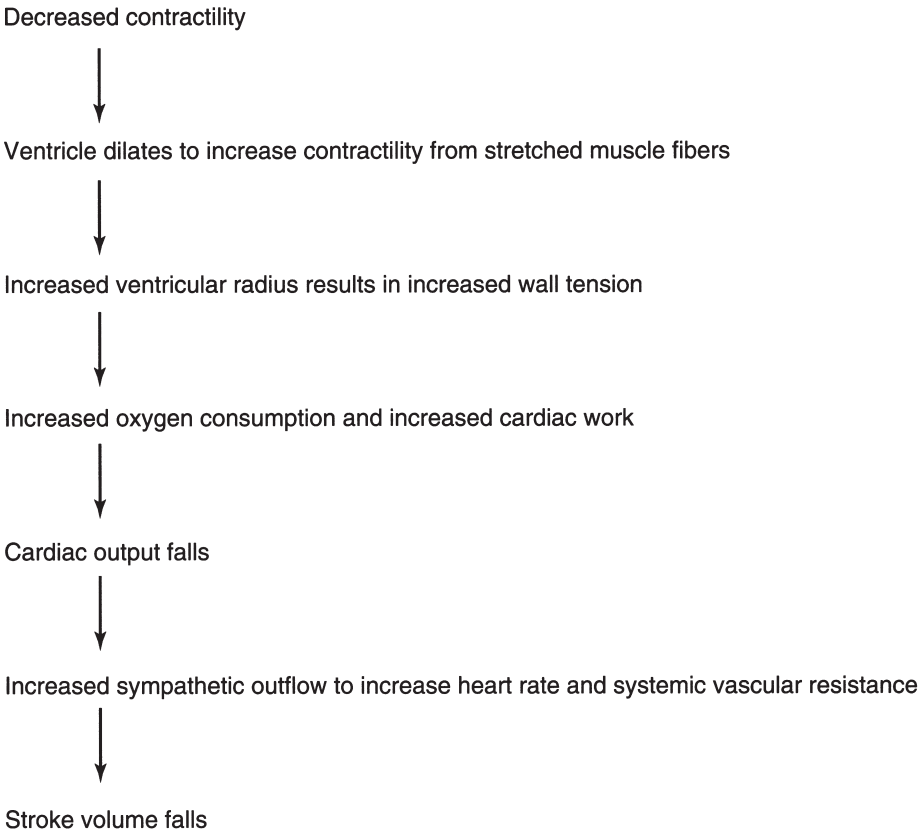


**FIGURE 3-1** ■ Pathophysiology of dilated cardiomyopathy.

**BOX 3-1 Manifestations of Ventricular Failure**

**"Forward": Diminished Cardiac Output and Organ Perfusion**

- Fatigue
- Hypotension
- Oliguria
- Activation of renin-angiotensin-aldosterone system

**"Backward": Elevated Ventricular Filling Pressures and Valvular Regurgitation**

- Left-sided
  - Orthopnea
  - Paroxysmal nocturnal dyspnea
  - Pulmonary edema
- Right-sided
  - Jugular venous distention
  - Hepatomegaly
  - Peripheral edema

"secondary" mitral regurgitation occurs secondary to the above-noted mechanisms. The manifestations of left-sided ventricular failure include orthopnea, paroxysmal nocturnal dyspnea, and pulmonary edema. The manifestations of right-sided ventricular failure include hepatomegaly, jugular venous distention, and peripheral edema.

### 3. Which monitors would you use for this patient in the perioperative period?

Electrocardiogram (ECG) monitoring is essential in the management of patients with DCM, particularly patients with myocarditis. Ventricular arrhythmias are common, and the development of complete heart block requires rapid diagnosis and pacing. The ECG is also useful for monitoring ischemic changes when CAD is associated with cardiomyopathy, as in amyloidosis. Invasive continuous intraarterial blood pressure monitoring during surgery provides continuous blood pressure information and a convenient route for obtaining arterial blood gases.

Many patients in CHF with a severely compromised myocardium who require anesthesia and surgery should have central venous access for monitoring and vasoactive drug administration. The use of a pulmonary artery catheter is much more controversial but is probably of value in patients with severely compromised left ventricular function. Although there is no evidenced-based medicine to support outcome differences, measuring left-sided filling pressures could be beneficial. Monitoring right-sided filling pressure is of equal importance in patients with pulmonary hypertension or cor pulmonale. In addition to measuring filling pressures, a thermodilution pulmonary artery catheter can be used to obtain cardiac output and to calculate systemic and pulmonary vascular resistance, which allow for serial evaluation of hemodynamic status. Additionally, pulmonary artery catheters with fiberoptic oximetry and rapid-response thermistor catheters that calculate right ventricular ejection fraction are available. Pacing catheters and external pacemakers provide distinct advantages in managing patients with myocarditis and associated heart block.

Two-dimensional transesophageal echocardiography (TEE) provides useful data on the ventricle's response to anesthetic and surgical manipulations. A transgastric short-axis view of the left ventricle provides real-time data on preload and ventricular performance that are valuable in judging the need for inotropic support or vasodilator therapy. The degree of mitral regurgitation could also be followed intraoperatively.

### 4. How would you anesthetize this patient?

Avoidance of myocardial depression is the goal of anesthetic management (Table 3-2) for patients with DCM. All the potent volatile anesthetic agents are myocardial depressants. For this reason, these agents, especially in high concentrations, are probably best avoided in patients with DCM. An opioid and sedative-hypnotic anesthetic can be employed instead. Etomidate and ketamine are acceptable anesthetic induction agents, whereas thiopental and propofol are relatively contraindicated.

For a patient with a severely compromised myocardium, the synthetic piperidine opioids (e.g., fentanyl, sufentanil,

TABLE 3-2 **Hemodynamic Goals in Congestive Heart Failure**

| Parameter | Goal | Indicated | Contraindicated |
|---|---|---|---|
| Heart rate | Normal to elevated | Dopamine<br>Dobutamine | High-dose β-adrenergic blockers |
| Preload | Normal to high | Intravenous fluids | Nitroglycerin<br>Propofol<br>Thiopental |
| Afterload | Low | Angiotensin-converting enzyme inhibitors<br>Nitroprusside<br>Milrinone | Phenylephrine |
| Contractility | Increased | Dopamine<br>Dobutamine<br>Epinephrine<br>Milrinone | High-dose volatile anesthetics<br>Nitric oxide<br>High-dose β-adrenergic blockers |

remifentanil, and alfentanil) are useful because myocardial contractility is not depressed. Chest wall rigidity associated with these medications is treated with muscle relaxants. Bradycardia associated with high-dose opioid anesthesia may be prevented by the use of pancuronium for muscle relaxation, anticholinergic drugs, or pacing. For peripheral or lower abdominal surgical procedures, regional anesthetic techniques are reasonable alternatives, provided that filling pressures are carefully controlled and the hemodynamic effects of the anesthetic are adequately monitored. However, regional techniques may be impossible in many patients because of anticoagulation for associated atrial fibrillation or mural thrombus prevention.

In planning the anesthetic management of patients with DCM, associated cardiovascular conditions, such as CAD, valvular abnormalities, outflow tract obstruction, and constrictive pericarditis, should also be considered. Patients with CHF often require circulatory support intraoperatively and postoperatively. Inotropic drugs, such as dopamine or dobutamine, have been shown to be effective in low-output states and produce modest changes in systemic vascular resistance at lower dosages. In severe heart failure, more potent drugs, such as epinephrine, may be required. However, the effects of β-adrenergic agents are limited by the downregulation of β-adrenergic receptors that occurs in chronic CHF. Milrinone is a phosphodiesterase III inhibitor with inotropic and vasodilator properties that may improve hemodynamic performance. As noted earlier, stroke volume is inversely related to afterload in the failing ventricle, and reducing left ventricular afterload with vasodilating drugs, such as nitroprusside and milrinone, is also effective in increasing cardiac output. In patients with myocarditis, especially with a viral cause, transvenous or external pacing may be required if heart block occurs. Intraaortic balloon counterpulsation and left ventricular assist devices are additional options to be considered in the case of a severely compromised ventricle.

Incidence of supraventricular and ventricular arrhythmias is increased in patients with myocarditis and DCM. These arrhythmias often require extensive electrophysiologic investigation and may be unresponsive to maximal medical therapy. Implantable cardioverter-defibrillators are often placed in these patients. During surgery requiring electrocautery, the tachy therapy functions of the cardioverter-defibrillators must be turned off, and external pacemaker pads should be placed in the event defibrillation becomes necessary. Proper ECG monitoring and access to a charged external cardioverter-defibrillator device are crucial in the management of patients with myocarditis and DCM.

**BOX 3-2 Anesthetic Management**

**Induction**
- Etomidate or ketamine

**Maintenance**
- Opioids: fentanyl, remifentanil, sufentanil, alfentanil
- Sedative-hypnotics
- ± Nitrous oxide

**Monitoring**
- ECG for arrhythmias or ischemia
- Arterial catheter
- Pulmonary artery catheter
- TEE

**Arrhythmia Management**
- Esmolol
- Amiodarone
- Cardioversion
- Transvenous/external pacing

**Inotropic Support**
- Dopamine
- Dobutamine
- Milrinone
- Epinephrine

**Vasodilators**
- Milrinone
- Nitroprusside

Amiodarone is a long-acting antiarrhythmic medication with intrinsic myocardial depressant properties. Nevertheless, amiodarone seems to have an overall beneficial effect in patients with CHF, especially patients who present with chronic atrial fibrillation. Amiodarone is currently the antiarrhythmic medication of choice for persistent ventricular tachycardia/ventricular fibrillation, which may be encountered at any time in patients with severely impaired myocardial function (Box 3-2).

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CASE 4

# Aortic Stenosis

**Amanda J. Rhee, MD • Alexander J. C. Mittnacht, MD • David L. Reich, MD**

## QUESTIONS

1. Describe the symptoms of and long-term prognosis for aortic stenosis.
2. Identify the etiology of aortic stenosis.
3. What is the significance of aortic valve area and how is it calculated?
4. Why is it important to maintain sinus rhythm?
5. What is the treatment for supraventricular tachyarrhythmias or bradyarrhythmias?
6. How is hypotension best treated in a patient with aortic stenosis?
7. How would you anesthetize this patient for cardiac or noncardiac surgery?
8. What are anesthetic considerations for transcatheter aortic valve implantation?

A 65-year-old woman presented for aortic valve replacement. She had a history of congestive heart failure (CHF). Cardiac catheterization showed a peak systolic gradient of 90 mm Hg between the left ventricle and the aorta. During anesthetic induction with fentanyl and vecuronium, the patient developed a junctional rhythm and severe hypotension.

### 1. Describe the symptoms of and long-term prognosis for aortic stenosis.

The classic symptoms in patients with severe aortic stenosis (AS) are angina, syncope, and CHF. Life expectancy in untreated cases is approximately 5 years after developing angina, 3 years after developing syncope, and 2 years after developing CHF. Angina is present in approximately 66% of patients with critical AS, but only about 50% have clinically significant coronary artery disease (CAD). Patients without CAD develop angina because of inadequate oxygen delivery to hypertrophied myocardium. There is also evidence that patients with moderate to critical AS (i.e., aortic valve area 0.7-1.5 $cm^2$) are at increased risk for morbidity, which worsens with the onset of symptoms. Some clinicians recommend that aortic valve replacement should be performed promptly in symptomatic patients. However, percutaneous interventions, such as balloon valvuloplasty and percutaneous transcatheter aortic valve implantation (TAVI), may be indicated depending on the clinical situation.

Concentric left ventricular hypertrophy occurs in AS, as defined by increasing left ventricular wall thickness in a symmetric fashion without ventricular dilation. The advantage of a hypertrophied myocardium is the greater intraventricular pressure generated with a smaller increase in wall tension. The relationship between wall tension (T), intracavitary pressure (P), left ventricular radius (R), and wall thickness (h) is described by the law of Laplace: $T = (P \times R)/2h$.

Tension generation in myocytes is the most inefficient way of performing cardiac work because it requires large amounts of oxygen. In patients with left ventricular hypertrophy, oxygen delivery is decreased because left ventricular end-diastolic pressure (LVEDP) is increased. Increased LVEDP decreases coronary perfusion pressure (CPP). CPP is defined as diastolic aortic pressure minus LVEDP.

As the severity of AS increases, a decrease in diastolic aortic pressure compromises CPP even more. The hypertrophied myocardium also results in decreased left ventricular compliance and higher left ventricular filling pressures, which leads to diastolic dysfunction and impaired cardiac filling. Neovascularization of the pressure-overloaded heart is inadequate for the degree of hypertrophy. Finally, the isovolumic phase of relaxation is inappropriately long, shortening the filling period of diastole, which diminishes the time for coronary perfusion. For all these reasons, patients with AS are prone to developing myocardial ischemia during anesthesia.

Syncope is the initial symptom of AS in 15%–30% of patients. It is usually exertional and is caused by exercise-induced vasodilation in the face of a fixed cardiac output. CHF portends the worst long-term prognosis. CHF occurs when the heart has exceeded its capacity to compensate for pressure work with myocardial hypertrophy. The heart progressively dilates, and symptoms of left ventricular failure appear.

### 2. Identify the etiology of aortic stenosis.

AS may be congenital or acquired. In adults, a congenitally bicuspid valve may become calcified and stenotic. Senile calcification of a trileaflet aortic valve is common in patients >70 years old. Rheumatic AS is almost always

associated with rheumatic mitral valve disease. This etiology is becoming less common in developed countries because of the widespread use of antibiotic therapy.

### 3. What is the significance of aortic valve area and how is it calculated?

The normal aortic valve area is 2.5-3.5 $cm^2$. According to the American College of Cardiology/American Heart Association (ACC/AHA) guidelines, valve area <1.0 $cm^2$, peak transvalvular velocity >4.0 m/sec, and mean transvalvular gradient >40 mm Hg are considered to be parameters of hemodynamically severe AS (Table 4-1).

In cardiac catheterization laboratories, aortic valve areas are calculated using the modified Gorlin equation, which in its simplified form states that the valve area is proportional to the flow across the valve divided by the square root of the mean pressure gradient. A variation of this formula is the Hakki equation: Valve area = cardiac output/√peak pressure gradient.

Using echocardiography, the aortic valve area can be calculated using the continuity equation, which is based on the principle that the stroke volume is equal in the left ventricular outflow tract (LVOT) and the aortic valve:

$$\text{Velocity-time-integral}_{(\text{LVOT})} \times \text{area}_{(\text{LVOT})} = \text{velocity-time-integral}_{(\text{aortic valve})} \times \text{area}_{(\text{aortic valve})}$$

Transvalvular peak-to-peak gradients are calculated using the modified Bernoulli equation:

$$\text{Transvalvular gradient} = 4 \times (\text{maximum velocity})^2$$

Transvalvular gradients underestimate the degree of AS in low cardiac output states because of diminished flow across the valve. Despite flow dependence, a mean pressure gradient >40 mm Hg or a peak pressure gradient >80 mm Hg implies severe AS. In the near future, new techniques that employ postprocessing of three-dimensional echocardiographic data may result in improved accuracy compared with current two-dimensional imaging and Doppler interrogation.

### 4. Why is it important to maintain sinus rhythm?

Atrial systole normally contributes approximately 15%–20% of the total stroke volume; in AS, this increases to 40%–50%. The atrial "kick" is crucial in preserving left ventricular filling (and stroke volume) in AS because passive filling is decreased owing to the noncompliant left ventricle. This diastolic dysfunction is characterized by a prolonged isovolumic relaxation phase and decreased early ventricular filling, which leads to increased dependence on the atrial kick. The onset of nonsinus rhythm is often associated with marked hypotension because stroke volume is decreased from loss of the atrial kick. It is difficult for patients with AS to compensate for the loss of sinus rhythm because marked increases in left atrial pressure would be required to maintain an adequate stroke volume.

TABLE 4-1 **Aortic Valve Area**

| Category | Valve Area ($cm^2$) |
|---|---|
| Normal | 2.5–3.5 |
| Mild stenosis | 1.5–2.5 |
| Moderate stenosis | 1.0–1.5 |
| Severe stenosis | 0.7–1.0 |
| Critical stenosis | <0.7 |

### 5. What is the treatment for supraventricular tachyarrhythmias or bradyarrhythmias?

Treatment of arrhythmias in patients with AS must be accomplished rapidly to prevent hemodynamic decompensation. Cardioversion should be considered as the first-line therapy in unstable patients with supraventricular tachyarrhythmias. In stable patients, a therapeutic diagnostic maneuver (e.g., vagal stimulation, adenosine) should be attempted.

When the exact underlying rhythm is identified, treatment usually consists of β-adrenergic blockers (e.g., esmolol), amiodarone, or cardioversion, depending on the rhythm. Amiodarone is the preferred drug in patients with impaired cardiac function (ejection fraction <40%, CHF) or when ventricular tachycardia cannot be ruled out. Volume loading may be beneficial to treat rhythms without an atrial kick, such as atrial fibrillation and junctional tachycardia.

Bradyarrhythmias should be treated with anticholinergics, combined α-adrenergic and β-adrenergic agonists, or atrioventricular sequential pacing. The ideal heart rate is probably 70–80 beats per minute. This rate allows for adequate diastolic filling, while providing sufficient cardiac output in a heart with a relatively fixed stroke volume.

### 6. How is hypotension best treated in a patient with aortic stenosis?

Patients with severe AS do not tolerate hypotension. Even brief episodes of hypotension may lead to hemodynamic decompensation. Based on optimization of preload, afterload, heart rate, and contractility (Table 4-2), the priorities of treatment to restore cardiac output should include the following:

- Preservation of blood pressure using vasoconstrictors to increase afterload
- Restoration of sinus rhythm
- Intravenous fluids to maintain preload
- Maintenance of heart rate in the normal range
- Maintenance of myocardial contractility

If the etiology of hypotension is not immediately obvious, empiric treatment with an α-adrenergic receptor agonist (e.g., phenylephrine) should be attempted to preserve CPP and avoid the vicious cycle of irreversible ischemia. Generally, pure α-adrenergic receptor agonists are the preferred vasoconstrictor agents because they do not cause tachycardia, which preserves diastolic filling time.

### 7. How would you anesthetize this patient for cardiac or noncardiac surgery?

Premedication in patients with AS should be administered carefully. Oversedation may lead to hypotension

TABLE 4-2 **Hemodynamic Goals in Aortic Stenosis**

| Parameter | Goal | Indicated | Relatively Contraindicated |
|---|---|---|---|
| Heart rate | Normal to slow sinus rhythm | Restore sinus rhythm<br>β blockers | Potent volatile agents (high doses) |
| Preload | Normal to high | Intravenous fluids | Nitroglycerin<br>Thiopental<br>Propofol |
| Afterload | High | Phenylephrine | Nitroprusside |
| Contractility | Normal to increased | Epinephrine (careful of increased heart rate)<br>Norepinephrine | High-dose β-adrenergic blockers<br>Potent volatile agents (high doses) |

and decreased CPP, whereas undersedation may result in anxiety, tachycardia, and myocardial ischemia. Patients with AS are critically sensitive to preload; adequate intravascular volume status has to be ensured before anesthesia induction. Systemic vascular resistance must be maintained at all times. Sympatholysis associated with neuraxial anesthesia often requires use of vasoconstrictive medications and invasive monitoring. Neuraxial techniques may be relatively contraindicated in patients with severe AS. Arrhythmias are poorly tolerated, so maintenance of a sinus rhythm is imperative. A defibrillator should be readily available, or defibrillator pads may be placed preemptively, especially in reoperative cardiac surgery and minimally invasive aortic valve replacement where internal paddles may not be as effective or may be impossible to use.

Perioperative monitoring should be guided by the recommendations of the American Society of Anesthesiologists (ASA). Patients with AS are at increased risk for ischemia and arrhythmias, and electrocardiogram (ECG) monitoring should include leads II and V5. Intraarterial monitoring should be used to monitor blood pressure precisely for rapid recognition and treatment of hemodynamic derangements, especially in situations where rapid fluid shifts or hemodynamic alterations are expected. Pulmonary artery catheters are no longer routinely used solely to estimate left-sided filling pressures because of absence of evidence to support the value of this information. If a pulmonary artery catheter is inserted, placement must be performed with extreme caution because arrhythmias and (rarely) heart block may occur. However, pulmonary artery catheters may be advantageous for monitoring mixed venous oxygen saturations, cardiac outputs, and transvenous pacing capability.

The main goals for inducing anesthesia in patients with AS are to avoid major alterations in preload, afterload, heart rate, and contractility (see Table 4-2). Etomidate, opioids, and midazolam are reasonably good choices but should be titrated to effect. Vecuronium and cisatracurium are neuromuscular blockers with favorable hemodynamic profiles. Ketamine and pancuronium may increase heart rate and should be avoided. Thiopental may cause decreased preload and myocardial contractility and probably should be avoided or titrated to effect at reduced dosages. The dosage and rate of administration of propofol should also be reduced to avoid hypotension.

Anesthesia can be maintained with many different techniques as long as preload, afterload, heart rate, and contractility are controlled to avoid adverse hemodynamic responses. Opioids, benzodiazepines, potent volatile anesthetics, and nitrous oxide all should be titrated, paying careful attention to maintaining perfusion pressure. Tachycardia, bradycardia, and loss of sinus rhythm all are problematic. Stroke volume across the stenotic aortic valve is relatively fixed and is lower than normal; an α-agonist, such as phenylephrine, is the agent of choice for treating hypotension.

## 8. What are anesthetic considerations for transcatheter aortic valve implantation?

TAVI is a method by which a bovine bioprosthetic aortic valve is inserted through a catheter superimposing the existing aortic valve and replacing its function. It is most commonly used in patients with severe AS. The first valve approved for TAVI by the U.S. Food and Drug Administration (FDA) is the Sapien valve (Edwards Lifesciences Corporation, Irvine, CA), which was approved in November 2011. The CoreValve (Medtronic Inc., Minneapolis, MN) is used in the United States at the present time for investigational purposes only. These two valves have similarities and individual limitations, but the overall procedure is similar.

Depending on the patient's comorbidities and procedural approach, either general anesthesia or monitored anesthesia care (deep sedation) can be performed. There are a few reports of neuraxial techniques, but they are not widely accepted. Monitoring should include standard ASA monitors, continuous intraarterial pressure monitoring before induction of anesthesia, and a large-bore central venous catheter through which pressures can be measured. Transesophageal echocardiography (TEE) is used to evaluate the patient's baseline disease, aid in determining suitability of valve placement, monitor the heart and valve during the procedure, and evaluate successful placement after valve deployment. Pulmonary artery catheters, cerebral oximetry, and anesthetic depth monitors should be considered. The need for rapid blood transfusion must also be anticipated and prepared for.

The CoreValve is a self-expanding device that continues to expand over 48 hours; the risk of new conduction abnormalities continues until expansion is complete.

Placement of a transvenous pacing wire is strongly recommended during this time period. The Sapien valve is not self-expanding, so the need for a transvenous pacing wire is evident immediately after deployment of the valve.

The most common approach is retrograde by transcatheter insertion through the femoral or axillary artery, which may be established percutaneously or via a surgical cutdown. TAVI can also be performed by direct access through the aorta after thoracotomy or sternotomy. Less common areas of insertion are through the carotid artery and transapically through the left ventricle. After arterial access is established and preliminary preparations are made, the right ventricle is paced at a rapid rate to decrease cardiac output while balloon valvuloplasty of the native aortic valve is performed. Subsequently, iatrogenic aortic regurgitation is seen with evidence of decreased forward flow. Blood pressure may need to be supported with vasopressors such as phenylephrine, norepinephrine, or vasopressin. After obtaining an angiogram to confirm positioning of the valve, rapid ventricular pacing is begun again to decrease cardiac output as the valve is rapidly deployed. There is a brief period during which valve expansion creates a significant obstruction of flow through the aorta. After the valve is deployed, pacing is stopped, and the blood pressure may need to be supported again with vasopressors. Successful valve placement should reestablish forward flow. After the procedure, the patient should recover in an intensive care setting.

Possible deployment complications include the following:

- Arrhythmia (e.g., complete heart block)
- Obstruction of the coronary arteries with native aortic valve leaflets that are pressed against the inner aortic wall
- Global ischemia from periods of low output during pacing
- Valve malfunction with inadequate opening of all leaflets
- Aortic regurgitation

During the procedure, wires and catheters in the heart may cause ventricular arrhythmia. Manipulation of the aorta, other arteries, or the heart can lead to vessel injury, perforation, or dissection with the potential for massive bleeding.

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CASE 5

# Mitral Stenosis

**Amanda J. Rhee, MD • Alexander J. C. Mittnacht, MD • David L. Reich, MD**

## QUESTIONS

1. What are the etiology and pathophysiology of mitral stenosis?
2. How are preload, afterload, heart rate, and contractility managed in patients with mitral stenosis?
3. Explain methods for optimizing the patient's condition preoperatively.
4. What intraoperative monitoring would be appropriate?
5. How would you anesthetize this patient?
6. Describe the treatment for hypotension in patients with mitral stenosis.
7. What therapies are recommended for perioperative right ventricular failure?
8. Describe specific considerations for mitral valve repair, replacement, or percutaneous techniques.

A 77-year-old woman with severe mitral stenosis was scheduled for mitral valve repair or replacement and tricuspid valve annuloplasty. On admission to the hospital, she had severe pulmonary edema and atrial fibrillation, with a rapid ventricular response. She weighed 55 kg. Cardiac catheterization revealed mitral stenosis, pulmonary hypertension, and tricuspid regurgitation.

## 1. What are the etiology and pathophysiology of mitral stenosis?

Mitral stenosis is frequently rheumatic in origin. In many patients, there is a latency period of 30–40 years between the episode of rheumatic fever and the onset of clinical symptoms. Dyspnea is the most common symptom. The initial presentation is often due to an episode of atrial fibrillation resulting from atrial dilation or an exacerbation of symptoms from an unrelated condition, such as pregnancy, thyrotoxicosis, anemia, fever, or sepsis. Other common symptoms include fatigue, palpitations, chest pain, thromboembolic events, and hemoptysis (from pulmonary vascular congestion).

The normal adult mitral valve orifice is 4–6 $cm^2$. As the orifice narrows to $<2$ $cm^2$, the pressure gradient between the left atrium and left ventricle increases to maintain adequate flow and filling of the left ventricle. The high left atrial pressure causes pulmonary venous congestion, which eventually leads to pulmonary edema, particularly in the presence of tachycardia (Figure 5-1). Tachycardia shortens diastole and diminishes the time available for flow across the mitral valve; this impairs left atrial emptying and left ventricular filling. Cardiac output decreases, pulmonary congestion increases, and decompensation ensues. A mitral valve area $<1$ $cm^2$ is considered critical. However, the decision to perform valve surgery is usually based on the severity of symptoms (i.e., New York Heart Association [NYHA] classification). The 10-year survival rate for patients with symptoms of dyspnea on exertion is approximately 80% without surgery. The 10-year survival rate for patients with disabling NYHA class III (dyspnea with minimal activity) and class IV (dyspnea at rest) symptoms is approximately 15% without surgery.

It previously had been thought that the left ventricle is "protected" from pressure or volume overload. Although some degree of left ventricular "protection" may be present for most cases of mild mitral stenosis, as the disease progresses, it is likely to cause varying degrees of left ventricular failure. Additionally, left ventricular contractility may be

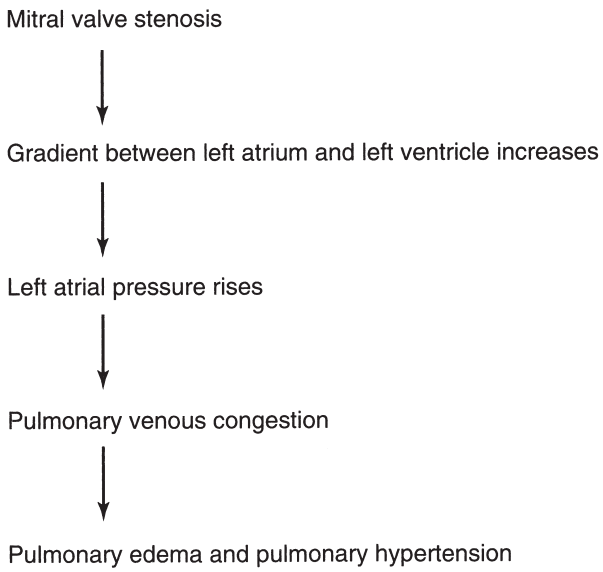


**FIGURE 5-1** ■ Pathophysiology of mitral stenosis.

impaired by rheumatic involvement of papillary muscles and mitral anulus. Left ventricular posterobasal regional wall motion abnormalities may result. However, it is possible that left ventricular function might also be impaired by a leftward shift of the interventricular septum owing to right ventricular pressure overload. Pulmonary hypertension and right ventricular failure are often observed in mitral stenosis.

## 2. How are preload, afterload, heart rate, and contractility managed in patients with mitral stenosis?

The goals for preload, afterload, heart rate, and contractility are the major guiding principles of intraoperative management for patients with mitral stenosis. High left atrial pressures are required to maintain filling of the left ventricle (preload) through the stenotic mitral valve. Hypovolemia and venodilating drugs should be avoided. Afterload (systemic vascular resistance) should be kept high to maintain perfusion pressure in the face of a relatively low and fixed cardiac output. Heart rate should be kept slow to maximize diastolic filling of the left ventricle. Contractility should be maintained to preserve stroke volume. The hemodynamic goals in mitral stenosis are summarized in Table 5-1.

Right ventricular failure is common in mitral stenosis. Parameters should be optimized for the right ventricle and the left ventricle. For example, optimization of left ventricular preload is important while also guarding against exacerbation of pulmonary congestion. Also, tachycardia can be detrimental in mitral stenosis; however, a normal to mildly elevated heart rate is beneficial in right ventricular failure, where the cardiac output of the right ventricle becomes more heart rate–dependent. These seemingly contradictory management goals must be balanced based on each patient's dynamic physiologic status and needs.

## 3. Explain methods for optimizing the patient's condition preoperatively.

In patients with mitral stenosis, it is essential to optimize hemodynamics preoperatively. There is no medical treatment for the fixed obstruction resulting from mitral stenosis. However, medical optimization is mainly geared toward heart rate control to promote ventricular filling and reduce pulmonary vascular congestion. Medical therapy includes β-adrenergic blockers or calcium-channel blockers or both for heart rate regulation or cardiac glycosides if there is left or right ventricular dysfunction. If there is bronchial reactivity, glucocorticoids may be helpful. Pulmonary vascular congestion is treated with diuretics and salt restriction. Diuretic-induced hypokalemia is corrected to prevent digitalis toxicity and arrhythmias. These medications are continued until the time of surgery.

Treatment of acute-onset rapid atrial fibrillation includes anticoagulation and rate control with digoxin, calcium-channel blockers, and β-adrenergic blockers. Hemodynamic instability requires immediate electrical cardioversion and pharmacologic cardioversion in select patients.

Patients with mitral stenosis are unusually hemodynamically sensitive to opioids and central nervous system depressants; however, adequate preanesthetic medication is important for preventing anxiety-induced tachycardia. Monitoring should be provided when administering these medications to avoid or treat decreases in systemic vascular resistance or preload.

## 4. What intraoperative monitoring would be appropriate?

In addition to the American Society of Anesthesiologists (ASA) standard monitoring requirements, insertion of an intraarterial catheter before induction is recommended to follow blood pressure carefully during induction. Tachycardia during intubation or hypotension related to induction agents should be recognized and treated rapidly to prevent catastrophic outcomes. Pulmonary artery catheters may be useful in these patients, but placement of a pulmonary artery catheter is not without risks. The risks include arrhythmias, heart block, and pulmonary artery perforation. Benefits of pulmonary artery catheters include data on left atrial filling pressure, pulmonary artery pressure, cardiac output, mixed venous oxygen saturation, and pulmonary

TABLE 5-1 **Hemodynamic Goals in Mitral Stenosis**

| Parameter | Goal | Indicated | Relatively Contraindicated |
|---|---|---|---|
| Heart rate | Slow | β-adrenergic blockers<br>Digoxin<br>Calcium-channel blockers | Dopamine<br>Dobutamine<br>Ketamine<br>Pancuronium |
| Preload | High | Intravenous fluids | Nitroglycerin<br>Thiopental<br>Propofol |
| Afterload | High | Phenylephrine | Angiotensin-converting enzyme inhibitors (except for right ventricular failure)<br>Nitroprusside |
| Contractility | Normal to increased | Norepinephrine | High-dose volatile anesthetics<br>High-dose β-adrenergic blockers |

and systemic vascular resistance. In the presence of right ventricular dysfunction, knowledge of pulmonary artery pressures is particularly important because successful therapy includes decreasing right ventricular afterload.

Transesophageal echocardiography (TEE) provides information about biventricular function, left atrial dimensions, and valvular function. TEE allows for visualization of left and right ventricular filling and function. Mitral valve area can be calculated using pressure half-time measurements or the continuity equation using Doppler interrogation techniques. TEE permits evaluation of valvular pathology and guidance for surgical decision making regarding repair versus replacement as well as evaluation of the valve or prosthesis after cardiopulmonary bypass.

## 5. How would you anesthetize this patient?

Opioids (e.g., fentanyl, sufentanil, remifentanil), benzodiazepines, and etomidate all are reasonable choices for anesthetic induction in patients with mitral stenosis (Table 5-2). Opioids also have the advantage of increasing vagal tone and slowing heart rate, usually without associated hypotension. Short-acting barbiturates, such as thiopental, produce undesirable venodilation and myocardial depression. Ketamine is relatively contraindicated on the basis of its tachycardic effects. Volatile agents produce both myocardial depression and vasodilation and should be used cautiously in low concentrations. Propofol should be used with caution. Theoretically, the most suitable neuromuscular blocking agents for mitral stenosis are succinylcholine, vecuronium, rocuronium, and cisatracurium. Large boluses of pancuronium are relatively contraindicated because they produce tachycardia.

## 6. Describe the treatment for hypotension in patients with mitral stenosis

Hypotension is best treated with an α-adrenergic agonist, such as phenylephrine, which increases arterial blood pressure and decreases heart rate via baroreceptor-mediated reflexes. Vasopressin can also be used and may be preferable in pulmonary hypertension because it does not cause pulmonary vasoconstriction. Vasoconstriction is necessary during hypotension because it is essential to preserve vital organ perfusion in the face of fixed low cardiac output. β-Adrenergic agonists cause tachycardia and vasodilation, which are undesirable effects in patients with mitral stenosis. Ephedrine, dopamine, dobutamine, and epinephrine are relatively contraindicated before valvular repair.

## 7. What therapies are recommended for perioperative right ventricular failure?

After mitral valve replacement, weaning from cardiopulmonary bypass is sometimes complicated by pulmonary hypertension and right ventricular failure. Monitoring left atrial pressure may be helpful in the most difficult cases because a gradient is often present between the pulmonary capillary wedge and left atrial pressures. Factors that predispose to pulmonary vasoconstriction (e.g., hypoxia, hypercarbia, acidosis, light anesthesia, and hypothermia) should be corrected.

The main goals in the anesthetic management of right ventricular failure are to reduce right ventricular afterload, optimize right ventricular preload, maintain right ventricular coronary perfusion, and support right ventricular contractility. In the presence of preexisting pulmonary hypertension and increased pulmonary vascular resistance, right ventricular failure responds favorably to pulmonary vasodilation. Drugs with pulmonary vasodilating activity that are used after termination of cardiopulmonary bypass include nitroprusside, nitroglycerin, prostaglandin $E_1$ (or other prostanoid therapies, such as prostacyclin or iloprost), or an endothelin antagonist. However, none of these medications is selective for the pulmonary circulation, and their use may be limited by systemic effects. Milrinone, a phosphodiesterase III inhibitor, increases right ventricular contractility and has pulmonary vasodilating properties. This pharmacologic profile makes phosphodiesterase III inhibitors appealing in the treatment of right ventricular failure. Inhaled aerosolized milrinone is an emerging therapy that may be used for selective pulmonary vasodilation.

TABLE 5-2 **Mitral Stenosis and Anesthesia**

| Category | Recommended | Not Recommended |
|---|---|---|
| Induction agents | Etomidate<br>Opioids<br>Benzodiazepines | Thiopental<br>Ketamine<br>Propofol |
| Maintenance agents | Opioids | Potent inhalation agents in high concentrations |
| Muscle relaxants | Succinylcholine<br>Vecuronium<br>Rocuronium<br>Cisatracurium | Pancuronium |
| Hypotension | Phenylephrine<br>Vasopressin | β-adrenergic agonists<br>Ephedrine<br>Epinephrine<br>Dopamine<br>Dobutamine |

**BOX 5-1 Treatment of Right Ventricular Failure**

- Reverse pulmonary vasoconstriction
  - Correct hypoxia, hypercarbia, acidosis, hypothermia
- Dilate pulmonary vasculature
  - Nitroglycerin
  - Prostaglandin $E_1$
  - Inhaled nitric oxide
  - Inhaled prostacyclin (e.g., iloprost)

Inhaled nitric oxide is an established therapy for pulmonary hypertension and right ventricular failure after mitral valve surgery. Inhaled nitric oxide selectively causes pulmonary vascular relaxation. Inhaled prostacyclin acts via specific prostaglandin receptors and has been shown to reduce pulmonary hypertension after cardiac surgery. Vasodilation is relatively selective for the pulmonary vasculature. Various newer prostacyclin analogues are now given for chronic pulmonary hypertension and may be useful in intraoperative situations in the future (Box 5-1).

Vasopressin or norepinephrine is particularly effective for the treatment of systemic hypotension in patients with right ventricular failure. Epinephrine is the preferred catecholamine in patients with pulmonary hypertension and right ventricular failure when right ventricular contractility is suspected to be severely impaired.

### 8. Describe specific considerations for mitral valve repair, replacement, or percutaneous techniques.

Percutaneous mitral valve commissurotomy may be performed using a balloon catheter that is inflated across the mitral valve. It has become the preferred procedure compared with surgery in select patients because success rates are comparable with surgical mitral commissurotomy. It is effective in the following patients:

- Asymptomatic patients with moderate to severe mitral stenosis with pulmonary hypertension
- Symptomatic patients (NYHA functional class II, III, or IV) with moderate or severe mitral stenosis
- Patients with favorable mitral valve pathology in the absence of left atrial thrombus and moderate to severe mitral regurgitation
- Gravid patients

Surgical mitral valve replacement or repair, if possible, is indicated in symptomatic patients (NYHA functional class III or IV) with moderate to severe mitral stenosis when percutaneous valvotomy is unavailable or unfavorable. Symptomatic patients with concomitant moderate to severe mitral regurgitation should also undergo surgical mitral valve repair or replacement. Known complications of mitral valve replacement include valve thrombosis, valve dehiscence, valve malfunction, valve infection, and embolic events.

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CASE 6

# Hypertrophic Obstructive Cardiomyopathy

**Amanda J. Rhee, MD • Alexander J. C. Mittnacht, MD • David L. Reich, MD**

## QUESTIONS

1. Describe the anatomic abnormalities in hypertrophic obstructive cardiomyopathy.
2. What changes in preload, afterload, heart rate, and contractility optimize hemodynamic performance for patients with hypertrophic obstructive cardiomyopathy?
3. What are the treatment options for hypertrophic obstructive cardiomyopathy?
4. What monitoring is required in patients with hypertrophic obstructive cardiomyopathy?
5. What are the considerations for anesthetic management of patients with hypertrophic obstructive cardiomyopathy?
6. What are special considerations for anesthetic management of labor and delivery in patients with hypertrophic obstructive cardiomyopathy?

A 28-year-old woman with hypertrophic obstructive cardiomyopathy (HOCM) presented for labor and delivery. She was initially managed by the obstetrician with intravenous butorphanol but became progressively more uncomfortable. The anesthesiologist was consulted for further management.

### 1. Describe the anatomic abnormalities in hypertrophic obstructive cardiomyopathy.

HOCM is the most common genetic cardiovascular disease, with a prevalence of approximately 1 in 500 young people in the United States. It is an autosomal dominant genetic disorder and is an important cause of heart failure at any age. HOCM is usually defined by a hypertrophied, nondilated left ventricle that occurs in the absence of other causative diseases for hypertrophy, such as chronic hypertension and aortic stenosis. It occurs in either obstructive or nonobstructive forms. The obstructive forms feature a dynamic pressure gradient across the left ventricular outflow tract (LVOT). Other conditions can produce the picture of obstructive cardiomyopathy secondary to significant infiltration of the ventricular wall, as in Pompe disease, in which a massive accumulation of cardiac glycogen in the ventricular wall produces ventricular outflow obstruction.

HOCM, hypertrophic cardiomyopathy, asymmetric septal hypertrophy, and idiopathic hypertrophic subaortic stenosis all are terms applied to the same disease process. The main anatomic feature of HOCM is a hypertrophied ventricular muscle at the septum base in the LVOT. The histologic appearance is a disorganized mass of hypertrophied myocardial cells extending from the left ventricular septal wall; the mass may involve the papillary muscles. Intramural (small vessel) coronary artery disease has been identified in autopsy specimens, especially in areas of myocardial fibrosis. This coronary artery disease may play some role in the etiology of myocardial ischemia in these patients.

Obstruction to left ventricular outflow is caused by hypertrophic muscle at the interventricular septum and systolic anterior motion (SAM) of the anterior leaflet of the mitral valve. SAM is associated with mitral regurgitation and a posteriorly directed jet. SAM previously was thought to be caused by a Venturi effect of the rapidly flowing blood in the LVOT. A more recent theory suggests that changes in the position of the leaflet coaptation zone relative to the interventricular septum and changes in blood flow caused by blood hitting the bulging septum may physically push the anterior mitral valve leaflet into the LVOT during systole. In other words, the hypertrophied ventricular septum causes the mitral valve to be positioned more anteriorly in the left ventricular cavity, bringing the leaflet coaptation point closer to the interventricular septum than normal. Excessive anterior mitral valve tissue in combination with the more anterior position of the mitral valve causes the anterior mitral valve leaflet to protrude into the LVOT. Additionally, the hypertrophied ventricular septum changes blood flow in the LVOT, redirecting it behind and lateral to the enlarged anterior mitral valve leaflet and pushing it into the septum.

Consequently, a dynamic subaortic pressure gradient is present. The outflow tract obstruction, by causing increased pressure in the ventricular chamber, can result in hypertrophy of the remainder of the ventricular muscle. As the ventricle hypertrophies, ventricular compliance decreases, and passive filling of the ventricle during diastole is limited. The ventricle increasingly depends on atrial systole (atrial kick) to maintain ventricular end-diastolic volume and, ultimately, cardiac output. Occasionally, HOCM is associated with right ventricular outflow tract obstruction as well.

## 2. What changes in preload, afterload, heart rate, and contractility optimize hemodynamic performance for patients with hypertrophic obstructive cardiomyopathy?

Determinants of the severity of the ventricular obstruction in HOCM are the following:

- Systolic volume of the ventricle
- Force of ventricular contraction
- Transmural pressure distending the outflow tract

Large systolic volumes in the ventricle distend the outflow tract and reduce the obstruction. Paradoxically, when ventricular contractility is increased, the outflow tract is narrowed, which increases the obstruction and decreases cardiac output. When aortic pressure (afterload) is elevated, there is an increased transmural pressure distending the LVOT during systole, and this reduces the degree of obstruction. Conversely, during periods of systemic vasodilation, the outflow tract is narrowed. This results in a marked decrease in cardiac output and mitral regurgitation, as the mitral valve becomes the relief point for ventricular pressure (Table 6-1).

## 3. What are the treatment options for hypertrophic obstructive cardiomyopathy?

Medical therapy of HOCM is based on the administration of β-adrenergic blockers (Table 6-1). The specific regimen is tailored to an individual patient's pathologic profile. The beneficial effects of β-adrenergic blockers are likely due to depressed systolic function, improved diastolic filling, and better relaxation. However, it is still unclear whether life expectancy is prolonged by this treatment. In patients whose symptoms are refractory to β-adrenergic blockers, verapamil is administered, which also depresses systolic function and improves diastolic function. Patients whose symptoms are refractory to this combination may be treated with disopyramide, a type IA antiarrhythmic medication that decreases systolic function and causes some peripheral vasoconstriction. Amiodarone is commonly administered for the control of supraventricular and ventricular dysrhythmias.

Nonmedical treatment options are surgical myotomy or myectomy, percutaneous transluminal septal myocardial ablation, alcohol septal ablation, septal coil embolization, mitral valve replacement or valvuloplasty, or a combination of these. Potential complications of surgical correction of the LVOT obstruction include complete heart block and immediate or late formation of a ventricular septal defect secondary to septal infarction. Dual chamber pacing and implantable cardioverter-defibrillator devices are helpful to maintain sinus rhythm and treat arrhythmias that might otherwise lead to sudden cardiac death. The reported annual mortality rate is 1% to 3%, with deaths mostly resulting from ventricular arrhythmias, sudden cardiac death, progressive heart failure, and atrial fibrillation with embolic stroke.

## 4. What monitoring is required in patients with hypertrophic obstructive cardiomyopathy?

Patients with HOCM may be extremely sensitive to slight changes in ventricular volume, blood pressure, heart rate, and rhythm resulting in hemodynamic catastrophe. Monitoring should allow for continuous assessment of these parameters, particularly in patients with severe obstruction. In patients with HOCM presenting for septal myectomy, an electrocardiogram (ECG), intraarterial catheter, and central venous catheter are necessary.

TABLE 6-1 **Hemodynamic Goals in Hypertrophic Obstructive Cardiomyopathy**

| Parameter | Goal | Indicated | Relatively Contraindicated |
|---|---|---|---|
| Heart rate | Slow | β-adrenergic blockers<br>Verapamil | Dopamine<br>Dobutamine<br>Ephedrine<br>Epinephrine<br>Isoproterenol<br>Atropine<br>Glycopyrrolate<br>Ketamine |
| Preload | Normal to high | Intravenous fluids | Nitroglycerin<br>Thiopental<br>Propofol<br>Spinal/epidural anesthesia |
| Afterload | High | Phenylephrine<br>Disopyramide | Angiotensin-converting enzyme inhibitors<br>Nitroprusside<br>Milrinone |
| Contractility | Decreased | Halothane<br>Sevoflurane<br>High-dose β-adrenergic blockers<br>Disopyramide<br>Verapamil | Dopamine<br>Dobutamine<br>Epinephrine<br>Milrinone |
| Heart rhythm | Normal sinus | Atrial pacing<br>Disopyramide<br>Amiodarone | |

A pulmonary artery catheter may be considered. Two-dimensional transesophageal echocardiography (TEE) provides useful data on ventricular performance, the dynamic mechanism of LVOT obstruction, and accompanying mitral regurgitation. After septal myectomy, TEE provides invaluable information about residual obstruction and mitral regurgitation. TEE can also be useful for detecting surgical complications, such as ventricular septal perforation.

In patients with HOCM scheduled for noncardiac procedures, monitoring should provide some indication of ventricular volume, force of ventricular contraction, and transmural pressure distending the outflow tract. Central venous pressure could be an indicator of ventricular volume in procedures that do not result in major volume shifts or alterations in ventricular function. An intraarterial catheter is almost always indicated for beat-to-beat blood pressure monitoring during major regional or general anesthesia in patients with symptomatic HOCM. Intraoperative TEE is the most accurate monitor of ventricular loading conditions and performance in HOCM.

## 5. What are the considerations for anesthetic management of patients with hypertrophic obstructive cardiomyopathy?

Anesthetic management of patients with HOCM revolves around optimization of intravascular volume, ventricular contractility, and transmural distending pressure of the outflow tract (see Table 6-1). Blood loss, sympathectomy secondary to spinal or epidural anesthesia, nitroglycerin, or postural changes can decrease preload. Sympathetic stimulation caused by tracheal intubation or surgical manipulation results in an increase in contractility and tachycardia, both of which may exacerbate LVOT obstruction. An effort should be made to blunt this response (e.g., deepening the anesthesia) before stimulation. Inotropes, β-adrenergic agonists, and calcium are relatively contraindicated for the same reason. Transmural distending pressure can be decreased by hypotension secondary to anesthetic drugs, hypovolemia, or positive pressure ventilation. Tachycardia is poorly tolerated in patients with HOCM because it decreases systolic ventricular volume, narrowing the outflow tract. Atrial contraction is extremely important to filling of the hypertrophied ventricle. Nodal rhythms should be aggressively treated, using atrial pacing if necessary.

Anesthesia can be induced intravenously or by inhalation of a potent anesthetic agent. Ketamine and pancuronium are best avoided because of their sympathomimetic effects. Historically, halothane was the most efficacious potent volatile agent because it decreases heart rate and myocardial contractility, has the least effect on systemic vascular resistance (SVR), and tends to minimize the severity of LVOT obstruction when volume replacement is adequate. Isoflurane and desflurane cause pronounced peripheral vasodilation and are less desirable. Sevoflurane decreases SVR to a lesser extent and may be the preferred inhaled volatile anesthetic at the present time. Agents that release histamine, such as morphine, are not recommended because of the venodilation and hypovolemia that they produce. High-dose opioid anesthesia causes minimal cardiovascular side effects along with bradycardia and may be a useful anesthetic technique in these patients. Preoperative β-adrenergic blocker or calcium channel blocker therapy should be continued. Intravenous propranolol, metoprolol, esmolol, or verapamil can be administered intraoperatively to improve hemodynamic performance (Table 6-2).

TABLE 6-2 **Anesthetic Agents and Hypertrophic Obstructive Cardiomyopathy**

| Anesthetic Agent | Advantage | Disadvantage |
|---|---|---|
| Halothane | Decreases heart rate<br>Decreases contractility<br>Minimal decrease in SVR | |
| Sevoflurane | | More peripheral vasodilation than halothane but less than isoflurane and desflurane<br>Increases heart rate |
| Isoflurane | | More peripheral vasodilation than halothane<br>Increases heart rate |
| Desflurane | | More peripheral vasodilation than halothane<br>Increases heart rate |
| Fentanyl | Slows heart rate | |
| Morphine | | Histamine release, predisposing to peripheral vasodilation |
| Ketamine | | Sympathomimetic |
| Pancuronium | | Increases heart rate |

*SVR,* Systemic vascular resistance.

### 6. What are special considerations for anesthetic management of labor and delivery in patients with hypertrophic obstructive cardiomyopathy?

Anesthetic management for labor and delivery in a parturient with HOCM can be quite complex. β-Adrenergic blocker therapy may have been discontinued during pregnancy because of the association with intrauterine growth restriction and fetal bradycardia. The risks associated with pregnancy in patients with HOCM vary with severity of disease. Mortality is highest in patients with severe symptoms such as shortness of breath. Pregnancy avoidance may have already been discussed with these patients.

Successful cesarean deliveries with both general and epidural anesthetics have been reported. Careful titration of anesthetic agents and optimization of intravascular volume are imperative. The monitoring recommendations are the same as described previously with the addition of a fetal heart monitor. Finally, left uterine displacement should be established in the usual fashion. The hemodynamic goals should be the same as for a nonpregnant patient except that these goals must also be titrated to the well-being of the fetus. Care should be taken to balance treating perfusion pressures with vasopressors and vasoconstriction of the uterine vessels that may affect the fetus. If hypotension occurs during anesthesia, the use of β-adrenergic agonists, such as ephedrine, may result in worsening outflow tract obstruction. α-Adrenergic agonists, such as phenylephrine, previously thought to result in uterine vasoconstriction and fetal asphyxia, are now preferred for the treatment of hypotension.

Although maternal mortality is increased in women with HOCM, overall mortality seems to be low. The management of labor and delivery in the presence of HOCM is a challenging situation, and emergency delivery services should be available. Elective cesarean delivery should be considered if symptoms of HOCM are severe.

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CASE 7

# Cardiac Pacemakers and Defibrillators

**Marc E. Stone, MD • Himani Bhatt, MD**

## QUESTIONS



A 59-year-old man with diverticulitis and dilated cardiomyopathy presented for a hemicolectomy. Concurrent medical issues include coronary artery disease, coronary artery bypass graft, congestive heart failure, hypertension, mild renal insufficiency, and hiatal hernia. A pacemaker and implantable cardioverter-defibrillator (ICD) are present. Medications include aspirin, warfarin, enalapril, fluoxetine, metoprolol, lansoprazole, and zolpidem. He has no known drug allergies.

### 1. What are the different types of pacemakers?

In modern practice, cardiac pacing can be provided in numerous ways and by a range of devices, including transcutaneous pacing pads; temporary external pacing devices connected to transvenous or epicardial wires; and highly sophisticated, multifunctional, programmable, permanently implanted pulse generators with permanent intracardiac or epicardial leads. Indications for cardiac pacing are generally guided by two main factors: symptomatic arrhythmias and conduction abnormalities (Box 7-1).

Pacing impulses can be delivered to a single chamber (atrium *or* ventricle), dual chambers (atrium *and* ventricle), or multiple chambers (e.g., biventricular pacing for cardiac resynchronization therapy [CRT]). Bipolar leads (cathode and anode present on the lead itself) have predominantly been used since the late 1990s. The advantage of bipolar leads (compared with unipolar leads where the pulse generator functions as anode) is that the distance between the anode and cathode is much smaller, and this confers a reduced susceptibility to electromagnetic interference (EMI). Typically, pacemaker leads are placed in the right atrial appendage, in the right ventricle, or in both in a dual-chamber device (Figure 7-1).

**BOX 7-1 Indications for Implantation of Cardiac Pacemakers**

- Sinus node dysfunction (symptomatic bradycardia)
- AV conduction block
- Postablation of AV node or junction
- Third-degree AV block after myocardial infarction
- Significant carotid sinus hypersensitivity
- Congenital complete heart block
- Long QT syndrome
- Refractory heart failure (cardiac resynchronization therapy)

*AV,* Atrioventricular.

### 2. How does a pacemaker work?

In an asynchronous mode of programming, pacing impulses are delivered to the chamber where a lead resides at a set rate regardless of spontaneous electrical activity. In a sensing mode, electrical activity can be detected in the chamber where a lead resides, and depending on device

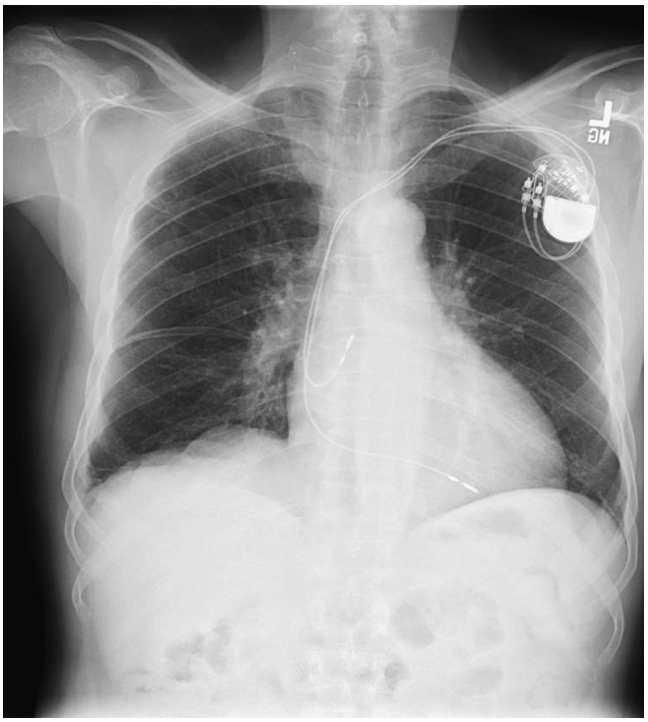

**FIGURE 7-1** ■ Chest x-ray appearance of a pacemaker.

programming, what is sensed can cause either inhibition or triggering of pacing in that chamber. For example, in a sensing mode of programming, if a spontaneous depolarization is sensed, the device inhibits itself from delivering a pacing stimulus, and it looks for a subsequent depolarization during the next preset time interval. If no spontaneous depolarization of the chamber is sensed within the programmed limits, the device delivers a pacing stimulus and looks for a subsequent depolarization during the next preset time interval. Regardless of the device used or the configuration of the leads, pacemaker function always must be programmed to the needs of the individual patient.

## 3. What do the pacemaker codes represent?

The current North American Society of Pacing and Electrophysiology/British Pacing and Electrophysiology Group (NASPE/BPEG) generic five-position code for antibradycardia, adaptive-rate, and multisite pacing is presented in Table 7-1.

- Position I: The first letter specifies the chamber or chambers being paced.
- Position II: The second letter specifies the chamber or chambers where sensing takes place.
- Position III: The third letter specifies the response to sensed events.
- Position IV: The fourth letter specifies the presence or absence of potential rate modulation.
- Position V: The fifth position specifies the location or absence of multisite pacing (when present).

It is important to understand what these letters imply so that one knows what pacing behavior to expect from a patient's device. In addition to basic sensing and pacing functionality, modern devices may include additional features such as mode switching and rate responsiveness that allow for improved performance.

Perhaps the easiest way to understand these codes is by starting with the second letter, the chamber where sensing takes place, because that is really where the activity starts. For example, in a theoretical VAT mode, a sensed atrial depolarization triggers ventricular pacing. Such a mode might be useful for patients after ablation of the atrioventricular (AV) node and would be physiologic. However, the risk of such a mode would be tracking of a fast atrial rate, resulting in a fast ventricular rate.

Commonly employed modes include the following:

*AAI mode*—ensures adequate heart rate in a patient with symptomatic sinus bradycardia and normal AV conduction. In AAI mode, if no atrial depolarization occurs within a preset time interval, the device provides atrial pacing at a preset rate, while a sensed spontaneous atrial depolarization inhibits the device from pacing the atrium.

*VVI mode*—ensures adequate ventricular rate (e.g., in a patient with atrial fibrillation and a slow ventricular response or in a patient with impaired AV conduction). In VVI mode, if no ventricular depolarization occurs within a preset time interval, the device provides ventricular pacing at a preset rate, while a sensed ventricular depolarization inhibits the device from pacing the ventricle. When an external pacing box is in use with temporary pacing leads (e.g., after cardiac surgery), VVI mode is preferred to the default DDD mode in patients with a ventricular lead only.

*DDD mode*—ensures that each spontaneous atrial depolarization is followed by a ventricular depolarization because it enables sensing and subsequent

TABLE 7-1 **Pacemaker Five-Digit Nomenclature**

| Position I: Chamber Paced | Position II: Chamber Sensed | Position III: Sensing Response | Position IV: Rate Modulation | Position V: Multisite Pacing |
|---|---|---|---|---|
| **A** = Atrium | **A** = Atrium | **I** = Inhibited | **R** = Rate modulation | **A** = Atrium |
| **V** = Ventricle | **V** = Ventricle | **T** = Triggered | **O** = None | **V** = Ventricle |
| **D** = Dual (A+V) | **D** = Dual (A+V)<br>**O** = None | **D** = Dual (I+T)<br>**O** = None | | **D** = Dual (A+V)<br>**O** = None |

Adapted from Bernstein AD, Daubert JC, Fletcher RD, et al.: The revised NASPE/BPEG generic code for antibradycardia, adaptive-rate and multisite pacing. Pacing Clin Electrophysiol 25:260, 2002.

inhibition or triggering of pacing of both the atrium and the ventricle. DDD mode is a very versatile and physiologic mode that is commonly programmed for various clinical scenarios.

Asynchronous modes (e.g., AOO, VOO, DOO) are most often used for emergency situations (e.g., acute high-degree AV conduction block, asystole) or in an environment (e.g., operating room) where EMI (e.g., electrocautery) can cause inhibition of pacing based on sensed intrinsic electrical activity, especially in patients who are pacemaker dependent. A risk of an asynchronous mode of pacing is competition with a spontaneous underlying rhythm and the potential to deliver a pacing impulse at a vulnerable portion of the cardiac cycle, leading to an arrhythmia (e.g., ventricular fibrillation from an "R on T" phenomenon).

### 4. Explain physiologic pacing.

AV synchrony optimizes ventricular filling and, ultimately, cardiac output. Dual-chamber pacing modes can sense and trigger or inhibit pacing in one or both chambers. Such a mode of pacing (i.e., AAI, DDD) is "physiologic" because it ensures that the atrial rate is the same as the ventricular rate and that an atrial systole immediately precedes every ventricular systole. This pacing can be especially important in patients with ischemic cardiomyopathy or diastolic dysfunction, where an atrial kick and AV synchrony improve cardiac output. In addition to improved hemodynamics, physiologic pacing modes minimize AV valvular insufficiency that occurs with isolated ventricular pacing and retrograde atrial depolarization. These modes may reduce the incidence of atrial tachyarrhythmias, reducing potential thromboembolic events from stasis in a noncontracting atrium.

### 5. What is mode switching?

Mode switching refers to an automatic reprogramming of a pacemaker to prevent tracking of a sudden rapid atrial rate to the ventricle. Once sinus rhythm has been restored, the pacemaker should revert quickly to the original programming. Mode switching refers to an automatic, temporary reprogramming of the device to prevent symptoms resulting from a rapidly paced ventricular rate.

### 6. Describe rate-adaptive pacing

The ability to increase the heart rate when needed is crucial to optimal systemic perfusion. Rate modulation (also called rate adaptation) is a functionality incorporated into most modern pacemakers that allows the device to increase the paced heart rate automatically when needed to meet metabolic demands. The fourth letter of the NASPE/BPEG code designates the presence or absence of rate modulation. This functionality is accomplished according to a computerized algorithm in proportion to the change in certain monitored physiologic variables. The most common sensor currently employed is a piezoelectric accelerometer to sense vibrations and accelerations secondary to bodily motion. Sensors detecting a change in thoracic impedance ostensibly secondary to increased minute ventilation are also available, and a blended sensor detecting both accelerations and changes in thoracic impedance are used in certain devices. Preoperatively, it may be beneficial to disable the rate-adaptive pacing function for some patients to avoid unnecessarily rapid rates of pacing that may be diagnostically confusing in the perioperative period.

### 7. What is cardiac resynchronization therapy?

The fifth position in the NASPE/BPEG code provides information about the presence or absence of multisite pacing, which implies either there is more than one lead in a single cardiac chamber or there is biventricular pacing. The former refers to attempts to suppress atrial fibrillation with more than one lead in the atrium, but this is not currently clinically relevant. The latter refers to biventricular pacing as CRT, which is beneficial in restoring synchrony in some patients with heart failure and left ventricular dysfunction.

Advanced cardiac failure is often accompanied by sinus or AV node dysfunction and intraventricular conduction defects that delay the onset and completeness of right or left ventricular systole in at least one third of patients with heart failure. This delay causes dyssynchrony between and within left and right ventricular contractions, further impairing cardiac output, and has been shown to increase the risk of death in these patients.

CRT entails AV sequential biventricular pacing to optimize the timing and completeness of the right and left ventricular contractions, "resynchronizing" and optimizing cardiac function. CRT has been shown to improve cardiac output, hemodynamics, heart failure symptoms, and quality of life in patients with heart failure. CRT is currently indicated for reduction of symptoms in patients with moderate to severe heart failure (New York Heart Association [NYHA] class III or IV) who remain symptomatic despite stable, optimal medical therapy and who have a left ventricular ejection fraction (LVEF) of $<35\%$ and QRS duration $>130$ msec.

### 8. What is an implantable cardioverter-defibrillator?

An ICD is a device capable of detecting a malignant ventricular arrhythmia and delivering therapy (e.g., shock) to terminate the arrhythmia. Sensing of electrical activity from the right ventricular lead enables the ICD to detect and classify the apparent heart rate as ventricular fibrillation (VF) or ventricular tachycardia (VT) based on predetermined and programmed heart rate "zones" and to provide an appropriate treatment. All modern ICDs also have pacemaker capabilities in case defibrillation results in bradycardia or asystole ("post shock therapy"—often VVI mode at 55–60 beats per minute) and programming that allows for antitachycardia pacing that can potentially terminate VT.

The main indication for implantation of an ICD is the prevention of death caused by a lethal arrhythmia (e.g., VF or VT). Modern ICDs can terminate VF in $>98\%$ of episodes, and prevention of sudden death secondary to arrhythmia has been shown to increase survival in

**BOX 7-2 Indications for Implantable Cardioverter-Defibrillator Placement**

**Primary Prevention**

- Prior myocardial infarction with LVEF<30%
- Cardiomyopathy with NYHA class II or III and LVEF < 35%

**Secondary Prevention**

- Prior episode of resuscitated VT/VF without reversible cause
- Spontaneous sustained VT in presence of heart disease

*LVEF*, Left ventricular ejection fraction; *NYHA*, New York Heart Association; *VF*, ventricular fibrillation; *VT*, ventricular tachycardia.

patients with both ischemic and nonischemic cardiomyopathy. Several large clinical trials have demonstrated a survival benefit of prophylactic ICD implantation compared with medical therapy in patients with cardiomyopathy and decreased left ventricular function (LVEF ≤35%). ICDs have increasingly become a definitive therapy for patients at high risk for malignant ventricular arrhythmias (primary prevention) and for patients who have survived a malignant arrhythmia (secondary prevention) (Box 7-2).

Although "pacemakers" do not have ICD functionality, *all* ICDs have potential pacemaker functionality (as explained earlier) that can be programmed as a backup, as a therapy, and as a primary functionality for patients who require it. It is important to elucidate the type of device present and how it is programmed before going to the operating room because not every device that appears to be pacing is a simple pacemaker.

## 9. How is a patient with a cardiac implantable electronic device managed in the perioperative period?

Care for patients with cardiac implantable electronic devices (CIEDs) requires an understanding of the type of device (i.e., pacemaker or ICD), the programming of the device, the extent of patient dependency on the device, and whether the device is functioning as intended. This information is used to determine the need for reprogramming CIEDs to protect against EMI in the perioperative period.

It is not always feasible for the assigned anesthesiologist to "manage" a patient's CIED independently on the day of surgery without the requisite knowledge and technological equipment. It is often necessary to enlist the assistance of an experienced colleague (e.g., cardiologist) or a manufacturer's representative.

A consensus statement regarding recommended perioperative CIED management was published in 2011 by the Heart Rhythm Society (HRS) in collaboration with the American Society of Anesthesiologists (ASA), the American Heart Association (AHA), and the Society of Thoracic Surgeons (STS). This expert consensus statement calls for a change in the current perioperative management of patients with a CIED to a multidisciplinary approach before the day of surgery.

As per the new consensus, for elective situations, "best practice" results from advanced determination of the appropriate perioperative management by the "CIED team" (i.e., physicians and their assistants who usually manage the patient) because they already have all the information needed about the device. Each patient requires individualized management; "one size does *not* fit all." Essential elements of the advocated process include the following:

1. Advance provision of specific information to the CIED team by the procedural team (surgeon and anesthesiologist) to include:
   - Type of surgery
   - Anatomic location of the surgery with respect to the device
   - Positioning of the patient during the surgery
   - Whether or not cautery (or other type of EMI) will be encountered
   - Postoperative disposition of the patient
   - Special circumstances
2. In return, the CIED team provides a "prescription" for perioperative device management to the procedural team. Although the exact form of this prescription is not specified, the essential information needed to manage the device perioperatively should be included. Examples of this prescription might be as follows:
   - "There is a Medtronic ICD present that should be deactivated for the procedure. Magnet application may be used to accomplish this in the operating room. Magnet removal will restore ICD settings to baseline."
   - "There is a St. Jude pacemaker present (DDD mode, backup rate 60 beats per minute). The patient is not pacemaker dependent. No reprogramming is necessary. If needed, magnet application will result in an asynchronous mode of pacing at 85 beats per minute."
   - "There is a Medtronic ICD present. The planned site of surgery is remote from the location of the device, and it is unlikely that EMI will be detected by the device assuming electrocautery grounding pads are placed so as to direct the current away from the device. There is probably no need to deactivate the ICD, but magnet application can be used to suspend detection if desired."
   - "There is a Boston Scientific ICD present. The patient is in atrial fibrillation with a slow ventricular response and is pacemaker dependent. For the procedure, the pacemaker should be reprogrammed to an asynchronous mode using a manufacturer's programmer, and the ICD can be deactivated with a magnet. Based on history, the patient is at high risk of an arrhythmia, and removal of the magnet will allow for more rapid defibrillation (if necessary) than would attempting to reprogram the device intraoperatively. The

device should be formally interrogated after the procedure if defibrillation was necessary, and all settings must be restored to baseline by a manufacturer's programmer."

Getting the necessary information to and from the CIED team in a timely fashion is key. Arranging for an Industry Employed Allied Healthcare Professional (also known as a "pacemaker rep") or other knowledgeable colleague to assist with any recommended reprogramming requires advance planning.

As ideal as the proposed new system sounds for elective situations, there will always be situations in which such idealized communication cannot take place (e.g., urgent or emergent surgery, nights, weekends, and holidays). In many cases, immediate consultation with a cardiologist or industry representative may be necessary, and interrogation of the device with a manufacturer-specific programming device may be performed. However, depending on the clinical setting, the time of day, and the urgency of the procedure, a formal interrogation of the device may or may not be convenient or even possible. It is important for all anesthesia practitioners to familiarize themselves with the recommendations for using CIEDs in the perioperative period that are contained within an ASA Practice Advisory on the topic.

## 10. How is the type of device present determined?

There are numerous ways to determine what type of device is present. All patients with implanted devices are given a device information card that contains the necessary information. If the card is unavailable, one can contact the cardiologist managing the patient's device or the device manufacturer. Failing that, one can look at the chest x-ray because the appearance of ICD leads differ from those of a pacemaker (Figure 7-2). However, the chest x-ray alone cannot provide information about the programming of the device, pacemaker dependency, or whether the device is functioning as intended (although the identification of a fractured lead would suggest that it is not).

## 11. What is electromagnetic interference, and how does it affect cardiac implantable electronic devices?

Radiofrequency waves between 0 and $10^9$ Hz may electromagnetically interfere with appropriate device function. Classic examples of EMI commonly encountered in the perioperative period include electromagnetic waves emanating from the surgical electrocautery (the "Bovie"), nerve stimulators, and evoked potential monitors. Other clinically relevant sources of EMI may include fasciculations, shivering, and large tidal volumes. Telemetry can also cause interference with certain functions under specific circumstances. Higher frequency waves (e.g., x-rays, gamma rays, infrared, ultraviolet light) are unlikely to cause interference with CIED function. However, large cumulative exposures to some kinds of radiation can cause short circuits or other electrical problems.

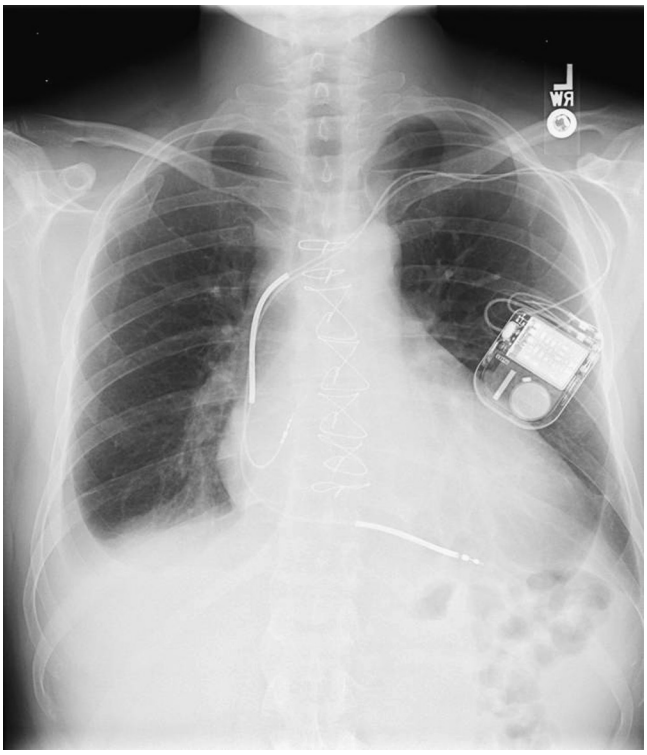

**FIGURE 7-2** ■ Chest x-ray appearance of ICD. Note the thick radiopaque sections on the right ventricular lead of ICD.

Generally, EMI-induced inhibition of pacing owing to oversensing is the most common problem for a pacemaker. Brief exposure generally is not a problem. However, prolonged exposure EMI can convert the pacemaker to asynchronous pacing or reversion to programmed "noise reversion" mode (often VVI or VOO). If an ICD is present, EMI can cause inappropriate delivery of a defibrillatory shock. However, the vulnerability of modern devices is decreased as a result of the nearly routine use of bipolar leads and sophisticated noise protection algorithms. A site of surgery remote from the location of the device may also be protective (e.g., infrainguinal surgery in a patient with a subpectoral device and the electrocautery grounding pad placed on the thigh or buttocks contralateral to the side of surgery). Regardless, any sudden changes to pacing behavior or an inappropriate attempt at defibrillation or overdrive pacing should be considered as unrecognized EMI, and steps should be taken to prevent further exposure. Such steps may include (as appropriate) immediate cessation of cautery activity until hemodynamic stability is restored and the limitation of cautery to short bursts thereafter, magnet application to a pacemaker to suspend detection and create an asynchronous mode of pacing, or magnet application to a defibrillator to suspend detection and prevent accidental unwarranted discharge. Caveats to magnet use are discussed in detail later on.

EMI-CIED interactions can be avoided by taking appropriate precautions, including reprogramming devices

where significant EMI is anticipated intraoperatively. Reprogramming of a pacemaker to an asynchronous mode is recommended at the present time only for pacemaker-dependent patients. This reprogramming can potentially be accomplished with a manufacturer-specific programmer or by magnet application (discussed later). Patients who are not pacemaker dependent should not be reprogrammed to an asynchronous mode because of the risk of competition of paced beats with a spontaneous rhythm and the potential "R on T" phenomenon that may produce ventricular fibrillation. However, it is recommended that rate modulation should be suspended (if feasible) for patients who do not require reprogramming (rate modulation is not a consideration in asynchronous modes of pacing).

## 12. How do you determine if a patient is pacemaker dependent, and how should this be managed in the perioperative period?

It is critical to know if patients are dependent on their pacemakers before going to the operating room. This information may be available in chart notes or may be ascertainable from the patient, the family, the manufacturer of the device, or the pacemaker clinic where the patient receives care. A history that the device was implanted for symptomatic bradycardia or syncope or after a successful AV nodal ablation suggests pacemaker dependence. If such information is unavailable, one should examine or obtain an electrocardiogram (ECG). Pacemaker dependence should be assumed if every P-wave or QRS complex on the ECG is preceded by a pacemaker spike. If an Industry Employed Allied Healthcare Professional or other consultant interrogates the device, he or she would be able to recognize pacemaker dependency (there would be no spontaneous ventricular activity when the pacemaker is programmed to VVI mode at a low rate). Provocative maneuvers to elicit bradycardia (e.g., prolonged Valsalva maneuver; administration of a small dose of esmolol, adenosine, or edrophonium) are not recommended.

The recognition (or assumption) of pacemaker dependence should prompt a plan to protect the CIED from effects of EMI intraoperatively. Current recommendations state that pacemaker-dependent patients should have their devices reprogrammed to an asynchronous mode to protect from EMI intraoperatively, when the site of surgery or EMI is close (e.g., $<15$ cm) to the location of the device and leads. This reprogramming can be accomplished with a manufacturer-specific programming device or, potentially, with a magnet (assuming no ICD is present, magnet response is enabled, and the device is accessible during the procedure). If the site of surgery or EMI is remote (e.g., $>15$ cm) from the location of the device and leads, magnet response is known, and the device would be accessible during the surgical procedure, one may decline reprogramming the device in advance, reserving magnet application to create an asynchronous mode of pacing as a rescue maneuver, if needed.

Magnet application to an ICD would not create an asynchronous mode of pacing from the associated pacemaker programming. Any desired reprogramming of the pacemaker in a patient with an ICD would require a manufacturer-specific programming device to effect alterations to the programming (as explained subsequently).

## 13. Should a magnet be used?

It has become common practice to use a magnet to alter the behavior of a CIED perioperatively because it is often more convenient and may be safer for the patient than formal reprogramming. However, the programmed magnet response of a device should ideally be ascertained in advance if magnet application is to be considered a rational plan to prevent (or rescue from) inhibition of pacing or prevention of a defibrillatory shock owing to EMI.

Application of a magnet to a modern pacemaker usually produces an asynchronous mode of pacing. The configuration and the programming of the device determine the specific mode of asynchronous pacing one obtains (e.g., AOO, VOO, DOO), and the remaining battery life determines the rate. There may also be default settings that vary by manufacturer. Assuming an appropriate magnet response is programmed, once the magnet is applied over the pulse generator, asynchronous pacing persists for as long as the magnet remains in place. Removal of the magnet results in reversion to baseline settings. This response is always seen with a Medtronic pacemaker (Minneapolis, Minnesota), (and would likely be seen with pacemakers from other manufacturers), but the magnet response is programmable in devices from Boston Scientific (Natick, Massachusetts), St. Jude (St. Paul, Minnesota), and Biotronik (Berlin, Germany), and the response may vary (e.g., there may be none, or the device may first capture a snapshot of recent events or conduct a battery test). The more recent introduction of magnetic resonance imaging–compatible devices with programmable magnet responses brings a new set of considerations, emphasizing the need to know what is present and how it is programmed before proceeding into the operating room and simply assuming that a magnet application would produce an asynchronous mode of pacing when needed.

Application of a magnet to an ICD should disable detection of arrhythmias and would protect against an inappropriately delivered defibrillatory shock as a result of exposure to EMI; however, the magnet response is potentially programmable in devices from Boston Scientific, St. Jude, and Biotronik, and one needs to ensure that magnet response is enabled in a given patient's device. Assuming the magnet response to be enabled, a critical concept to understand is that the nominal magnet response across the industry is to deactivate an ICD. In other words, if a patient has an ICD that is also providing pacing, magnet application would deactivate only the ICD, and one would not obtain an asynchronous mode of pacing from the device. If one desires asynchronous pacing in a patient with an ICD, the device must be programmed with a manufacturer-specific programmer. This situation

underscores the need to know what is present and how it is programmed.

An ICD can also be "deactivated" using a programmer, but it is thought to be safer to use a magnet to accomplish this where feasible owing to the rapid reversion to active detection and defibrillation with magnet removal. It is also more convenient at the end of the procedure simply to remove a magnet to restore baseline settings than it may be to wait for formal reprogramming.

Any patient with an intentionally deactivated ICD should be continuously monitored in an appropriate setting with the immediate availability of defibrillation or backup pacing, or both, if necessary. External defibrillation or pacing pads should be placed on any patient whose ICD is deactivated perioperatively and stay connected to a bedside monitor or defibrillator until reactivation of the ICD is confirmed. When placing the pads, an anterior-posterior position is preferred to minimize the current that might be induced down the leads.

### 14. Does an implantable cardioverter-defibrillator have to be deactivated in the perioperative period?

A standard of care that seeks the highest possible level of safety for patients would probably answer this question in the affirmative, the risk being that the high-frequency EMI emanating from the surgical electrocautery would be sensed and interpreted as VF, which the ICD would try to treat. This is especially likely if the source of the EMI is close to the ICD and leads (<15 cm). It may also be the case that modern ICDs would not likely detect EMI generated from a routine surgical electrocautery >15 cm from the device and leads. However, it stands to reason that not every ICD encountered would be one of the latest models, and it is also understood that surgical equipment continues to evolve. Each practitioner should be familiar with the current recommendations and should individualize his or her plan based on the needs of the patient and recommendations of consultants (Box 7-3).

### 15. What should be done if a patient with a deactivated implantable cardioverter-defibrillator experiences fibrillation?

If the patient experiences fibrillation and a magnet has been used to deactivate an ICD, the magnet should be removed and the device allowed to detect the arrhythmia and defibrillate the patient. Usual advanced cardiac life support (ACLS) protocols should be implemented as appropriate. Any observed delays in (or failures to) defibrillate should prompt immediate external defibrillation and implementation of ACLS protocols. The convention for any patient with a subpectoral CIED with transvenous leads is to place the defibrillation pads or paddles in an anterior-posterior configuration, instead of the usual apex-base locations, to minimize induction of current down the leads. One should also avoid placing the defibrillation current directly over the device or leads.

**BOX 7-3 Points for Management of Cardiac Implantable Electronic Devices (CIEDs) in the Perioperative Period**

- An individualized, multidisciplinary approach is recommended for perioperative management of patients with CIEDs (pacemakers and defibrillators).
- It is imperative for the anesthesiologist to know what device is present, understand how it is programmed, ensure it is functioning as intended, and implement appropriate perioperative management *before* going to the operating room.
- Device information can be obtained from the patient's device information card, the cardiologist managing the device, and the manufacturer. An x-ray can reveal the manufacturer, whether or not an ICD is present, and if the leads are intact. A formal interrogation of the device also can provide all necessary information but is not always necessary.
- If a pacemaker only is present, magnet application would most likely temporarily program the device to an asynchronous mode. If an ICD is present, the magnet would deactivate the ICD.
- Magnet application would not produce an asynchronous mode of pacing if an ICD is present.
- All device settings should be returned to baseline postoperatively.

### 16. How can one know if a cardiac implantable electronic device requires interrogation before discharging the patient from an intensive care setting?

Defining when a formal immediate postoperative interrogation is warranted remains a challenging and controversial topic. Many practitioners are uncomfortable discharging patients with CIEDs from a monitored setting postoperatively without formally interrogating the device. Because this situation evinces a high level of concern for patient safety and may involve medicolegal factors, there are situations in which a formal postoperative interrogation is recommended. However, in many instances, such an interrogation is not feasible in a timely fashion in all practice settings, and there may or may not be a need for it depending primarily on the device itself and the manner in which the device programming was temporarily altered for the surgical procedure (e.g., magnet vs. programmer). However, various intraoperative factors may also come into play, and the routine need for postoperative interrogation of all devices remains controversial. Recommendations of the HRS Consensus Statement (Box 7-4) outlines situations in which postoperative interrogation by knowledgeable personnel would promote the highest possible level of safety for patients.

**BOX 7-4 Recommended Indications for Interrogation of Cardiac Implantable Electronic Devices (CIEDs) before Patient Discharge or Transfer from a Monitored Environment***

- Hemodynamically challenging surgeries, such as cardiac surgery or significant vascular surgery (e.g., abdominal aortic aneurysm repair)
- Significant intraoperative events, including cardiac arrest requiring temporary pacing or cardiopulmonary resuscitation and events that required external electrical cardioversion
- Emergent surgery where the site of EMI exposure was above the umbilicus
- Cardiothoracic surgery
- Procedures that emit EMI with a greater probability of affecting device function
- Logistic limitations that would prevent reliable device evaluation within 1 month from their procedure

*Patients with CIEDs reprogrammed before the procedure that left the device nonfunctional, such as disabling tachycardia detection in an ICD.
*EMI*, electromagnetic interference.
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CASE 8

# Cardiac Tamponade

**Cesar Rodriguez-Diaz, MD**

QUESTIONS



A 54-year-old man with atrial fibrillation underwent percutaneous pulmonary vein isolation under general anesthesia earlier in the day. In the recovery room, he became tachycardic, hypotensive, and short of breath and complained of chest tightness. Electrocardiogram (ECG) revealed low QRS complexes and electrical alternans. Cardiac tamponade is suspected.

## 1. What is cardiac tamponade?

Cardiac tamponade is defined as accumulation of fluid in the pericardial sac that interferes with cardiac filling and causes hypotension. The pericardial sac encloses the heart. It is composed of two membranes, an outer fibrous pericardium and an inner serous pericardium. The serous pericardium is composed of a visceral layer fused to the epicardium and a parietal layer fused to the fibrous pericardium. The pericardial sac normally contains 15–50 mL of straw-colored fluid.

Cardiac tamponade can be classified further as acute or subacute based on the time it takes to develop. Acute cardiac tamponade can occur with 150 mL of fluid in the pericardial space owing to poor compliance of the fibrous pericardium. In subacute cardiac tamponade, a large amount of fluid (>1000 mL) might be present if the pericardium has had time to stretch.

The progression of tamponade physiology as described by Reddy occurs in three phases. Initially, when fluid starts accumulating in the pericardial sac, the intrapericardial pressure begins to increase, but a compensatory increase in central venous pressure allows for maintenance of right ventricular and left ventricular filling. As more fluid accumulates, the intrapericardial pressure equalizes first with the right ventricular filling pressure, interfering with ventricular filling. The right ventricle is compromised first because it is more compliant than the left ventricle and has a lower filling pressure. At this phase, stroke volume is diminished, but cardiac output may be maintained by a higher heart rate. Last, as further fluid accumulates, intrapericardial pressure equalizes with left ventricular filling pressure, and cardiac output becomes severely compromised.

## 2. What are the etiologies of cardiac tamponade?

Acute tamponade can be caused by chest trauma, ascending aortic dissection, percutaneous coronary interventions, and intracardiac arrhythmia ablations. Indwelling central venous catheters have also been identified by the American Society of Anesthesiologists (ASA) Closed Claims Project as a cause of tamponade. Recent pericardiotomy, as performed during cardiac surgery, has also been implicated in the development of cardiac tamponade, even though the pericardial sac has been left open; in this situation, a localized hematoma can cause regional cardiac tamponade (i.e., a specific chamber is compressed).

Subacute cardiac tamponade can be caused by malignancy, renal failure, infections such as tuberculosis, and hypothyroidism.

## 3. What are the signs and symptoms of cardiac tamponade?

Depending on the severity and acuity of development of cardiac tamponade, shortness of breath, chest tightness, dizziness, distended neck veins, and shock are nonspecific signs and symptoms. Classic signs of cardiac tamponade include the following:

- Pulsus paradoxus—an exaggerated decrease in systolic arterial blood pressure associated with inspiration (>10 mm Hg)

- Beck triad—dilated neck veins, muffled heart tones, and hypotension
- ECG signs
  - Low voltage in all leads
  - Electrical alternans—changing electrical axis caused by the heart swinging freely in the pericardial fluid

Equalization of central venous pressure (CVP), pulmonary artery diastolic pressure (PADP), and pulmonary artery capillary wedge pressure (PACWP) and absent y descent in right atrial and wedge pressure tracings are signs seen when a pulmonary artery catheter is present. Chest x-ray might show an enlarged cardiac silhouette if there is >250 mL of pericardial fluid (Box 8-1).

### 4. How is cardiac tamponade diagnosed?

Diagnosis of cardiac tamponade requires a high index of suspicion. Transthoracic echocardiography has proved to be the imaging modality of choice because of its portability and availability. It allows visualization of pericardial fluid and its effect on cardiac filling. Expected echocardiographic findings of cardiac tamponade are summarized in Box 8-2. Chest x-ray might be useful for large pericardial effusions as previously discussed.

### 5. How does spontaneous respiration affect ventricular filling in cardiac tamponade?

Spontaneous inspiration in healthy subjects promotes right ventricular filling secondary to increased intrathoracic venous flow caused by negative intrathoracic pressure. In contrast, during inspiration, left ventricular filling is decreased because of expansion of the pulmonary vascular bed. In tamponade physiology, this phenomenon is exaggerated. During inspiration, the right ventricle fills, causing the ventricular septum to bulge into the left ventricle and result in a markedly reduced left ventricular stroke volume; this is the physiologic basis for pulsus paradoxus. Because cardiac tamponade tends to affect right ventricular filling more than left ventricular filling, it is beneficial to maintain spontaneous inspiration.

**BOX 8-1 Cardiac Tamponade Findings**

**Nonspecific Symptoms**

- Shortness of breath
- Chest tightness
- Dizziness
- Distended neck veins
- Shock

**Classic Findings**

- Pulsus paradoxus
- Beck triad (dilated neck veins, muffled heart tones, hypotension)
- ECG
  - Low voltage in all leads
  - Electrical alternans
- Pulmonary artery catheter
  - CVP = PADP = PACWP
  - Absent y descent on right atrial and wedge pressures
- Enlarged cardiac silhouette on chest x-ray

*CVP*, central venous pressure; *ECG*, electrocardiogram; *PACWP*, pulmonary artery capillary wedge pressure; *PADP*, pulmoanry artery diastolic pressure.

**BOX 8-2 Echocardiographic Findings in Cardiac Tamponade**

- Right atrial systolic collapse
  - Collapse sustained for one third of cardiac cycle
  - High sensitivity and specificity
- Right ventricular early diastolic collapse
  - Lowest ventricular pressure during early diastole
  - Less sensitivity but high specificity
- Left ventricular chamber collapse
  - Highest specificity
- Inferior vena cava plethora

### 6. What variants of cardiac tamponade have been described?

Usually in cardiac tamponade, CVP and PACWP range from 15–30 mm Hg. Low-pressure cardiac tamponade has been described in hypovolemic patients with a CVP of 6–12 mm Hg. A fluid challenge might unmask classic tamponade signs. Hypertensive cardiac tamponade has been described when hypertensive patients develop tamponade physiology but maintain an elevated blood pressure, presumably from increased sympathetic activity. Regional tamponade occurs when a loculated effusion obstructs filling of a single chamber.

### 7. How is cardiac tamponade treated?

The goal of management of cardiac tamponade ultimately is to relieve intrapericardial pressure by pericardiocentesis. Medical management of cardiac tamponade aims at maintaining cardiac output and perfusion pressure while the pericardial effusion can be drained. Aggressive fluid hydration to maintain increased CVP to overcome intrapericardial pressure is the initial step in management. Tachycardia should be maintained and promoted to maximize cardiac output in the setting of low stroke volume. Systemic vascular resistance should be optimized to maintain coronary perfusion pressure in the setting of low cardiac output. Contractility should be maintained or increased to optimize cardiac output. β-Receptor and α-receptor agonist infusions, such as epinephrine, dobutamine, dopamine, and norepinephrine, should be instituted if needed.

Pericardiocentesis can be performed bedside under echocardiographic guidance, in the catheterization laboratory under fluoroscopic guidance, or in the operating room under direct surgical vision. Possible complications of pericardiocentesis include arrhythmias, coronary artery injury, hemothorax, pneumothorax, and hepatic injury. In rare cases, transient biventricular dysfunction accompanied by pulmonary edema has been described; the mechanism for this is unclear. Sudden increases in ventricular filling, neurohormonal etiology, or reduced coronary artery flow during cardiac tamponade have been implicated in the mechanism.

### 8. How would you anesthetize a patient with cardiac tamponade?

The primary anesthetic goal is to maintain cardiac output with:

- Spontaneous respiration
- Tachycardia
- Maintained vascular tone
- Aggressive hydration
- Promoting contractility

Standard ASA monitors are applied. An intraarterial catheter is placed for beat-to-beat monitoring of hemodynamic status; however, the procedure should not be delayed because of difficulty obtaining access. Preferentially, pericardiocentesis should be performed in an awake patient with local anesthesia to avoid potentially deleterious hemodynamic effects of anesthetic drugs. Vasodilation, myocardial depression, or positive pressure ventilation could lead to cardiovascular collapse. However, awake pericardiocentesis is not always possible in an uncooperative patient, especially a child.

If general anesthesia is necessary, intravenous ketamine is the drug of choice because it usually maintains spontaneous respiration, has indirect sympathomimetic activity, provides analgesia, and produces hypnosis. Local anesthesia should still be used to minimize the amount of ketamine required. After the procedure, the patient should be monitored closely, preferentially in an intensive care unit, to watch for complications or effusion reaccumulation.

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CASE 9

# Patient with a Left Ventricular Assist Device Presenting for Noncardiac Surgery

**Muoi A. Trinh, MD • Marc E. Stone, MD**

## QUESTIONS

1. What is a ventricular assist device?
2. What are important preanesthetic considerations for patients with a left ventricular assist device?
3. What anesthetic agents and techniques are appropriate for a patient with a left ventricular assist device?
4. What are the goals for fluid management in a patient with a left ventricular assist device?
5. Should anticoagulation be reversed for the surgical procedure?
6. What antibiotic coverage is necessary for a patient with a left ventricular assist device?
7. How should implantable cardioverter-defibrillators and pacemakers be managed perioperatively in a patient with a left ventricular assist device?
8. Which monitoring devices are necessary for anesthetic management of a patient with a left ventricular assist device?
9. When are central venous catheters or pulmonary artery catheters helpful in patients with a left ventricular assist device?
10. What are the parameters on the HeartMate II left ventricular assist device console?
11. How long do HeartMate II device batteries last?
12. What alarms might I hear annunciated, and of what alert conditions do I need to be aware?
13. What are important postoperative considerations in a patient with a left ventricular assist device?

A 60-year-old man with end-stage heart failure presented for colonoscopy. He had a left ventricular assist device (LVAD) as a bridge-to-transplantation. He last took warfarin 5 days ago.

A 55-year-old man with an LVAD and stage IV sacral decubitus ulcer presented for débridement and myocutaneous flap closure. The surgeon requested the prone position. The patient was receiving a continuous heparin infusion with a partial thromboplastin time of 70 seconds.

A 64-year-old man with intraabdominal hemorrhage presented for exploratory laparoscopy and possible laparotomy 2 days after appendectomy. He had an LVAD as destination therapy. His international normalized ratio (INR) was 2.0 and his hematocrit was 23% after receiving 2 units of packed red blood cells.

### 1. What is a ventricular assist device?

Ventricular assist devices (VADs) are pumps implanted to assist the failing ventricle and maintain systemic perfusion. Various VADs are approved for use in the United States, and an even larger variety are used worldwide. Some VADs are intended for short-term use after an acute cardiac event as a "bridge-to-recovery," and some devices are intended for intermediate-term or long-term use as a "bridge-to-transplantation." In patients who are not eligible for transplantation, some devices have been approved as "destination therapy" as a final, permanent management strategy for end-stage heart failure. In many instances, a period of VAD support can improve multiorgan failure and improve a patient's status to become eligible for transplantation; in such instances, VADs are used as a "bridge-to-improved-candidacy." Devices also are available that can provide circulatory support as a "bridge-to-immediate-survival" (e.g., from acute cardiogenic shock) and as a "bridge-to-next-decision" (e.g., in a patient with uncertain neurologic or multiorgan status after a cardiac arrest).

VADs function by collecting blood from the failing ventricle and pumping it downstream into the systemic circulation. An LVAD provides support for the left ventricle by draining blood most commonly from the apex of the left ventricle and returning it by pump to the ascending aorta. A right ventricular (RV) assist device provides support for the right ventricle by draining blood from the right atrium and returning it by pump to the main pulmonary artery. Some VADs are implanted within the body, and some remain paracorporeal during support, connected to long cannulas implanted in the heart and great vessels.

First-generation LVADs (approved in the mid-1990s) were pulsatile devices that were intended to capture the entire potential output of the failed ventricle and eject a physiologic stroke volume. Their output was pulsatile, although the "pulse" rarely coincided with the underlying cardiac rhythm because the devices were generally set to eject only when they were full. Outputs were generally about 5 to 8 L per minute as long as intravascular volume status and RV function were adequate. Filling relied on gravity drainage augmented by residual ventricular contractions. Ejection was accomplished by either pneumatic or electrically controlled mechanical compression of the blood chamber within the device. First-generation pulsatile VADs have essentially been supplanted worldwide by the second generation of VADs and are now rarely used.

Second-generation VADs (currently being implanted) provide nonpulsatile circulatory support with miniaturized impellers. The design of the impeller varies but can essentially be "axial" (similar to an Archimedean screw) or centrifugal. Although some devices use bearings and impellers with fixed attachment, the impellers can also be magnetically levitated, and some are hydrodynamically suspended by the patient's flowing blood (so-called third-generation devices).

The next generation devices generally are much smaller than the first-generation devices, which has increased not only the ease of implantation but also the relative percentage of patients who can receive one. Further miniaturized devices are available for pediatric patients. Several advantages have been demonstrated for continuous flow compared with pulsatile flow, including potentially less hemolysis, lower incidence of thromboembolic complications, reduced stroke rate, silent operation, and decreased incidence of RV failure during LVAD support. Continuous flow devices do not seek to decompress the left ventricle completely (which alters the geometry of the right ventricle in an unfavorable way) but instead provide true left ventricular "assistance."

As of this writing, in the United States, it is most likely that a patient with an LVAD presenting for a noncardiac surgery has a HeartMate II LVAD (Thoratec Corporation, Pleasanton, CA) (Figure 9-1). The HeartMate II is a miniaturized axial flow pump with an internal volume of 63 mL and a potential maximum output of 10 L per minute against a mean arterial pressure (MAP) of 100 mm Hg. The U.S. Food and Drug Administration approved the HeartMate II as a bridge-to-transplantation in 2008 and for destination therapy in 2010.

More widespread acceptance of VADs has occurred as a result of a demonstrated decreased incidence of complications associated with the HeartMate II compared with previous LVADs, new understandings of risk factors that may result in complications, increased patient management

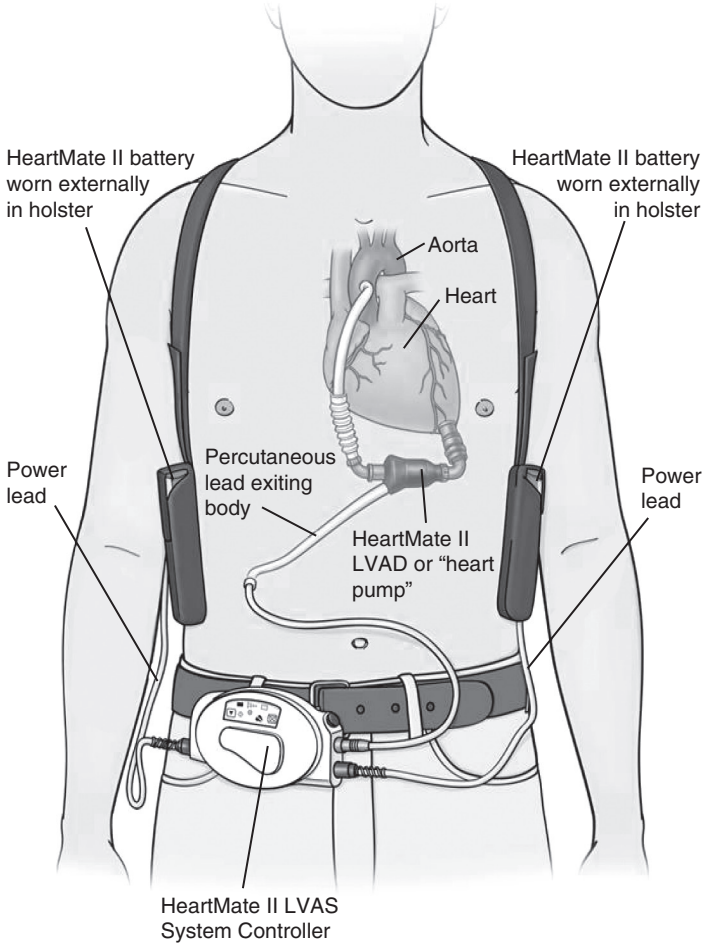


**FIGURE 9-1** ■ Schematic of implanted HeartMate II. (Reprinted with the permission of Thoratec Corporation, Pleasanton, CA.)

experience over the years, significant improvement in multiorgan function in patients with VADs, and very favorable published data from clinical trials of new continuous flow devices. The increasing use of VADs and enhanced survival of patients with VADs mean that more and more patients with devices are presenting for elective noncardiac procedures. Anesthesiologists should become familiar with VADs and related physiology.

## 2. What are important preanesthetic considerations for patients with a left ventricular assist device?

The preoperative clinical status of a patient with an LVAD is the result of multiple factors, including end-organ damage sustained during low cardiac output states before VAD implantation, complications following implantation, current surgical problems, and preexisting comorbidities. Some patients with an LVAD are ambulatory and appear to be uncompromised. Others have varying degrees of renal, hepatic, pulmonary, or central nervous system insufficiency. A thorough preoperative evaluation of all major organ systems is essential even for minor procedures. Another consideration is that further deterioration in the perioperative period may preclude full recovery or disqualify a patient from later heart transplantation. Preoperative discussions with knowledgeable colleagues, the surgeon, and the physician managing the VAD are strongly encouraged. Issues to be considered include the following:

- Perioperative fluid management
- Perioperative anticoagulation
- Perioperative antibiotic prophylaxis
- Perioperative management of pacemakers and implantable cardioverter-defibrillators (ICDs)
- Appropriate location for postoperative recovery (i.e., postanesthesia care unit [PACU] vs. intensive care unit [ICU])
- Postoperative pain management

## 3. What anesthetic agents and techniques are appropriate for a patient with a left ventricular assist device?

No specific anesthetic agents are contraindicated in the presence of a VAD. The selection of anesthetic agents and the dosages used should be appropriate for the procedure and should take into account the potentially dysfunctional unsupported right ventricle in a patient with an LVAD as well as any other existing comorbidities as in any other patient. Most patients with a VAD receive a general anesthetic because of the requisite anticoagulation associated with extracorporeal support through the VAD. However, in select cases, superficial regional blocks placed with ultrasound guidance or a regional intravenous technique (e.g., a Bier block) may be appropriate. Major conduction anesthetics (e.g., spinals, epidurals) are generally contraindicated. Intubation and extubation criteria are the same as for any patient. First-generation VADs were large and were implanted in a preperitoneal pocket, requiring "full stomach" precautions (e.g., consideration of rapid sequence induction, etc). The current generation of VADs has been miniaturized, and patients are no longer necessarily relegated to "full stomach" status. Whenever possible, early (if not immediately postoperative) extubation is desirable because prolonged intubation predisposes to pulmonary infections and requires prolonged sedation. There is no reason for patients to remain intubated just because they have a VAD.

## 4. What are the goals for fluid management in a patient with a left ventricular assist device?

Intravascular volume status is a critical determinant of LVAD output. Regardless of the type of device present (pulsatile or continuous), intravascular volume must be optimally maintained. Adequate "preload" was especially important with first-generation pulsatile devices that depended on a full blood chamber to trigger ejection, but it is also very important for the current generation of nonpulsatile LVADs. Hypovolemia resulted in hypotension with pulsatile devices because the rate of LVAD filling slowed, which led to a slower rate of LVAD ejection and a decrease in overall output because the stroke volume was fixed. With nonpulsatile devices, hypovolemia results in an underfilled arterial tree and possibly left ventricular "suckdown" owing to the continuous nature of the LVAD pumping action ("suckdown" is the industry word used to refer to the physical sucking empty of the LV). The goal for perioperative fluid management is to maintain a euvolemic, if not slightly hypervolemic, state (assuming the right ventricle is able to handle the volume load).

Decreased RV function is another important reason for inadequate "preload" to an LVAD, and all attempts must be made to prevent abrupt increases in pulmonary vascular resistance that may impair the ability of the right ventricle to get blood to the left ventricle (e.g., as a result of hypercarbia, hypoxia, hypothermia, acidosis, pain, administered α-agonist vasoconstrictors). The effect of surgical positioning and retractors also must be considered in regard to "preload," and high intrathoracic pressures (e.g., from excessively large tidal volumes) should be avoided because venous return to the heart is impeded.

## 5. Should anticoagulation be reversed for the surgical procedure?

There is a significant risk of thromboembolic events associated with extracorporeal circulation, and this requires anticoagulation during VAD support. For example, the HeartMate II currently requires an INR in the vicinity of twice the normal value, but ongoing experience is defining the optimal level of maintenance anticoagulation further. The anesthesiologist, the surgeon, and the physician managing the VAD should discuss this important issue in advance to determine a safe anticoagulation regimen for the perioperative period that balances the concern for surgical bleeding with the risk of thrombus formation and thromboembolism. In elective situations, requisite warfarin therapy is sometimes discontinued preoperatively and converted to carefully monitored heparin infusions. Unless it has been discussed and agreed to beforehand, heparin infusions should not be routinely and automatically discontinued "on call to the operating room" by the anesthesia staff. Although the surgeon usually desires discontinuation of anticoagulation perioperatively, full reversal should not occur without agreement of the physician managing the VAD because this may result in a thromboembolic event. If anticoagulation is to be fully

reversed, the perioperative plan must be clearly elucidated, understood, and followed by all parties involved in the care of the patient. Most surgical procedures (except possibly neurosurgical, ophthalmologic, and spine cases) can proceed in the presence of mild or even moderate anticoagulation; however, scrupulous attention to hemostasis is required intraoperatively. Fresh frozen plasma or cryoprecipitate or both may be infused to decrease the level of anticoagulation toward the lower limit of manufacturer's recommendations. Frequent measurements of hemostatic potential (e.g., partial thromboplastin time, thromboelastography, INR) are important to balance the dual potential complications of hemorrhage and thromboembolism. Antiplatelet medications should be discussed in advance.

### 6. What antibiotic coverage is necessary for a patient with a left ventricular assist device?

The perioperative antibiotic regimen should be appropriate for the planned procedure but needs to be discussed among the surgeon, the anesthesiologist, and the physician managing the VAD. Preoperative antibiotic coverage for most procedures includes broad-spectrum antibiotics for gram-positive and gram-negative bacteria, taking local flora into account. Antibiotics for anaerobes are prudent for intraabdominal procedures. Antifungals should be considered in patients who may be at higher risk; this may include patients with recent treatment with an antibiotic course or multiple indwelling catheters. Infection of an LVAD itself is a catastrophic but rare complication. The most common site of infection involving LVADs is in the tract of the percutaneous driveline that generally exits the body on the right side of the abdomen, often between the upper and lower quadrants. Drivelines should be excluded from the sterile field by sterile drapes.

### 7. How should implantable cardioverter-defibrillators and pacemakers be managed perioperatively in a patient with a left ventricular assist device?

Perioperative management of pacemakers and ICDs are the same in patients with LVADs as in other patients. To devise a rational plan for perioperative management, one needs to ascertain what is present, how it is programmed, and that it is functioning as intended. One needs to understand the level of dependency on any pacemaker present and the expected response to magnet application. Generally, for any procedure in which electromagnetic interference (EMI) may be encountered (e.g., from surgical electrocautery), ICDs should be deactivated (either with a magnet or with a programmer) after placement of external defibrillator pads, and patients with pacemakers should have their device reprogrammed to an asynchronous mode (by programmer if an ICD is also present or possibly by a magnet if no ICD is present). A magnet would not affect the behavior of a pacemaker if an ICD is present. More recent recommendations suggest that a site of EMI distant from the device (e.g., subumbilical site of surgery) poses little risk of interference with device behavior. Vigilance must be maintained intraoperatively for appropriate device function, cautery dispersal pads should be appropriately placed to divert current away from the device, and sudden hemodynamic changes associated with altered device behavior should be assumed to be due to unrecognized EMI. All settings should be returned to baseline after the procedure.

A full discourse on the perioperative management of pacemakers and ICDs is beyond the scope of this chapter (see Chapter 7), but a comprehensive up-to-date review on the subject was published more recently (see Suggested Readings). All anesthesia practitioners should become familiar with the recommendations in the current American Society of Anesthesiologists (ASA) practice advisory regarding perioperative management of patients with pacemakers and ICDs and in the 2011 expert consensus statement on this subject from the Heart Rhythm Society.

### 8. Which monitoring devices are necessary for anesthetic management of a patient with a left ventricular assist device?

Standard ASA monitors (cardiac rhythm, blood pressure, oxygenation, ventilation, and temperature) are routine for every patient undergoing anesthetic procedures. First-generation LVADs essentially captured the entire output of the failed side of the heart and, when full, ejected their physiologic "stroke volume" in a pulsatile fashion into the arterial circulation immediately downstream from the failing ventricle. Standard perioperative monitoring was reliable; however, this is not the case with newer generation LVADs. Newer continuous flow devices provide nonpulsatile flow, although some pulsatility is often manifest during support. The two standard ASA monitors that are potentially most affected by a nonpulsatile circulation are noninvasive blood pressure and pulse oximetry measurements.

Noninvasive blood pressure measurements work in a patient with a continuous flow LVAD as long as there is sufficient pulsatility. Although the MAP may be normal, the pulse pressure often is small. Completely normal readings (e.g., 120/80 mm Hg, MAP 93 mm Hg) may be present in partially recovered, well-compensated euvolemic patients; however, readings such as 86/65 mm Hg (MAP 72 mm Hg) are commonly encountered and do not necessarily indicate a problem. After induction, a brief period of relative hypovolemia from associated vasodilation results in lost pulsatility unless preload is adequately replenished. Pulsatility is routinely lost if a patient with a VAD becomes significantly hypovolemic from blood loss or major fluid shift. An invasive arterial monitoring catheter is often needed for cases with anticipated major fluid shifts. Because it can be difficult to place arterial catheters in patients without a pulse, ultrasound guidance is necessary. Alternatively, it is possible to decrease pump speed transiently to allow for increased pulsation in patients who can tolerate it. An arterial line is also helpful for assessment of oxygenation because pulse oximetry does not work without a pulse. Cerebral oximetry is a very helpful monitor of oxygenation in situations where pulsatility is lost or there is minimal pulsatility at baseline.

### 9. When are central venous catheters or pulmonary artery catheters helpful in patients with a left ventricular assist device?

Trending of central venous pressure (CVP) measurements can be helpful to understand the RV volume status,

and central vascular access is often used when large fluid shifts are anticipated. Optimal LVAD function depends on adequate intravascular volume. Although the incidence may be less with second-generation devices being implanted at the present time, LVADs do increase the risk of RV failure. Decompression of the left ventricle by an LVAD causes a leftward shift of the interventricular septum, resulting in altered RV geometry, increased RV compliance, and decreased RV contractility. Also, high output from an LVAD increases RV preload. Sometimes this increased RV preload alone is enough to exacerbate RV dysfunction in patients with moderate-to-severe RV dysfunction. Although an optimally functioning LVAD reduces RV afterload and often improves RV function in patients with normal pulmonary vascular resistance (PVR), patients with fixed elevated PVR may experience increased RV afterload owing to increased right-sided and pulmonary artery flows. Finally, moderate-to-severe tricuspid regurgitation occasionally results from dilation of the tricuspid anullus during LVAD support.

In addition to monitoring CVP to detect developing RV failure and to guide fluid management, central venous access is useful for drug infusions and the potential introduction of transvenous pacing wires. Additionally, one can calculate systemic vascular resistance (SVR) by substituting the VAD output for the cardiac output in the hemodynamic formula. The calculation is as follows:

$$SVR = [(MAP - CVP)/LVAD\ output] \times 80\ dynes/sec/cm^5$$

Central catheters are a potential source of sepsis and should be avoided when not absolutely necessary. Pulmonary artery catheters are a "double edged sword." Although they allow for sampling of mixed venous oxygen saturation and monitoring of pulmonary artery pressures, they provide little other useful information in patients with an LVAD, because the LVAD console offers a continuous display of the "cardiac" output. Pulmonary artery catheters increase the risk of pulmonary artery rupture in patients with pulmonary hypertension. Pulmonary artery catheters can be helpful in the pharmacologic management of pulmonary hypertension. If the patient has a CVP catheter, SVR can be calculated without a pulmonary artery catheter as outlined previously. Although it is not quantitative, one can sometimes infer that the SVR has abruptly increased a patient with an LVAD when the residual volume in the pump abruptly increases (first-generation LVADs only) or if the power readout (described subsequently) abruptly increases (second-generation LVADs only). Transesophageal echocardiography is the intraoperative monitor of choice if one is concerned about failure of an unassisted ventricle, if one needs to confirm volume status, or if one suspects a device-related problem.

## 10. What are the parameters on the HeartMate II left ventricular assist device console?

Understanding and correctly interpreting the parameters displayed on the HeartMate II clinical screen is helpful for monitoring and managing the patient. It is extremely rare that changes would ever need to be made to previously stable device settings during the course of an anesthetic if volume status and RV function are kept optimized.

There are four parameters on the display: pump flow, pump speed, pump power, and pulsatility index (Figure 9-2).

*Pump flow* (L per minute) is an estimate of device output derived from the speed of impeller rotation and power consumption. Flows encountered clinically usually range from 4 to 6 L per minute, but the device is capable of flowing 10 L per minute against an MAP of 100 mm Hg.

*Pump speed* (rpm) is the number of revolutions per minute at which the impeller is rotating. In most situations, this is a set and fixed value. Speeds encountered clinically usually range from 9000 to 9600 rpm. Increases in speed facilitate ventricular unloading by increasing flow through the pump. If the amount of flow exceeds the available volume in the ventricle, a "suck-down" occurs. Decreasing the speed increases the volume in the left ventricle.

*Pump power* (watts) is the power required to spin the impeller at the set speed and is partially determined by flow. Increases in speed or flow require increased power. Power is generally 5 to 7 W. A gradual increase in power over time suggests developing thrombus in the pump. A sudden increase in power requirement may suggest significantly increased afterload, thrombus, or other obstruction to rotor rotation. One should always investigate abrupt increases in power not explainable by an increase in pump speed.

*Pulsatility index* is a unitless measure of the flow pulse (the difference between maximum flow and minimum flow) through the device averaged over 15-second intervals. Pulsatility index is affected by myocardial contractility and preload and directly reflects the amount of assistance provided by the device. The relationship between pulsatility index and the amount of assistance is an inverse one (e.g., a higher pulsatility index indicates less assistance being provided, and a lower pulsatility index indicates more assistance). Unless the ventricle is completely akinetic (or perhaps fibrillating), there is always some contractility, which creates pulses of flow through the device, and this is what is being measured. Optimization of preload improves the contractility of any ventricle through the Starling

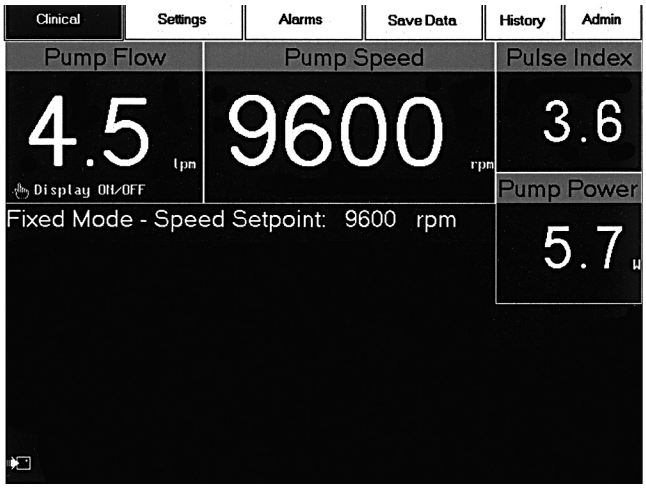


**FIGURE 9-2** ■ HeartMate II control console clinical screen. (Reprinted with the permission of Thoratec Corporation, Pleasanton, CA.)

mechanism. In a euvolemic patient, pulsatility index is usually in the range of 4 to 6. Pulsatility index decreases with hypovolemia and increases with myocardial recovery. A low (or decreasing) pulsatility index likely indicates the need to increase preload or possibly to increase contractility. RV dysfunction can lead to a decreased filling of the left ventricle.

## 11. How long do HeartMate II device batteries last?

According to the manufacturer, a pair of wearable, rechargeable HeartMate II batteries powers the HeartMate II LVAD for approximately 3 to 5 hours, depending on the charge status of the batteries and the hemodynamic condition of the patient. The patient is always transported to the procedural suite or operating room on battery power, and unless there is a very good reason not to, as with all other life-support and lifesaving equipment in the operating room, it is prudent to ensure a connection to main A/C power during the intraoperative period and in the recovery location (e.g., PACU).

## 12. What alarms might I hear annunciated, and of what alert conditions do I need to be aware?

Various alerts may be annunciated from the controller or displayed on the clinical screen, but a thorough discussion of all possible conditions is beyond the scope of this chapter. Figure 9-3 shows alarm conditions, potential causes,

| Warning Lights | Audio Tone | Alarm Message | Meaning | Action |
|---|---|---|---|---|
| Red Heart  | Steady Audio Tone | LOW FLOW HAZARD (on Display Module) LOW FLOW, PUMP OFF and/or PUMP DISCONNECTED (on System Monitor) | Pump flow <2.5 lpm, pump has stopped, perc lead is disconnected, or pump is not working properly. | 1. Make sure System Controller is connected to the pump.<br>2. Make sure the System Controller is connected to a power source (batteries, PBU, or EPP).<br>3. If alarm continues, immediately seek additional help. |
| NONE: No Warning Light and No Green Power Symbol | Steady Audio Tone | NONE | System Controller is not receiving power. | 1. Make sure System Controller is connected to a power source (batteries, PBU, or EPP).<br>2. If connected and alarm continues, switch to alternate power source.<br>3. If alarm continues after switching power source, replace System Controller. |
| Red Battery  | Steady Audio Tone | LOW VOLTAGE | Less than 5 minutes of battery power remain, voltage is too low, or the System Controller is not getting enough power from the PBU. | Immediately replace depleted batteries with new, fully-charged set. Change batteries **one at a time**. If fully charged batteries are not available, switch to PBU or EPP. **WARNING! Do NOT remove power from both power leads at the same time, or the pump will stop.**<br>**Note:** Pump speed will gradually decrease to "Power Saver Mode" until the condition is resolved and the alarm clears. |
| Yellow Battery  | 1 Beep Every 4 Seconds | Low Voltage Advisory | Less than 15 minutes of battery power remain, voltage is too low, or the System Controller is not getting enough power from the PBU. | Immediately replace depleted batteries with new, fully charged set. Change batteries **one at a time**. If fully-charged batteries are not available, switch to PBU or EPP. **WARNING! Do NOT remove power from both power leads at the same time, or the pump will stop.** |
| NONE: No Warning Light | Broken Audio Tone (repeating cycle of 1 beep/sec. for 2 seconds, followed by 2 seconds of silence) | REPLACE SYSTEM CONTROLLER (on System Monitor) REPLACE SYSTEM DRIVER (on Display Module) | System Controller is operating on backup system. | 1. Replace the System Controller.<br>2. Notify the patient's physician.<br>3. Obtain a new backup System Controller.<br>4. Program the new backup Controller with settings described for this patient. |
| Yellow Controller Cell  | 1 Beep Every 4 Seconds | SC CELL MODULE LOW (on System Monitor) DRIVER CELL LOW (on Display Module) | The battery module that powers the System Controller audible alarm is depleted. | Replace the System Controller Battery Module. |
| Rapidly Flashing Green Power Symbol  and 4 Green Battery Fuel Gauge Lights  Flashing Once Per Second | 1 Beep Every Second | POWER CABLE DISCONNECTED | One of the power leads is damaged or disconnected. | 1. Reconnect or tighten disconnected/loose power lead.<br>2. If alarm continues, check System Controller power lead and PBU power lead for damage.<br>3. If System Controller power lead or PBU power lead is damaged, replace the Controller and/or replace thr PBU cable.<br>4. Obtain a new backup System Controller for this patient, if necessary. |
| NONE: No Warning Light | NONE on PBU w/System Monitor<br>1 Beep Every 4 Seconds when on Batteries or PBU w/Display Module | WARNING: Low Speed Operation | Pump is operating below low speed limit. | Connect System Controller to System Monitor (audio alarm will stop) and increase fixed speed setting or reduce low speed limit. |

**FIGURE 9-3** ■ Summary of HeartMate II alarm conditions and manufacturer-suggested actions. (Reprinted with the permission of Thoratec Corporation, Pleasanton, CA.)

and appropriate corrective actions. Although problems are exceedingly rare if intravascular volume status and RV function are kept optimized, and one rarely if ever needs to make adjustments to previously stable device settings, a serious device problem (beyond simply plugging the device in if the batteries run low) requires the assistance of knowledgeable colleagues and requires attempts at resuscitation using standard advanced cardiopulmonary life-support protocols. Chest compressions have been successfully employed in patients with a VAD, but they should be performed with caution because left ventricle apical cannula dislodgment can perforate the heart. The potential consequence of not performing chest compressions when needed is even worse. Chest compression in patients with a VAD is a controversial subject.

### 13. What are important postoperative considerations in a patient with a left ventricular assist device?

The patient is transported on battery power from the operating room to the recovery location. It is important to reconnect the VAD to main A/C power and the system base unit on arrival. The recovery location itself (e.g., PACU vs. ICU vs. VAD floor) may warrant discussion in advance to ensure the receiving staff are able to care for a patient with a LVAD. Excessive anxiety on the part of nursing or other receiving staff is not in the best interest of the patient but is generally amenable to education and experience over time.

Volume status should be optimally maintained. Pain, temperature aberrations, hypercarbia, and acidosis can increase PVR, which may put a strain on a potentially dysfunctional right ventricle, decreasing the "preload" to the LVAD. All pacemaker and ICD settings should be restored to baseline before discharge from a monitored setting.

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CASE 10

# Noncardiac Surgery after Heart Transplantation

**Terence Wallace, MD • Marc E. Stone, MD**

## QUESTIONS

1. Explain the physiology of transplanted hearts.
2. Is reinnervation of the transplanted heart a concern?
3. Which immunosuppressive medications are typically used after heart transplantation?
4. What are the preanesthetic concerns for patients with a heart transplant?
5. What anesthetic techniques are applicable to patients with a heart transplant?
6. Which intraoperative monitors are recommended for patients with a heart transplant?
7. Which emergency drugs are likely to be effective in a patient with a heart transplant?
8. When antagonizing neuromuscular blockade in a patient with a heart transplant, do anticholinergics also need to be given?

A 57-year-old man with hypertension, elevated serum cholesterol, and mild renal insufficiency presented for laparoscopic cholecystectomy. His past medical history was significant for heart transplantation at age 55 for idiopathic dilated cardiomyopathy. His medications included nifedipine, tacrolimus, azathioprine, prednisone, atorvastatin, and omeprazole.

### 1. Explain the physiology of transplanted hearts.

The donor heart is denervated during harvesting, and once it is transplanted into the recipient, there is neither direct efferent nor afferent neural innervation of the graft through autonomic or somatic pathways. Although denervation results in inability of the transplanted heart to respond to extrinsic neural signals, intrinsic myocardial mechanisms and reflexes remain intact. Although the transplanted heart functions in isolation from the nervous system, it retains the ability to respond to humoral factors circulating in the blood (e.g., catecholamines) directly through myocardial receptors. The overall result is a predictable physiology.

The results of cardiac denervation are as follows:

- Lack of tonic vagal input to the transplanted heart results in relative tachycardia, usually around 90 to 100 beats per minute.
- All autonomic reflexes that would normally alter the heart rate are gone. One should expect no change in heart rate with carotid massage, from acute hypertension or hypotension, or from a Valsalva maneuver.
- Drugs that alter the heart rate indirectly (i.e., via the autonomic nervous system), either by intent or by side effect, do not have their usual effects on a transplanted heart. One should not expect an increased heart rate from drugs with vagolytic actions (e.g., atropine, pancuronium, meperidine), and similarly one should not expect a decreased heart rate from drugs with vagotonic actions (e.g., acetylcholinesterase inhibitors, opioids). Drugs that have both direct and indirect actions maintain their direct effects on the denervated heart. Digoxin maintains its positive inotropic effects on the graft but does not slow the heart rate through its parasympathetic mediated effects on the atrioventricular (AV) node.
- Because of lack of direct sympathetic innervation of the heart, there are delayed and decreased sympathetic responses to laryngoscopy, intubation, painful stimuli, and light anesthesia. However, if a stimulus is prolonged, increasing levels of circulating catecholamines eventually result in an appropriate tachycardia or perhaps an exaggerated one through direct stimulation of myocardial adrenergic receptors.

Despite denervation, intrinsic myocardial mechanisms remain intact in the transplanted heart, as follows:

- The denervated myocardium responds normally to circulating or administered catecholamines (e.g., epinephrine, norepinephrine) and direct-acting sympathomimetic agents (e.g., isoproterenol, dobutamine) through direct stimulation of myocardial adrenergic receptors. In this regard, one should be aware that denervation appears to induce a downregulation of $\beta_1$ receptors, so most β-adrenergic receptors on the denervated myocardium tend to be of the $\beta_2$ subtype.
- The Frank-Starling mechanism (i.e., increased preload results in increased stroke volume) remains

intact and is the primary mechanism for increased cardiac output in response to exercise or stress. For this reason, it is important to maintain adequate preload in a patient after heart transplantation. Because they already have an elevated heart rate, the only way patients after heart transplantation can initially increase cardiac output in response to increased metabolic demand is through increased stroke volume. Any further increases in heart rate and cardiac output with prolonged exercise or stress are the results of increased levels of circulating catecholamines and are slightly delayed in onset (and resolution).

- Metabolic autoregulation of coronary blood flow in response to changes in acid-base status (pH) and carbon dioxide tension remains intact.
- There is normal electrical impulse formation and conductivity in the transplanted heart along the usual pathways from the donor sinoatrial (SA) node, but first-degree AV block is a common finding. Previous techniques for heart transplantation involved leaving behind cuffs of native right and left atrial tissue to facilitate the anastomoses. As a result, two P waves were seen on the electrocardiogram (ECG), one from the native heart and the other from the donor heart (Figure 10-1). The electrical discharge from the native SA node was unable to cross the suture line and did not result in depolarization of the donor heart. Current surgical technique involves bicaval anastomoses, so there is no native SA node left behind, and subsequently only a single P wave is expected to be seen on the ECG. The cuff of left atrial tissue contains the entry site for the four pulmonary veins.

## 2. Is reinnervation of the transplanted heart a concern?

Whether or not significant reinnervation occurs in transplanted human hearts remains to be determined. There is laboratory evidence of varying levels of functional reinnervation in nonhuman experimental models of cardiac transplantation, and there are some reports in the literature supporting varying degrees of apparent sympathetic reinnervation late in the posttransplantation period (>5 years postoperatively) in human patients. However, reinnervation appears to be incomplete at best in the human graft, and there is no evidence at the present time that reinnervation of transplanted human hearts is a clinically important phenomenon in the first few years after transplantation.

## 3. Which immunosuppressive medications are typically used after heart transplantation?

A typical immunosuppressive maintenance regimen might consist of a selective T-cell inhibitor such as tacrolimus, a nonspecific purine antimetabolite such as mycophenolate mofetil, and a corticosteroid such as prednisone. Characteristics of these medications are summarized in Table 10-1. Tacrolimus has replaced cyclosporine because of a more favorable side-effect profile. Mycophenolate is preferred over azathioprine because of decreased mortality and rejection. When nephrotoxicity or malignancy is present, antiproliferative agents such as sirolimus and everolimus may be employed. In the immediate postoperative period, cardiac transplant recipients may be given interleukin-2 receptor antagonists such as basiliximab or polyclonal antithymocyte antibodies (Thymoglobulin), but these are unlikely to be encountered when patients present for noncardiac surgery.

Although immunosuppressive agents are key to survival after cardiac transplantation, they also have some very detrimental side effects. Cyclosporine and tacrolimus tend to cause renal insufficiency, hepatotoxicity, hypertension, neurotoxicity, and potentially seizures by lowering the seizure threshold. Azathioprine primarily causes hematologic toxicity, resulting in thrombocytopenia and anemia, but also causes hepatotoxicity. Steroids can cause hypertension, diabetes, adrenal insufficiency, pancreatitis, and psychiatric disturbances.

Side effects such as those listed in Table 10-1 may require medical management. However, other side effects of these medications often necessitate surgical management, and these side effects constitute some of the most frequent indications for noncardiac surgery in patients after transplantation. For example, steroids not only impair white blood cell function but also predispose to peptic ulceration, aseptic bone necrosis, and cataracts. Patients taking long-term high-dose steroids may present for drainage of abscesses; orthopedic procedures on the hip, knee, elbow, or shoulder; exploratory laparotomy; bowel resection for perforated viscus

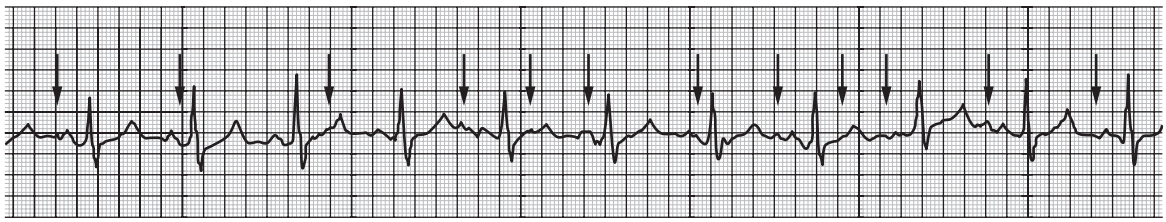

**FIGURE 10-1** ■ ECG strip of lead II from a patient with a cardiac transplant in sinus rhythm. Although the graft SA node is depolarizing the transplanted heart at approximately 80 beats per minute, there is another, smaller P wave marching through this strip at an independent rate, reflecting depolarization of the retained native SA node. The *arrows* indicate several native P waves; however, others may be present, buried within the complexes, giving the appearance of an irregular rate of native SA node discharge.

TABLE 10-1 **Characteristics of Immunosuppressive Agents Commonly Used after Cardiac Transplantation**

| Agent | Mechanism of Action | Main Side Effects |
|---|---|---|
| **Cyclosporine** *(Neoral, Sandimmune, SangCya)* | Selective T-cell inhibitor | Nephrotoxicity<br>Hypertension<br>Hepatotoxicity<br>Neurotoxicity (seizures) |
| **Tacrolimus** *(Prograf, FK-506)* | Selective T-cell inhibitor with 10× potency of cyclosporine | Less nephrotoxic than cyclosporine |
| **Azathioprine** *(Imuran)* | Purine antimetabolite | Thrombocytopenia<br>Anemia<br>Leukopenia<br>Hepatotoxicity |
| **Mycophenolate** *(CellCept)* | | Gastrointestinal disturbances<br>Leukopenia<br>Anemia |
| **Sirolimus** *(Rapamune)*<br>**Everolimus** *(Certican)* | Proliferation signal inhibitor | Oral ulcerations<br>Hyperlipidemia<br>Lower extremity edema<br>Poor wound healing |
| **Corticosteroids** *(e.g., prednisone)* | Decreased circulating lymphocytes<br>Impairment of antigen presentation<br>Interference with cytokine production<br>Impairment of phagocytosis<br>Inhibition of T-cell proliferation<br>Impaired lymphocyte adhesion<br>Impaired lymphocyte margination | Hypertension<br>Diabetes<br>Pancreatitis<br>Potential adrenal insufficiency<br>Psychiatric disturbances |

and diverticulitis; and ophthalmologic procedures related to cataracts and retinal detachments.

Cyclosporine, tacrolimus, and azathioprine tend to cause biliary stasis, and patients taking these agents often present for cholecystectomy. Nonspecific gastrointestinal toxicities of these agents can also cause severe symptoms (e.g., nausea, vomiting, diarrhea, anorexia, abdominal pain) mimicking an intraabdominal process that occasionally prompts exploratory laparotomy. Sirolimus may cause oral ulcerations and poor wound healing along with severe lower extremity edema.

Immunosuppression in general predisposes patients to certain types of malignancies. Immunosuppressed patients sometimes present for diagnostic procedures such as lymphoma staging, node sampling, and resection of gynecologic or skin malignancies.

## 4. What are the preanesthetic concerns for patients with a heart transplant?

The primary concern preoperatively is the function of the transplanted heart. Unless there is rejection, a patient with a heart transplant does not usually perceive any functional limitations and is classified as New York Heart Association class I or II status. Because of a lack of afferent innervation, patients do not experience angina in response to myocardial ischemia. However, just as in any other patient, one needs to assess the adequacy of ventricular function. If the preanesthetic history and physical examination do not provide adequate assessment information, further information regarding prior episodes of rejection (if any) and ventricular function can usually be obtained from the patient's cardiologist. This information from the cardiologist is especially important in patients whose transplantation was performed a few years ago because a patient after cardiac transplantation is subject to accelerated atherosclerotic coronary artery disease (possibly the result of a vasculitis from low-level, subclinical rejection). The likelihood of significant coronary artery occlusion increases directly with time from transplantation, with a reported 10% to 20% incidence at 1 year, 25% to 45% incidence at 3 years, and 50% incidence at 5 years.

Although some benign arrhythmias are common after transplantation (e.g., incomplete right bundle-branch block, premature atrial contractions, occasional premature ventricular contractions, and first-degree AV block), more ominous rhythms in the perioperative period might be a sign of acute rejection. Given the propensity toward accelerated atherosclerotic disease, one should always consider that new perioperative arrhythmias accompanied by hypotension might be a sign of ischemia.

During the preoperative evaluation, special attention should be paid to renal and hepatic function because impairment of these organs is a major side effect of immunosuppressive therapy. When impairment is present, one must carefully evaluate for acid-base and electrolyte derangements. A complete blood count should be reviewed for anemia and thrombocytopenia because hematologic toxicity is a major side effect of azathioprine.

Infection is a major source of morbidity and mortality for immunosuppressed patients after transplantation. Aseptic technique is mandatory for all invasive procedures, including intravenous line placement. Prophylactic antibiotics are routinely employed where appropriate.

Many immunosuppressive regimens include fairly high doses of corticosteroids at some point. Unless the patient has recently been tapered off steroids, the issue of a preoperative "stress dose" should be discussed with the primary physician.

Finally, given the dependence of the graft on the Frank-Starling mechanism (discussed previously), one must ensure an adequate intravascular volume status before anesthetic induction.

### 5. What anesthetic techniques are applicable to patients with a heart transplant?

General, spinal, and epidural anesthesia; regional blockade (e.g., axillary block, wrist block, ankle block, Bier block); and local anesthetic infiltration all have been used successfully in patients with a heart transplant, and the requirements are similar to other patient populations. In terms of general anesthesia, the choice of agent is not so crucial as how the agent is employed. Generally, the overwhelming experience is that induction agents, benzodiazepines, opioids, and inhaled potent volatile agents are usually well tolerated. All the usual caveats apply in the presence of renal or hepatic dysfunction. Just as in any other patient, one must titrate to effect. Whenever possible, one should plan a technique that allows early (if not immediate) postoperative extubation because prolonged intubation may increase the chances of pulmonary infection.

The plasma levels of various anesthetic agents that depend on P-450 metabolism may be increased or decreased by immunosuppressive agents and anticonvulsants and can themselves alter immunosuppressant blood levels. This situation can be potentially dangerous if increased blood levels of immunosuppressant agents result in undesirable side effects (e.g., nephrotoxicity of cyclosporine and tacrolimus). For example, agents that compete for P-450 metabolism (e.g., furosemide) can decrease cyclosporine elimination resulting in increased blood levels. Conversely, agents that increase cyclosporine metabolism (e.g., barbiturates) can reduce blood levels.

It is believed that neuromuscular blockade is augmented by cyclosporine and can be antagonized by anticonvulsants often given to patients taking azathioprine, but this should not pose a problem if neuromuscular blockade is closely monitored. The dose for muscle relaxants is not altered.

Regardless of technique, volume depletion and acute vasodilation (e.g., as may occur with spinal anesthesia) are poorly tolerated because the transplanted heart initially depends on the Frank-Starling mechanism to maintain cardiac output. Sudden vasodilation is not compensated by reflex tachycardia. One can perform a spinal anesthetic in a patient with a heart transplant, but one must be prepared to augment preload and prevent sudden decreases in systemic vascular resistance. An epidural technique with a gradual increase of anesthetic level results in better hemodynamic stability.

### 6. Which intraoperative monitors are recommended for patients with a heart transplant?

Monitoring requirements are the same for patients with a heart transplant undergoing a noncardiac procedure as for other patients. In the absence of rejection, graft function is usually fairly good, and a noninvasive blood pressure cuff and standard American Society of Anesthesiologists monitors usually suffice. Invasive monitoring of arterial and central venous pressures is generally employed only if there is hemodynamic instability or if indicated by the planned procedure. Required endomyocardial biopsies to monitor rejection are preferentially performed via the right internal jugular vein, and one should use the left internal jugular or subclavian veins for central access if possible. When available, transesophageal echocardiography may be preferable to invasive monitoring.

### 7. Which emergency drugs are likely to be effective in a patient with a heart transplant?

Only direct-acting inotropic and chronotropic agents are immediately effective. Epinephrine is usually the direct-acting inotropic agent of choice. Direct-acting chronotropic agents include epinephrine, isoproterenol, and dobutamine. Pacing (via external pacing pads or a transvenous pacing wire) is also an option to increase heart rate. For reasons previously discussed, atropine is not likely to increase heart rate in the denervated graft. Vasoconstrictors (including phenylephrine, norepinephrine, and vasopressin) act on the vasculature directly and are not affected by the denervated status of donor organs. For most situations, small bolus doses of epinephrine and phenylephrine are effective, and these are used as first-line agents when necessary.

Ephedrine is a noncatecholamine sympathomimetic agent with direct and indirect actions on α-adrenergic and β-adrenergic receptors. The indirect actions of ephedrine come from enhanced release of norepinephrine. Although ephedrine can be used advantageously in a patient with a heart transplant, it is not usually considered a first-line emergency drug because at least part of its desired action must await the subsequent release of norepinephrine.

Dopamine has both direct and indirect effects. It is the immediate precursor of and causes the release of norepinephrine. In a patient after cardiac transplantation, dopamine would initially be expected to exert only its direct dopaminergic effects (e.g., coronary and splanchnic arterial vasodilation) through dopaminergic receptors. The vasoconstrictive α-adrenergic effects and the desired β-adrenergic effects on heart rate and contractility come only from subsequently released norepinephrine. Taking into account all of these effects, dopamine may not be the optimal first-line choice when inotropy or chronotropy is urgently needed.

### 8. When antagonizing neuromuscular blockade in a patient with a heart transplant, do anticholinergics also need to be given?

Although bradycardia is unlikely to occur after the administration of an acetylcholinesterase inhibitor (e.g., neostigmine) to a patient after cardiac transplantation, the usual muscarinic blockers (e.g., glycopyrrolate) should be given concurrently to prevent noncardiac cholinergic side effects (e.g., bronchospasm). Another reason to provide an anticholinergic is that significantly increased levels of acetylcholine can cause coronary artery vasospasm in the denervated heart. Although there is some evidence that neostigmine has direct effects on the myocardium, and there are a few case reports of bradycardia after neostigmine administration in this population, it should not deter one from antagonizing neuromuscular blockade when appropriate because prolonged intubation may predispose to pulmonary infection.

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CASE 11

# Coronary Artery Bypass Grafting

**Menachem M. Weiner, MD**

## QUESTIONS

1. What are the major determinants of myocardial oxygen supply and demand?
2. How is coronary artery disease treated, and which medications should be continued perioperatively?
3. What are the preanesthetic concerns in a patient with coronary artery disease?
4. What anesthetic technique is used for coronary artery bypass grafting?
5. What intraoperative monitoring techniques can be used to detect myocardial ischemia?
6. What are the advantages and disadvantages of on-pump versus off-pump coronary artery bypass grafting?
7. What are unique anesthetic considerations related to off-pump coronary artery bypass grafting?

A 72-year-old man with a history of smoking, hypertension, diabetes mellitus type 2, and mild chronic renal insufficiency presented for off-pump coronary artery bypass grafting (OPCAB). Preoperative cardiac catheterization revealed three-vessel coronary artery disease (CAD) with 65% stenosis of the left main coronary artery, 95% stenosis of the mid-left anterior descending artery, 75% stenosis of the circumflex artery, and 80% stenosis of the right coronary artery. Transthoracic echocardiography showed normal left ventricular function without significant valvular abnormalities. His medications were metoprolol, lisinopril, aspirin, metformin, and sublingual nitroglycerin.

### 1. What are the major determinants of myocardial oxygen supply and demand?

The myocardium normally extracts 65% of the oxygen in arterial blood compared with extraction of 25% by other tissues. An increase in myocardial demand for oxygen can be met only by an increase in coronary blood flow, not by increased oxygen extraction.

The major determinants of myocardial oxygen supply include the following:

- *Coronary anatomy*. Myocardial blood supply derives from the left and right coronary arteries. The right coronary artery normally supplies the right atrium and most of the right ventricle and in right dominant circulation (85% of people) gives rise to the posterior descending artery, which supplies part of the interventricular septum and the inferior wall of the left ventricle. It also usually supplies the sinoatrial node (60% of patients) and the atrioventricular node (85% of patients). The left coronary artery bifurcates into the left anterior descending artery and the circumflex arteries. The left anterior descending artery supplies the septum of the left ventricle and the anterior wall, whereas the circumflex artery supplies the lateral wall and in left dominant circulation (15% of people) gives rise to the posterior descending artery.
- *Coronary perfusion pressure (CPP)*. CPP is determined by the difference between aortic pressure and ventricular pressure. During systolic contraction, the pressure in the left ventricle approaches aortic pressure, so no coronary perfusion occurs during this time. The left ventricle is almost entirely perfused during diastole, whereas the right ventricle is perfused during both systole and diastole. CPP for the left ventricle is the difference between the aortic diastolic pressure (ADP) and the left ventricular end-diastolic pressure (LVEDP):

$$CPP = ADP - LVEDP$$

- *Heart rate*. Because nearly all perfusion of the left ventricle occurs during diastole, the duration of diastole is also a significant determinant of coronary perfusion. Increases in heart rate result in a disproportionately greater decrease in diastolic time resulting in decreased coronary perfusion.
- *Arterial oxygen content*. Hemoglobin concentration and oxygen saturation need to be optimized to maintain adequate supply. The optimal hemoglobin concentration and transfusion trigger remain a matter of debate.

The major determinants of myocardial oxygen demand include the following:

- *Basal oxygen requirements*. Basal requirements account for about 20% of the oxygen requirements.
- *Left ventricular wall tension (T)*. T is directly proportional to the intraventricular pressure (P) and ventricular radius (r) and inversely proportional to ventricular wall thickness (h): $T = Pr/2h$. Increases in either preload (increased radius) or afterload (increased pressure)

increase T and oxygen demand. The increase in oxygen demand secondary to an increase in afterload is usually compensated by an increase in CPP and oxygen supply.
- *Heart rate.* Increases in heart rate increase oxygen demand, while decreasing oxygen supply, increasing the potential for myocardial ischemia.
- *Contractility.* Decreased myocardial contractility is associated with smaller oxygen requirements. However, if CPP is decreased, the oxygen supply is decreased.

## 2. How is coronary artery disease treated, and which medications should be continued perioperatively?

To avoid ischemia, a balance between myocardial oxygen supply and demand must be maintained. The medications used to treat CAD attempt to maintain this balance by either reducing the demand for or increasing the supply of myocardial oxygen.

### β-Adrenergic Blockers

By antagonizing the effects at β receptors, these agents reduce heart rate (increasing diastolic time) and contractility. Myocardial oxygen consumption is decreased, and coronary perfusion is improved. β Blockers are beneficial for most patients with CAD, particularly if their heart rates are increased. When acutely administered in adequate dosage, β blockers have been shown to significantly reduce myocardial oxygen demand and the incidence of atrial and ventricular arrhythmias. The current American College of Cardiology/American Heart Association (ACC/AHA) guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery recommend that β blockers should be continued in patients who have been taking them before surgery and should be started in patients who are at high risk for cardiovascular disease, as defined by the presence of more than one clinical risk factor (Box 11-1), and who are undergoing high-risk or intermediate-risk surgery.

### Antiplatelet Agents

Many patients present for coronary artery bypass grafting (CABG) while being treated with platelet inhibitors. Aspirin is a well-recognized component of primary and secondary prevention strategies for all patients with CAD. The combination of aspirin and clopidogrel has been shown to improve outcome after acute coronary syndrome. Many patients presenting for CABG underwent a previous coronary artery stent procedure, necessitating treatment with aspirin and clopidogrel to prevent early stent thrombosis. Antiplatelet therapy is also used after CABG to reduce postoperative ischemic complications. Aspirin has strong efficacy in the prevention of early graft thrombosis after CABG. However, controversy exists in regard to preoperative antiplatelet therapy. The risk of hemorrhagic complications needs to be weighed against the potential antiischemic benefits of antiplatelet therapy.

The premature discontinuation of antiplatelet therapy in patients with coronary artery stents presenting for noncardiac surgery increases the risk of stent thrombosis, myocardial infarction, and death. It is ideal to delay elective noncardiac surgery for 4 to 6 weeks after bare metal stent implantation and at least 12 months after drug-eluting stent implantation. If surgery cannot be postponed, a discussion with the surgeon and the patient's cardiologist is necessary to determine the risk versus benefit of temporarily stopping antiplatelet therapy compared with the risk of bleeding complications. If it is determined that clopidogrel therapy needs to be interrupted, owing to the risk of bleeding complications, aspirin therapy should be continued if possible, and clopidogrel should be restarted as soon as possible.

**BOX 11-1 Clinical Risk Factors (Revised Cardiac Risk Index)**

- History of ischemic heart disease
- History of congestive heart failure
- History of cerebrovascular disease
- Diabetes mellitus
- Renal insufficiency

### 3-Hydroxy-3-methylglutaryl-coenzyme A Reductase Inhibitors (Statins)

3-Hydroxy-3-methylglutaryl-coenzyme A (HMG CoA) reductase inhibitors have a variety of important effects independent of their primary purpose as lipid-lowering agents. They appear to possess potent antiinflammatory and antithrombotic effects. Statins have also been shown to decrease myocardial reperfusion injury after cardiac surgery. The current ACC/AHA guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery recommend continuing statins in patients currently taking them and considering starting statins in patients with at least one clinical risk factor (see Box 11-1) undergoing intermediate-risk surgery. Postoperative withdrawal of statin treatment is independently associated with increased in-hospital mortality after CABG.

### Intraaortic Balloon Pump

An intraaortic balloon pump is a mechanical device that increases myocardial oxygen perfusion while increasing cardiac output and myocardial oxygen delivery. It actively deflates in systole, increasing forward blood flow by reducing afterload. It actively inflates in diastole, increasing blood flow to the coronary arteries. These actions combine to decrease myocardial oxygen demand and increase myocardial oxygen supply. The preoperative use of intraaortic balloon pumps in high-risk patients undergoing CABG has shown promising results in improving outcomes.

## 3. What are the preanesthetic concerns in a patient with coronary artery disease?

The anesthesiologist needs to be aware of any comorbidities the patient has and plan accordingly. Patients

with CAD often have a history of hypertension, diabetes, cerebrovascular disease, and chronic renal disease. Many also have a history of smoking.

Patients with hypertension have intravascular hypovolemia and may become hypotensive after induction of anesthesia. Patients with severe diabetes mellitus are at risk for autonomic and peripheral neuropathy that can lead to silent myocardial ischemia and delayed gastric emptying. Appropriate prophylaxis for a "full stomach" should be considered. If a patient has significant cerebrovascular disease, a higher blood pressure is required to maintain cerebral perfusion pressure. Chronic renal disease may affect the elimination of certain medications.

Premedication in the preoperative period may be very important in a patient presenting for CABG. Premedication with benzodiazepines and opioids reduces apprehension and provides analgesia for potentially painful events before induction (e.g., vascular cannulation). This premedication may help prevent preoperative anginal episodes elicited by tachycardia secondary to anxiety or painful stimuli. After premedication, all patients should receive supplemental oxygen and monitoring with pulse oximetry, electrocardiogram (ECG), and noninvasive blood pressure.

## 4. What anesthetic technique is used for coronary artery bypass grafting?

A balanced general anesthetic is the most commonly performed anesthetic technique, but it needs to be tailored to the individual patient. Most hypnotics, opioids, and volatile agents have been used in different combinations for the induction and maintenance of anesthesia with good results. The main considerations in choosing an induction technique for patients undergoing CABG are left ventricular function and coronary pathology. Additionally, limiting the amount of opioids or the use of short-acting drugs is encouraged in patients eligible for fast-tracking and early extubation.

Interest in thoracic epidural anesthesia for cardiac surgery, whether as the primary anesthetic technique or as a supplement to general anesthesia, has steadily increased. Thoracic sympathectomy appears to have favorable effects on the heart and coronary circulation. Heightened concerns about the risk of devastating neurologic injury secondary to the profound anticoagulation needed for cardiopulmonary bypass (CPB) have limited its routine use in the United States.

Steadily increasing evidence from laboratory and clinical studies suggests that inhalation anesthetic agents have favorable properties in patients undergoing CABG. There has been a major resurgence in their popularity as the primary anesthetic in patients undergoing cardiac surgery owing to the current routine use of fast-track anesthesia techniques. Inhalation anesthetics are thought to protect the myocardium against ischemia by their ability to elicit the same protective cellular responses that are seen with ischemic preconditioning. The latter has been shown to reduce myocardial infarction size after periods of ischemia.

## 5. What intraoperative monitoring techniques can be used to detect myocardial ischemia?

Intraoperative detection of ischemia depends on the recognition of ischemic changes by ECG, hemodynamic manifestations, and new-onset regional wall motion abnormalities (RWMAs) seen on transesophageal echocardiography (TEE).

- *ECG.* The simultaneous monitoring of leads $V_5$ (anterior wall) and II (inferior wall) allows for the detection of 90% of ischemic episodes. In addition, this monitoring allows for detection of atrial and ventricular dysrhythmias, another possible manifestation of ischemia. Early ischemic changes usually involve T-wave inversions followed by ST segment depression.
- *TEE.* The earliest sign of myocardial ischemia is systolic RWMAs, which occur within seconds of reduced coronary perfusion. TEE is more sensitive than ECG at detecting myocardial ischemia. The routine use of TEE is now recommended for all patients undergoing CABG or OPCAB surgery. The transgastric short-axis midpapillary muscle view of the left ventricle is commonly used because it visualizes myocardium supplied by all three major coronary arteries. New RWMAs detected intraoperatively are not specific for myocardial ischemia because they may frequently occur secondary to nonischemic causes, such as changes in loading conditions, alteration in cardiac electrical conduction, post-CPB pacing, or poor myocardial preservation.

## 6. What are the advantages and disadvantages of on-pump versus off-pump coronary artery bypass grafting?

For many years, CABG was primarily performed with the use of CPB, which allowed for a bloodless and immobile surgical field. Conventional CPB and aortic cross-clamping risks generalized systemic inflammatory responses that cause hemodynamic instability and affects all organs, especially the heart, lungs, and kidneys. Cerebral dysfunction likely results from emboli that dislodge from the aorta during cross-clamping, cannulation, and proximal vein graft anastomosis. The introduction of OPCAB into practice was an attempt to decrease the adverse clinical consequences of conventional CPB and aortic cross-clamping.

The introduction of mechanical stabilizer devices that minimized motion around the anastomosis site (independent of heart rate) allowed for performing CABG without the use of CPB (i.e., "off-pump"). The ability to expose the posterior surface of the heart to access the posterior descending and circumflex arteries was vital for the multivessel application of this technique. This ability depends on placing suction devices on the apex of the heart without producing major hemodynamic compromise. About 30% of CABG procedures are likely performed off-pump.

Numerous studies analyzing whether OPCAB reduces morbidity and mortality compared with conventional CABG have reported conflicting results. The final word

regarding difference in outcome and which patients may benefit from an OPCAB technique is still years away.

### 7. What are unique anesthetic considerations related to off-pump coronary artery bypass grafting?

The continuous, intensive involvement of the anesthesiologist is perhaps more crucial during OPCAB than during on-pump CABG. Relative to on-pump CABG, OPCAB extends the range of surgeon-induced hemodynamic changes the anesthesiologist encounters. Surgical manipulations can cause various cardiac anatomic distortions including compression of the right ventricle and distortion of the mitral valve anulus. Anesthesiologists must be able to anticipate and communicate with surgeons to minimize the adverse impact of these changes on the heart and other vital organs. With a skilled surgeon, the changes are usually modest or easily treated by the Trendelenburg position, judicious volume expansion, and use of vasoconstrictors or inotropes. However, severe changes secondary to acute ischemia, unrecognized right ventricular compression, or severe mitral regurgitation may occur, necessitating emergent conversion to CPB.

The anesthesia technique in patients undergoing OPCAB does not differ much from the anesthesia technique for on-pump CABG. It can depend on the indication for OPCAB. Patients with advanced age, significant ascending aortic disease, poor left ventricular function, and multiple comorbidities may be scheduled for OPCAB to avoid CPB and aortic cross-clamping.

Anticoagulation in patients undergoing OPCAB is an area of controversy. Some surgeons prefer low-dose heparinization (e.g., 100 to 200 units/kg heparin) with a target activated clotting time (ACT) of 250 to 300 seconds, whereas others choose full heparinization (e.g., 300 units/kg) with a target ACT of greater than 480 seconds during the procedure. ACT is measured every 30 minutes, and heparin is administered to maintain the target ACT.

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SECTION 2

# RESPIRATORY SYSTEM

CASE 12

# One-Lung Ventilation

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## QUESTIONS

1. Describe the anesthetic evaluation before lung resection.
2. How are ventilation and oxygenation monitored noninvasively during surgery, and how do these monitors work?
3. What are the indications for one-lung ventilation?
4. Describe the use of single-lumen endotracheal tubes and bronchial blockers for one-lung ventilation.
5. If a double-lumen tube is to be used, which would be preferable, a left-side or right-side tube?
6. Describe the proper technique for placing a double-lumen endobronchial tube.
7. How is correct positioning of the double-lumen endobronchial tube assessed?
8. What clinical problems are associated with placement and use of double-lumen endobronchial tubes?
9. What complications are related to placing the patient in the lateral decubitus position?
10. How are pulmonary perfusion and ventilation altered during one-lung ventilation?
11. How is hypoxemia that occurs during one-lung ventilation treated?
12. Describe the role of a thoracostomy tube after pulmonary resection.
13. Describe a commonly used pleural drainage system.
14. What are the potential complications after thoracotomy?

A 70-year-old man presents for resection of a left upper lobe tumor. He has a long history of cigarette smoking.

### 1. Describe the anesthetic evaluation before lung resection.

Preoperative evaluation begins with the same basic information required before all anesthetics. Next, it is determined whether the patient is in optimal condition for the planned procedure or whether further preoperative evaluation or preparation is indicated. Finally, an assessment is made to predict lung function after resection. Specific pulmonary evaluation includes history of cough, sputum production, chest pain (possibly pleuritic), dyspnea, wheezing, arm pain (resulting from a Pancoast tumor invading the brachial plexus), weakness (resulting from myasthenic syndrome), other endocrine syndromes (caused by tumors secreting hormones), and weight loss (hypoproteinemia). Physical examination includes auscultation for wheezing, rales, and rhonchi. Wheezing may require treatment with bronchodilators, and infected sputum is treated with antibiotics. Chest radiograph, tomography, computed tomography, and magnetic resonance imaging provide further information about the tumor site, structures involved, and possible airway compromise.

Lung function tests are indicated to predict the risk of respiratory failure, right heart failure (cor pulmonale), and atelectasis and to guide bronchodilator therapy. Spirometry is a noninvasive test that provides data on lung volumes and gas flow rates. Flows are tested before and after bronchodilator therapy, such as albuterol by inhaler, to determine reversible obstructive airway disease. Improved flows after bronchodilator therapy indicate preoperative adjustments in the bronchodilator regimen.

Pulmonary function tests that may correlate with outcome include forced expiratory volume in 1 second ($FEV_1$), forced vital capacity (FVC), maximum voluntary ventilation, and ratio of residual volume to total lung capacity (RV/TLC). Based on how much lung tissue is to be resected, predicted postoperative (PPO) function can be calculated. A PPO $FEV_1$ >40% has been associated with improved outcome. FVC <50% of predicted or RV/TLC >50% of predicted may indicate higher risk.

Spirometry reflects respiratory mechanics, whereas gas exchange is assessed by measuring the diffusing capacity for carbon monoxide (DLCO). A PPO DLCO <40% indicates reduced lung parenchymal function and is a predictor of increased risk.

Cardiopulmonary reserve can be evaluated by measuring the maximal oxygen consumption ($\dot{V}O_2max$). A $\dot{V}O_2max$ <10 mL/kg/min indicates very high risk, and a $\dot{V}O_2max$ >20 mL/kg/min indicates reduced risk. Other tests of cardiopulmonary reserve include exercise oximetry, in which a decrease in oxygen saturation by pulse oximetry ($SpO_2$) of 4% during exercise may indicate increased risk. A simple

test is stair climbing; inability to climb more than one flight of stairs is associated with increased risk, and ability to climb three or more flights of stairs reflects decreased risk.

If lung function results are poor, split lung function testing (ventilation/perfusion radiospirometric studies) can be done to allow calculation of PPO lung function. Ultimately, the operative decision to perform pneumonectomy versus lobectomy versus wedge resection is a clinical one in which the patient's overall condition is considered.

## 2. How are ventilation and oxygenation monitored noninvasively during surgery, and how do these monitors work?

The purpose of ventilation is to remove carbon dioxide ($CO_2$) from the lungs. The average 70-kg man produces approximately 220 mL per minute of $CO_2$ and normally maintains an arterial carbon dioxide tension ($PaCO_2$) of 40 mm Hg. If removal of $CO_2$ is impaired or if production increases and ventilation does not increase, $PaCO_2$ increases. Arterial blood gas analysis provides the ultimate monitor of ventilation: $PaCO_2$. In the lungs, $CO_2$ diffuses into alveoli, and in areas where ventilation and perfusion are well matched, alveolar $CO_2$ tension ($P_ACO_2$) approximates $PaCO_2$. $P_ACO_2$ may be sampled as end-tidal carbon dioxide ($P_{ET}CO_2$) and analyzed by various technologies to provide a noninvasive estimation of $PaCO_2$. Overall, $P_{ET}CO_2$ is normally 4–6 mm Hg less than $PaCO_2$. Increases in physiologic dead space or a decrease in alveolar ventilation results in increased $PaCO_2$.

Capnography is the science of measuring and displaying $CO_2$ as a concentration plotted against time (capnogram). The $CO_2$ concentration in gas mixtures may be measured using many technologies, the most common of which is infrared light spectroscopy. Although mass spectrometry, infrared (IR) acoustic spectroscopy, and Raman scattering have been used in the past, the monitors that used these technologies are no longer in production. IR light spectroscopy is based on 4.3 μm (4300 nm) wavelength IR radiation absorbance by intermolecular bonds in the $CO_2$ molecule. The greater the number of $CO_2$ molecules present, the greater the absorbance of radiation. Gas is drawn through a sample cell (cuvette), and IR light of 4.3 μm is passed through the cell. Transmission of light through the gas sample to a photodetector is inversely proportional to the tension of $CO_2$ in the gas sample. Such systems are in widespread use, and sampling may be of the sidestream or mainstream (in the airway) design.

By continuously following the tension of $CO_2$ against time, the highest value is designated end-tidal and defines exhalation, and the lowest value is designated inspiratory and defines inspiration. Continuous capnography is considered the standard of care because it provides a continuous monitor of ventilation and, with certain limitations, can provide a noninvasive estimate of $PaCO_2$.

Oxygenation is monitored best by sampling arterial blood and analyzing it for tension ($PaO_2$), hemoglobin (Hb) saturation with oxygen (fractional saturation, i.e., $O_2Hb$/total Hb), and total Hb. The oxygen content of arterial blood ($CaO_2$) is given by the following equation:

$$CaO_2 = [(Hb \times 1.34 \times SaO_2) + (PaO_2 \times 0.003)]$$

Normal arterial oxygen content can be calculated by substituting variables as shown, assuming that the patient is breathing room air, the $SpO_2$ is 97%, and the $PaO_2$ is 97 mm Hg:

$$\begin{aligned} CaO_2 &= [(15 \times 1.34 \times 0.97) + (97 \times 0.003)] \\ &= 19.5 + 0.29 \\ &= \text{approximately 20 mL oxygen/100 mL blood} \end{aligned}$$

However, this calculation requires invasion of an artery for blood sampling.

Noninvasive monitoring of oxygenation is most commonly achieved using pulse oximetry, which is a standard of care. Pulse oximetry uses a combination of two technologies: (1) spectrophotometry of oxygenated and deoxygenated Hb and (2) optical plethysmography. The latter detects pulsatile components of changes in light transmitted through tissue. Each pulse oximeter probe has two light-emitting diodes that emit light at 660 nm and 940 nm as well as one photodetector. The ratio of the pulse-added absorbances at 660 nm to that at 940 nm is related through an empirically derived algorithm, to a saturation estimate that is designated $SpO_2$. Pulse oximeter readings have a standard deviation of approximately +2% in the saturation range of 70%–100%. The accuracy decreases at lower $SpO_2$ levels. Nevertheless, pulse oximeters are valuable as monitors of saturation trends. Pulse oximeters are inaccurate or may fail in the presence of poor perfusion (e.g., vasoconstriction from low cardiac output or cold extremities), venous pulsations, severe peripheral vascular disease, intravascular dyes, dyshemoglobins, certain nail polishes, and certain pigmentations. If doubt exists regarding the validity of pulse oximeter readings, an arterial blood gas sample should be drawn for blood gas tension analysis and saturation analysis in a laboratory cooximeter.

## 3. What are the indications for one-lung ventilation?

One-lung ventilation is indicated for isolation and protection of one lung from contamination by the other lung or for selective ventilation of one lung only. Indications for separating the lungs include prevention of blood or pus spillage and bronchopulmonary lavage. Situations in which hemorrhage or infectious material might affect the contralateral lung include bronchiectasis, lung abscess, and hemoptysis. The ability to control the distribution of ventilation between lungs improves exposure for thoracic surgery. Positive pressure ventilation through a single-lumen tube risks losing large amounts of tidal volume through a bronchopleural fistula or pneumothorax in the case of a giant unilateral lung cyst. Surgical exposure is improved during pneumonectomy, descending thoracoabdominal aortic aneurysm repair, and resection of midesophageal and upper esophageal lesions. One-lung ventilation is needed for video-assisted thoracoscopy because the surgeon cannot operate endoscopically on an inflated lung.

### 4. Describe the use of single-lumen endotracheal tubes and bronchial blockers for one-lung ventilation.

Bronchial blockers can be placed through single-lumen tracheal tubes. This practice eliminates the need for changing a single-lumen tube to a double-lumen tube (DLT) at the beginning of a case in which single-lumen tubes had been placed for an initial bronchoscopy. It also eliminates the need for replacing DLTs with single-lumen tubes at the conclusion of surgery. That might be required if bronchoscopy is performed or preferred if the patient's airway is to be kept intubated. When using bronchial blockers, single-lumen tubes of sufficient diameter are employed to accommodate both the blocker and a fiberscope, which is needed for correct placement. Endotracheal tubes cannot be too close to the carina, especially in the case of left-sided thoracic surgery, because there will not be enough space to manipulate a blocker into the left main stem bronchus. It may be necessary to rotate the endotracheal tube such that the concave side is on the left or to turn the patient's head to the right for the bronchial blocker to enter the left main stem bronchus.

The most commonly used bronchial blockers are the Uniblocker (Fuji Systems, Tokyo, Japan), Cohen blocker (Cook, Bloomington, IN), and Arndt blocker (Cook). The first commercially available blocker was the Univent tube (Fuji Systems). The Univent tube is a combined single-lumen endotracheal tube and an integral bronchial blocker. The single-lumen tube is equipped with a narrow internal lumen through which a balloon-tipped bronchial blocker is advanced into the right or left main stem bronchus. With the bronchial blocker retracted and deflated, the tube is positioned by standard techniques into the trachea. The tube is turned 90 degrees toward the side to be blocked, and the blocker is advanced under flexible fiberoptic bronchoscopic guidance into the appropriate bronchus. The balloon is inflated, and lung separation is confirmed by auscultation of breath sounds. More rapid collapse of the lung follows deflation of the blocker balloon and disconnection from the anesthesia breathing circuit. After successful lung collapse, reinflation of the blocker's balloon and connection to the anesthesia breathing circuit allow for ventilation of one lung and collapse of the other. The blocker of the Univent tube is now available as an independent blocker, the Uniblocker, which is bent near the tip. Because the lumen of a bronchial blocker is small, deflation of the blocked lung is slower than when a DLT with larger lumens is used. When placed, a blocker tends to dislocate more than a DLT, especially when placed on the right side because of its location near the carina. There is more space in the left main stem bronchus to seat the balloon of the bronchial blocker.

### 5. If a double-lumen tube is to be used, which would be preferable, a left-side or right-side tube?

There is no one correct answer to this question. Different approaches to the choice of DLTs depend on the side of thoracotomy. Placement of a left-side DLT is frequently prudent. In an adult, the left main stem bronchus is 5–6 cm in length, and the right main stem bronchus is 1.5 cm in length. The right upper lobe bronchus is more likely to be accidentally occluded by the endobronchial tube than the left upper lobe bronchus. Resection of the left lung necessitates continuous ventilation of the right lung. Obstruction of the right upper lobe bronchus is likely to lead to hypoxemia during one-lung ventilation. For this reason, some anesthesiologists routinely place a left-side DLT regardless of the side of surgery, unless it is specifically contraindicated because of the presence of a diseased left main stem bronchus or if the bronchus is likely to become part of the surgical field, such as in a sleeve resection. If a left-side DLT is placed too distally, it may lead to hypoxemia if the left upper lobe is not adequately ventilated.

Some anesthesiologists routinely place the endobronchial tube on the side ipsilateral to the pulmonary resection. With this arrangement, obstruction of the upper lobe bronchus by the endobronchial tube is not as likely to cause hypoxemia because this is the lung that is deflated during one-lung ventilation, and oxygenation continues via the tracheal lumen. Also, before chest closure, reinflation of the remaining lung ipsilateral to the tube can be verified by direct inspection. If the upper lobe fails to reinflate, the bronchial cuff is deflated so that the upper lobe can be ventilated from the tracheal lumen. Alternatively, the DLT can be withdrawn until the distal end of the endobronchial tube is proximal to the upper lobe bronchial orifice, or the side opening in the DLT can be realigned with the right upper lobe orifice. In the case of a pneumonectomy, an ipsilaterally placed tube must be withdrawn to a position where the distal end of the tube is in the trachea before division of the main stem bronchus. Withdrawal may also become necessary if the intubated bronchus is involved in the surgery.

A different approach used by a smaller percentage of anesthesiologists is to place the DLT routinely into the nonoperative side. This strategy prevents damage from placing the tube into a diseased bronchus. However, placement of a right-side DLT for a left thoracotomy may lead to hypoxemia during one-lung ventilation, as discussed earlier. This approach may be the most prudent course in the case of pneumonectomy, or sleeve resection, because surgery would not be affected by the presence of a tube.

### 6. Describe the proper technique for placing a double-lumen endobronchial tube.

The largest size DLT that can easily pass the glottis may be preferred. The advantages of placing a larger size tube are as follows:

- Less air is required to inflate the endobronchial tube cuff.
- A large lumen facilitates suctioning.
- Malposition of the tube distally in the bronchus is less likely.

Clear polyvinyl chloride disposable Robertshaw-type DLTs are available in sizes 41F, 39F, 37F, 35F, and 28F

(French size = external diameter of tube in mm × 3). Sizes 39F, 37F, and 35F fit most adults.

Curved laryngoscope blades usually provide more space in the mouth than straight blades for DLT passage. DLTs are bulky compared with single-lumen tubes. However, a straight blade may be required in some patients. Videolaryngoscopy can be used to facilitate tube placement.

Induction agents are selected based on the patient's medical condition. Nondepolarizing neuromuscular blocking drugs offer the advantage of a longer duration of action than succinylcholine. The greater duration of muscle relaxation facilitates DLT placement.

A DLT is placed orally, with its distal (bronchial) concave curve directed anteriorly. When the endobronchial cuff has passed through the glottic opening, an assistant removes the stylet. The tube is rotated 90 degrees toward the side of intended bronchial intubation and advanced to approximately 27–30 cm at the lips, or until resistance is encountered. If the tube advances into the unintended side, the endobronchial lumen can be withdrawn to the trachea and then advanced over a flexible fiberoptic bronchoscope into the appropriate bronchus. Air is injected into the tracheal cuff, and the tube's position is checked.

## 7. How is correct positioning of the double-lumen endobronchial tube assessed?

Correct placement of the endobronchial tube must be confirmed immediately after intubation and after turning the patient into the lateral decubitus position. The patient's lungs are initially ventilated through both lumens with the tracheal cuff inflated. Bilateral breath sounds, bilateral chest excursion, and bilateral fogging of the DLT lumens should be present, unless there is significant lung disease on one side. Gas should not leak around the cuff. The capnogram should be examined for the presence of $CO_2$. Successful response to these maneuvers ensures that the distal end of the tracheal lumen is in the trachea and is above the carina. Unilateral breath sounds and chest movement indicate that the tube has been inserted too far, and the tracheal lumen is in the bronchus, ipsilateral to the side on which breath sounds are present. In this case, the tracheal cuff should be deflated and the tube withdrawn until bilateral ventilation is established.

Next, the bronchial cuff is inflated with <2 mL of air. The tracheal lumen is clamped, and the access cap is opened. Ventilation should result in chest movement and breath sounds on the endobronchial side, which identifies for the practitioner the side in which the tube resides (Figure 12-1). The presence of bilateral breath sounds and chest movement indicates that the orifice of the bronchial lumen is proximal to the carina (Figure 12-2). Unilateral breath sounds and chest movement on the side opposite the bronchus intended for intubation indicate that the tube has been placed in the wrong side (Figure 12-3). Both cuffs should be deflated if the tube has been placed in the wrong side, and the tube should be withdrawn to a point where the distal end of the endobronchial tube is in the trachea. The tube is rotated and advanced again until there is resistance to further movement. An alternative method is to insert a fiberscope through the bronchial lumen, visualize the carina, pass the fiberscope down into the bronchus

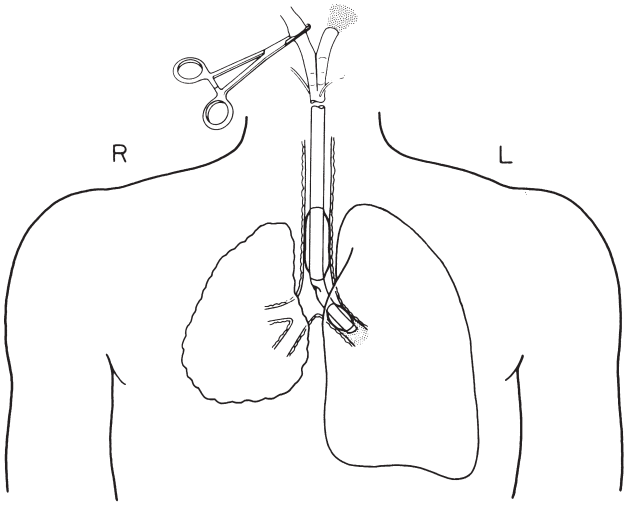


**FIGURE 12-1** ■ Left endobronchial tube is properly placed. Separation of lungs is achieved.

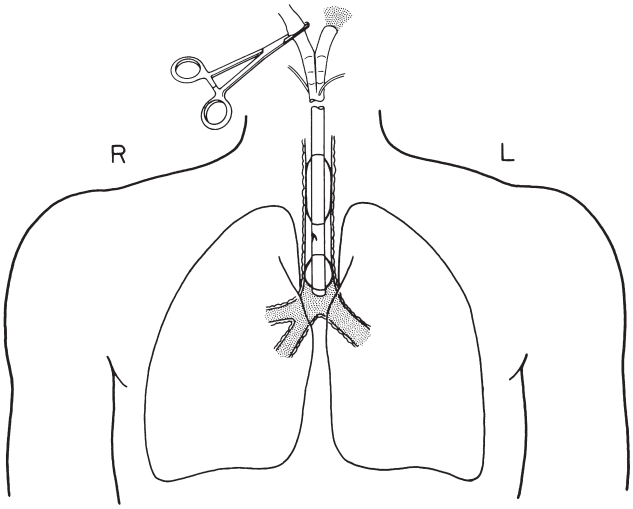


**FIGURE 12-2** ■ Left endobronchial tube is placed too shallow.

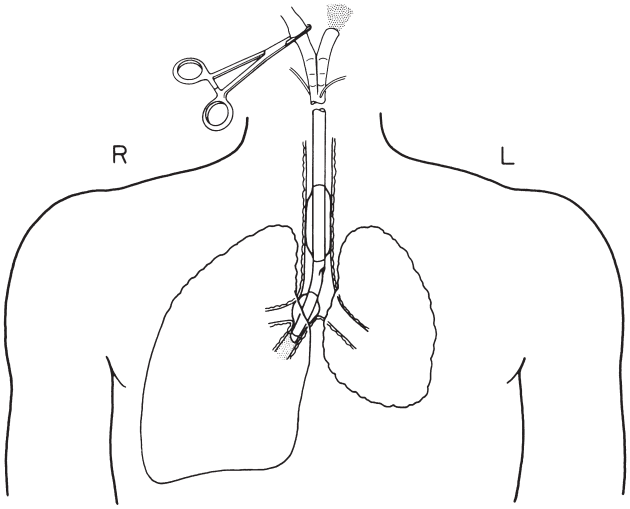


**FIGURE 12-3** ■ Left endobronchial tube is inserted into the right bronchus.

intended for intubation, and slide the tube distally using the fiberscope as a guide until resistance is met. If the trachea was easy to intubate, instead of remanipulating the tube within the patient, the tube can be removed from the patient entirely, and the procedure can be repeated.

A right-side tube almost always goes to the correct (right) side, but a left-side tube sometimes passes to the wrong side. A left-side tube should not be allowed to remain in the contralateral side because there is no opening for the right upper lobe bronchus on a left-side tube. Rotating the patient's head to the right, as is performed for left endobronchial rigid bronchoscopy, may facilitate passage of the tube to the left side.

Ventilation of the lung while the endobronchial lumen is clamped should provide breath sounds and chest movement only on the side opposite the bronchus intended for intubation, provided that the tube has been placed in the appropriate bronchus (Figure 12-4). Inability to ventilate

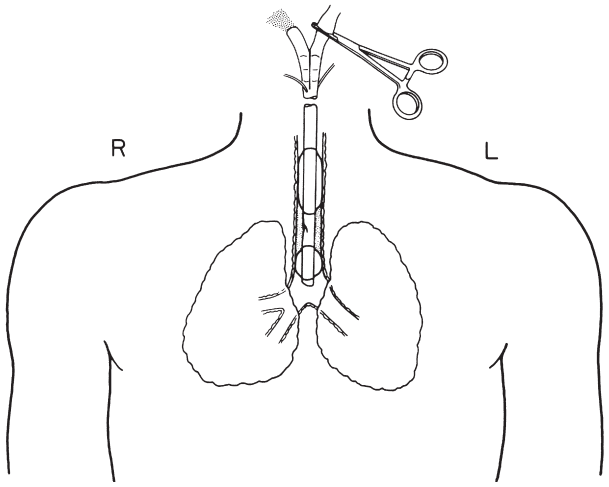


**FIGURE 12-6** ■ Left endobronchial tube is placed too shallow in the trachea (endobronchial cuff is inflated).

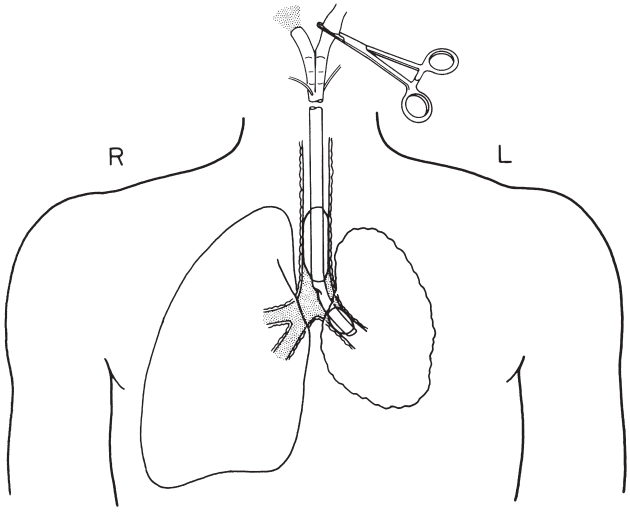


**FIGURE 12-4** ■ Left endobronchial tube is inserted correctly for right lung ventilation.

during this maneuver indicates that the tube is malpositioned and is either too deep in the bronchus (Figure 12-5) or too shallow in the trachea (Figure 12-6). Deflation of the endobronchial cuff while keeping the endobronchial lumen clamped allows ventilation of only one lung if the tube is too deep in the bronchus (Figure 12-7) or bilateral lung ventilation if the tube is too shallow in the trachea (Figure 12-8). Ventilation of the lung contralateral to the position of the endobronchial lumen and only the upper lobe of the side ipsilateral to endobronchial tube placement indicates that the cuff of the endobronchial tube is distal to the upper lobe bronchus and that the tube needs to be withdrawn.

The precise positioning of the tube should be evaluated with the use of a flexible fiberoptic bronchoscope, if possible. Passage down the tracheal lumen should reveal the carina and just the proximal tip of the blue cuff of the endobronchial tube in the opening of the main stem bronchus. Visualization of the tube passing into the

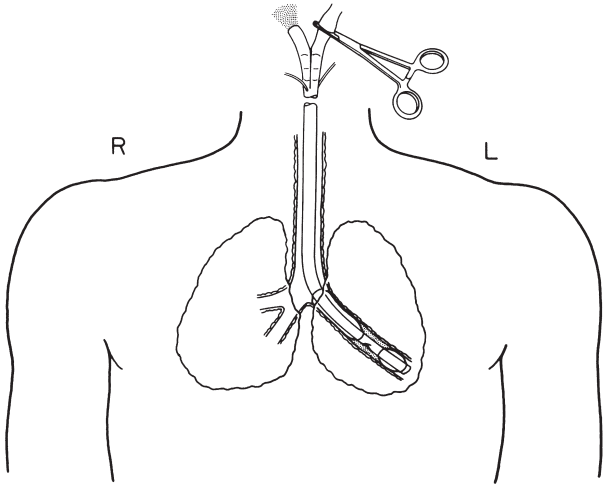


**FIGURE 12-5** ■ Left endobronchial tube is placed too deeply into the bronchus (both cuffs are inflated).

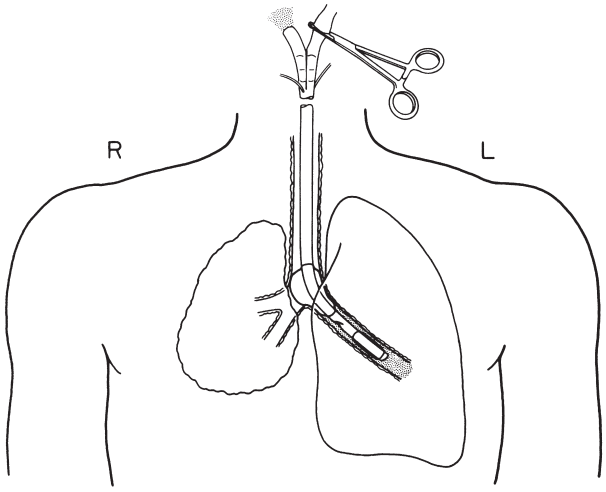


**FIGURE 12-7** ■ Left endobronchial tube is placed too deep in the left bronchus (only the tracheal cuff is inflated).

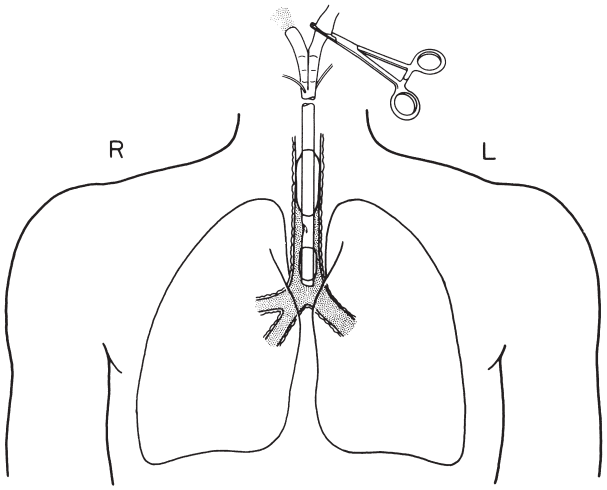


**FIGURE 12-8** ■ Left endobronchial tube is placed too shallow (endobronchial cuff is deflated).

bronchus beyond the carina without observation of the blue bronchial cuff indicates that the tube is positioned too deeply into the bronchus. Fiberscopic inspection via the bronchial lumen should reveal a patent bronchial lumen that is not occluded internally by the cuff. If the distal opening of the tube abuts the bronchial wall, ventilation of that lung becomes difficult because DLTs do not have Murphy eyes. Visualization of the bronchial carina indicates that the tube is not placed too deeply. If the tube is right-sided, visualization through the side opening should allow proper alignment with the right upper lobe bronchus. If the carina is not visualized after placing a fiberscope through the tracheal lumen, the tube is probably too shallow, too deep, or located in the unintended bronchus. If the tube is too shallow, deflation of the bronchial cuff should provide a view of the carina. If the tube is in the contralateral bronchus, deflation of the bronchial cuff does not reveal the tracheal carina, and instead anatomy of the opposite side is observed. For example, if a left-side tube lodges in the right bronchus, deflation of the bronchial cuff reveals the bronchus intermedius (right upper lobe, right middle lobe, and right lower lobe bronchi).

## 8. What clinical problems are associated with placement and use of double-lumen endobronchial tubes?

Depending on the type of tube malposition and the side of surgery, hypoxemia or poor surgical exposure may result. In the case of a bronchopleural fistula, poor separation of the lungs may lead to loss of tidal volume, hypercarbia, and hypoxemia. Inadequate isolation in the case of hemorrhage or empyema may lead to contamination of the uninvolved lung, which is in the dependent position during the surgical procedure and prone to contamination secondary to gravity.

Forcing the endobronchial tube too distally or using an excessive volume of air to inflate the bronchial cuff may lead to bronchial hemorrhage and perforation. Rupture may be more likely if the bronchus has been weakened by disease, such as a mediastinal tumor. A descending thoracic aortic aneurysm may impinge on the left main stem bronchus and possibly could be ruptured if an endobronchial tube is forced beyond this point of resistance. Movement of the tube without deflating the cuff could lead to airway trauma, especially by the endobronchial cuff.

## 9. What complications are related to placing the patient in the lateral decubitus position?

Pulmonary resection is usually performed with the patient in the lateral decubitus position. The operative lung is placed in the nondependent location. Cardiopulmonary complications of the lateral decubitus position depend mostly on the patient's preoperative condition (Box 12-1).

The patient should be well anesthetized and paralyzed before being turned to the lateral position to prevent coughing, hypertension, and tachycardia. The dependent lung is well perfused, and the nondependent lung is less well perfused, which is due to gravitational effects on the distribution of pulmonary blood flow.

In an awake spontaneously breathing patient, the dependent lung is better ventilated than the nondependent lung, which is due to more efficient contraction of the dependent hemidiaphragm. Greater curve (stretch) is present in the dependent diaphragm, which is due to the abdominal contents pushing cephalad.

In an anesthetized and paralyzed patient, most of the ventilation is distributed to the nondependent lung, while perfusion remains preferentially diverted to the dependent lung, creating a ventilation/perfusion mismatch. Reduction of lung volume attributed to induction of anesthesia moves the nondependent lung to a more compliant (steeper) portion of the volume-pressure (compliance) curve. With paralysis of the diaphragm, the abdominal contents impede movement of the dependent lung to a greater extent than the nondependent lung. Opening the chest further improves compliance of the nondependent lung, enhancing its ventilation. Downward pressure from the mediastinum and pressure from lying on the lateral chest wall exacerbate impaired dependent

**BOX 12-1 Complications Associated with Lateral Decubitus Position for Thoracic Surgery**

- Coughing, tachycardia, and hypertension during turn to lateral decubitus position
- Hypotension from blood pooling in dependent portions
- Ventilation/perfusion mismatching leading to hypoxemia
- Interstitial pulmonary edema of dependent lung (down-lung syndrome)
- Brachial plexus and peroneal nerve injuries
- Monocular blindness
- Outer ear ischemia
- Axillary artery compression

lung compliance and ventilation. Rolls beneath the hips and lower axilla lift the chest wall off the table and improve dependent lung ventilation.

Maintaining the lateral decubitus position for a long time leads to transudation of fluid in the dependent lung, causing interstitial pulmonary edema, known as "down-lung syndrome." Administration of large amounts of intravenous fluid increases left atrial pressure and leads to further transudation of fluid.

Peripheral nerve injuries from pressure or stretching may also occur. Padding the lower extremities and placing a low axillary roll help prevent injury to the peroneal nerve and brachial plexus. The dependent eye should remain clear of head supports, and the dependent ear pinna should not fold over itself. An arterial catheter placed in the dependent arm allows for constant monitoring of excessive pressure on the dependent axillary artery.

## 10. How are pulmonary perfusion and ventilation altered during one-lung ventilation?

During two-lung ventilation in the lateral decubitus position, ventilation is preferentially diverted to the nondependent lung, and perfusion is primarily directed to the dependent lung. When the nondependent lung is collapsed, ventilation to that side is eliminated, but some perfusion persists. Blood passing through the deflated lung does not exchange gas with alveoli and is called shunted blood. This unoxygenated venous (shunted) blood mixes with oxygenated blood from the dependent lung in the pulmonary vein and left atrium, resulting in a significant overall decrease in oxygen tension. Exchange of $CO_2$ is not affected by one-lung ventilation to the same extent as is oxygenation because $CO_2$ diffuses readily across alveolar-capillary membranes in the dependent (ventilated) lung.

Additionally, hypercarbia is better tolerated than hypoxia. There is a reduction in pulmonary blood flow to the nondependent lung during one-lung ventilation, which tends to decrease the shunt fraction (Box 12-2). Gravity, surgical compression, and ligation of nondependent pulmonary vessels all decrease blood flow to the nondependent lung. Alveolar hypoxia in the nondependent lung from atelectasis stimulates the hypoxic pulmonary vasoconstriction (HPV) response, which leads to further diversion of blood to the dependent (ventilated) lung. HPV is a local mechanism that constricts pulmonary vessels and diverts blood flow to the better oxygenated (ventilated) portions of the lung. Continued blood flow to the hypoxic lung constitutes true shunt. The stimulus for HPV appears to be related to mixed venous blood ($P_{\bar{V}}O_2$) and $P_AO_2$. Active HPV can decrease blood flow to hypoxic lung by approximately 50%, decreasing shunt and improving $PaO_2$.

In numerous in vitro and in vivo animal studies, HPV has been shown to be inhibited by potent inhaled anesthetics and vasodilators. Intravenous agents such as ketamine, opioids, and benzodiazepines do not appear to inhibit HPV. The effects of anesthetics on HPV are difficult to demonstrate clinically because of the many confounding variables present in patients undergoing surgery. If hypoxemia occurs secondary to shunting, adding remifentanil may allow less volatile agent to be used, decreasing the impact on HPV (Box 12-3).

## 11. How is hypoxemia that occurs during one-lung ventilation treated?

In the past, ventilation of the dependent lung with large tidal volumes (10–12 mL/kg) was recommended during one-lung ventilation to prevent atelectasis. Increased airway pressures also reduce transudation of fluid from pulmonary capillaries. However, too much of an increase in airway pressure may increase dependent lung pulmonary vascular resistance (PVR) and divert blood flow to the nondependent lung. Large tidal volumes create a risk for volutrauma and barotrauma from the associated higher airway pressures leading to acute lung injury. At the present time, most thoracic anesthesiologists ventilate the lung with tidal volumes of 5–8 mL/kg of ideal body weight. These smaller tidal volumes should be accompanied by positive end expiratory pressure (PEEP) to prevent atelectasis in the ventilated lung.

Ventilatory rate is adjusted to maintain $PaCO_2$ near 40 mm Hg; this is usually achieved with a rate similar to that employed during two-lung ventilation. During

**BOX 12-2 Ventilation and Perfusion Effects during One-Lung Ventilation**

Lateral decubitus position
- Perfusion best in dependent areas

Two-lung ventilation
- Ventilation best in nondependent areas
- Perfusion best in dependent areas

Nondependent lung collapsed
- Ventilation eliminated in nondependent lung and best in dependent areas
- Perfusion best in dependent area, but residual nondependent perfusion results in shunt
- HPV initiated by alveolar hypoxia and other factors
- $CO_2$ exchange minimally affected

*$CO_2$*, Carbon dioxide; *HPV*, hypoxic pulmonary vasoconstriction.

**BOX 12-3 Factors Affecting Hypoxic Pulmonary Vasoconstriction**

**Factors Inhibiting HPV**

Increased $P_{\bar{V}}O_2$
Potent inhaled anesthetics (controversial in humans)
Vasodilators (e.g., nitroglycerin, nitroprusside)
$\beta_2$-adrenergic agonists (e.g., isoproterenol)

**Factors that do not Appear to Affect HPV**

Ketamine
Opioids
Benzodiazepines

*HPV*, Hypoxic pulmonary vasoconstriction; $P_{\bar{V}}O_2$, mixed venous oxygen tension.

one-lung ventilation, 100% oxygen is administered. The benefits of 100% oxygen generally outweigh the possible risks of its use. The fraction of inspired oxygen ($FiO_2$) can be titrated lower as tolerated. Patients who received bleomycin are at risk for oxygen toxicity and should receive the lowest $FiO_2$ compatible with adequate oxygenation.

Temporarily reinflating and ventilating the nondependent lung with 100% oxygen rapidly corrects sudden and precipitous decreases in arterial oxygen saturation. Possible causes for hypoxia should be sought and corrected. Etiologies include the following:

- Malposition of DLT
- Kinking of tube
- Secretions
- Pneumothorax of dependent (ventilated) lung
- Bronchospasm
- Low cardiac output
- Low blood pressure
- Low $FiO_2$
- Hypoventilation

In the absence of an identifiable cause for hypoxemia, shunting of blood through the nondependent lung is most likely to be responsible. Continuous positive airway pressure (CPAP) of 5 cm $H_2O$ may be applied to the nondependent lung. CPAP to the nondependent lung opens alveoli so that they can participate in gas exchange and allows oxygenation of blood flowing through the nondependent lung. Insufflation of oxygen at zero airway pressure does not improve $PaO_2$, and using >10 cm $H_2O$ CPAP may lead to interference with surgical exposure. CPAP is usually effective in restoring $PaO_2$ to a safe level. CPAP interferes significantly with video-assisted thoracoscopy, which underscores the need to use PEEP to the dependent lung initially.

If functional residual capacity (FRC) is low, PEEP to the dependent lung may improve oxygenation by returning FRC toward normal and by decreasing PVR in the dependent lung. However, further increases of FRC may increase dependent lung PVR and decrease blood flow to the dependent lung. Other treatment modalities include intermittent ventilation of the nondependent lung with oxygen and clamping the nondependent pulmonary artery to eliminate shunting (Box 12-4).

**BOX 12-4 Prevention and Management of Hypoxemia during One-Lung Ventilation**

Ventilate dependent lung with tidal volumes of 5–7 mL/kg based on ideal body weight and PEEP 5–10 cm $H_2O$
Use 100% oxygen
Periodically reinflate nondependent lung with 100% oxygen
Search for causes of hypoxemia
  DLT malposition
  DLT kinking
  Secretions
  Pneumothorax
  Bronchospasm
  Low cardiac output
  Low $FiO_2$
  Hypoventilation
Apply CPAP 5–10 cm $H_2O$ to nondependent lung
Increase amount of PEEP if feasible
Clamp nondependent pulmonary artery when accessible during pneumonectomy

*CPAP*, Continuous positive airway pressure; *DLT*, double-lumen tube; *$FiO_2$*, fraction of inspired oxygen; *PEEP*, positive end expiratory pressure.

## 12. Describe the role of a thoracostomy tube after pulmonary resection.

Before chest closure, thoracostomy tubes are placed to drain air and fluid and to keep remaining lung tissue expanded. One tube is placed anteriorly at the apex for air drainage, and another is placed posteriorly for fluid drainage. The thoracostomy tubes are connected to underwater seals with negative 15–20 cm $H_2O$ pressure (suction). Inadequate suction may lead to tension pneumothorax if the rate of air removal from the pleural space is less than the rate of air leakage into the pleural space. Thoracostomy tubes are usually not placed after pneumonectomy because there is no remaining lung tissue to reexpand.

## 13. Describe a commonly used pleural drainage system.

Several different drainage systems are in use. The most commonly employed disposable system is a modification of the three-bottle system. It consists of a water seal, a low–negative pressure water limiter bottle, and a dry trap. The low–negative pressure water limiter bottle prevents application of excess negative pressure by allowing entrainment of atmospheric air. Use of only a dry trap bottle (single-bottle system) allows for reversal of air flow into the pleural space and for contamination of the suction source.

Clamping the thoracostomy tube is dangerous because it may lead to accumulation of air and fluid in the chest. Elevation of the underwater seal bottle above the patient is not recommended because it allows water to flow into the pleural space. Patency of the chest tube may be facilitated by "milking" and "stripping" (squeezing the tube toward and away from the chest, respectively).

## 14. What are the potential complications after thoracotomy?

Atelectasis is the most common cause for a decrease in oxygenation postoperatively, and respiratory failure is the most common serious complication. Patients presenting for thoracic surgery typically have a history of cigarette smoking and preoperative lung disease, which are risk factors.

Respiratory failure may be due to pulmonary edema, which can be cardiogenic or noncardiogenic in origin. Reexpansion pulmonary edema is usually unilateral and may occur after removal of large amounts of fluid or air from the pleural space in the case of a chronically

collapsed lung. Reexpansion pulmonary edema rarely occurs after short periods of lung isolation for thoracic surgery, unless lung collapse was present preoperatively. The etiology may be related to increased capillary permeability occurring with rapid reexpansion, similar to reperfusion injury.

There is a high incidence of arrhythmias after thoracic surgery. Sinus tachycardia, atrial fibrillation, and supraventricular tachycardia are the most common arrhythmias. Possible etiologies include manipulation of the heart, right atrial distention from pulmonary hypertension, and hypoxemia, especially in the setting of preexisting cardiac disease.

Right heart failure may occur after pneumonectomy. Heart failure can be due to an increase in right ventricular afterload or decrease in right ventricular contractility, or both. If the pulmonary vasculature is normal and distensible, the remaining lung can accommodate all of the pulmonary blood flow with only a small increase in pulmonary artery pressure. If there is a large increase in pressure, the right ventricle is prone to failure because of its relatively thin wall. Traditional treatment includes pulmonary vasodilation and inotropic support, using catecholamines and phosphodiesterase inhibitors. Nitric oxide may be beneficial in treating pulmonary hypertension after pneumonectomy because it does not have systemic effects.

Cardiac herniation is a rare complication that may occur after intrapericardial pneumonectomy, which involves opening the pericardium. This operation may be needed in cases of bronchogenic cancers or tumors invading the hilum. The heart can herniate through a pericardial defect into the empty thoracic cavity. Torsion may impede blood flow and lead to cardiovascular collapse. Following right-sided intrapericardial pneumonectomy, cardiac torsion may obstruct the superior vena cava resulting in superior vena cava syndrome. Following left-sided intrapericardial pneumonectomy, the apex of the heart may herniate through the defect, and the portion of the ventricle that herniates may become edematous. Obstruction to blood flow and ischemia may occur, which can lead to myocardial infarction and cardiac arrest.

Following intrapericardial pneumonectomy, the patient should not be positioned with the operative side dependent. Gravity may draw the heart downward through the pericardial defect into the empty hemithorax. If cardiac herniation occurs, the patient should be positioned in the lateral position with the operative side nondependent, which may improve cardiac function. Surgical treatment is almost always necessary.

Significant postoperative bleeding may occur and is usually diagnosed by measuring blood collected in drainage tubes. Blood loss continuing at a rate >100 mL per hour may warrant surgical reexploration. If bleeding is significant, drained blood may have a hematocrit >20%. Significant blood loss in the absence of blood drained into chest tubes can occur if the tubes are blocked by clot. In that case, tension hemothorax or pneumothorax is likely to occur.

Lobar torsion, which is seen on chest radiograph as a lobe that is collapsed or consolidated and in an abnormal position, requires immediate surgical correction. After rotation of the lobe or lung into the normal position, serosanguineous fluid may drain into the nonaffected lung, which needs to be suctioned. A late diagnosis may require further lung resection and may lead to death.

An air leak can be detected by air bubbles in the water-seal chamber of the thoracostomy tube drainage system. The defect causing an air leak usually heals postoperatively, eliminating the air leak. Return to spontaneous ventilation and negative pressure respiration facilitates reducing the air leak and healing of the defect. Failure of the defect to heal can lead to a bronchopleural fistula (BPF), which is a serious complication that can develop in the first 2 weeks after surgery. Less commonly, the development of a BPF may be delayed. A thoracostomy tube is necessary to provide adequate drainage and may facilitate closure of the BPF. Most patients with BPF need surgery during which a DLT and lung isolation are required.

Neural injuries may occur secondary to positioning or surgical trauma. Compression injuries to the brachial plexus or ulnar nerve may occur secondary to positioning. Surgery can lead to trauma to the intercostal, long thoracic, or thoracodorsal nerves. Most nerve injuries resulting from positioning typically resolve, but complete resolution may take 3–6 months (Box 12-5).

**BOX 12-5 Postthoracotomy Complications**

- Respiratory failure
  - Atelectasis
  - Pulmonary edema
    - Cardiogenic
    - Noncardiogenic (reexpansion)
- Dysrhythmias
  - Sinus tachycardia
  - Atrial fibrillation
  - Supraventricular tachycardia
- Right heart failure
- Cardiac herniation
- Bleeding
- Lobar torsion
- Bronchopleural fistula
- Nerve injuries
  - Brachial plexus
  - Ulnar nerve
  - Intercostal nerve
  - Long thoracic nerve
  - Thoracodorsal nerve

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CASE 13

# Thoracoscopy

**Steven M. Neustein, MD • James B. Eisenkraft, MD**

QUESTIONS



A 60-year-old man with a long history of cigarette smoking presents for video-assisted thoracoscopy (VAT) and wedge resection of a mass in the upper lobe of the right lung.

## 1. What procedures are performed under video-assisted thoracoscopy?

Minimally invasive thoracic surgery can be performed with VAT. Typically, three to five small incisions (portals) are created to allow entry of instruments into the thoracic cavity. A camera is connected to a monitor on which the visual field is displayed.

VAT can be used for biopsy of intrathoracic structures, such as lung, pleura, and mediastinal masses. If the biopsy is positive for cancer, open thoracotomy for a more extensive resection, such as lobectomy or pneumonectomy, may be the next step. Other lung surgical procedures that can be performed with VAT include resection of bullae, treatment of pneumothorax or empyema, and diagnosis and treatment of thoracic trauma.

Esophageal surgery can be performed with VAT, including esophagomyotomy for achalasia, which can also be performed via the abdomen with laparoscopy and thoracoscopy. Traditionally, the Ivor Lewis esophagectomy was performed through the use of laparotomy and right thoracotomy incisions.

Pericardial surgery can be performed with VAT, including pericardiectomy as treatment for pericardial effusion. Excision of a pericardial cyst and "takedown" of the internal mammary artery for coronary artery bypass grafting can also be performed with VAT.

## 2. What are the advantages of video-assisted thoracoscopy over traditional thoracotomy?

VAT requires only small incisions compared with a much larger thoracotomy incision. Surgery via thoracotomy requires cutting across chest wall muscles. Ribs are usually spread to allow intrathoracic access, and sometimes rib resection is required. There is a high incidence of tachyarrhythmias after thoracotomy, which may be related to postoperative pain. Epidural analgesia and intercostal nerve blocks are very effective for postoperative pain management and may lead to a lower incidence of arrhythmias. VAT is followed by less pain and respiratory impairment than open thoracotomy, allowing for earlier discharge to home.

## 3. What anesthetic techniques can be used for video-assisted thoracoscopy?

VAT is usually performed under general anesthesia. It is essential to provide excellent lung deflation and maintain oxygenation using one-lung ventilation (OLV). With a thoracotomy incision, surgeons can manually retract the lung if necessary, providing greater access and exposure. Under VAT, however, inadequate lung deflation hampers exposure and surgical access. Less than full lung collapse may necessitate thoracotomy, which is associated with greater morbidity and mortality.

OLV can be achieved with a double-lumen tube (DLT), which allows for lung deflation by egress of gas through the tracheal tube lumen. As soon as the patient is turned to the lateral decubitus position, and the position of the tube is rechecked, the lung to be operated on is deflated, and OLV is instituted.

An alternative to a DLT is a bronchial blocker. The most commonly used blockers are the Arndt (Cook, Bloomington, IN), Cohen (Cook), and Uniblocker (Fuji Systems, Tokyo, Japan). The first bronchial blocker available commercially was the Univent tube. This is a single-lumen silicone tube that has a small separate lumen along the anterior concave wall. The separate lumen contains a small hollow bronchial blocker that can be advanced 10 cm beyond the tip of the Univent tube. Once the blocker has been advanced into the bronchus to be blocked, a brief apneic period allows for partial lung collapse before

inflating the blocker's balloon. If the lung is not allowed to deflate before inflating the blocker balloon, lung deflation is delayed. The blocker's very narrow tube creates substantial resistance to gas flow, increasing the time for lung collapse. Once the lung is deflated, the blocker balloon is inflated, and ventilation (now of only the unblocked lung) is resumed. If necessary, the blocked lung can be collapsed by aspirating residual gas through the lumen of the blocker shaft.

Historically, the Arndt blocker was developed next. It has a lumen through which a wire loop extends beyond the distal tip. A fiberscope is passed through the loop and guides the blocker into the bronchus to be blocked. Once the blocker is positioned, the wire must be removed. Removal of the wire facilitates deflation of the lung via the blocker lumen and prevents unintentional stapling of the wire by surgeons.

The Cohen blocker is a bronchial blocker with a wheel at the proximal end that, when turned, bends the tip of the blocker. This blocker also has a lumen to allow lung deflation. The blocker of the Univent tube was made available more recently as an independent blocker, known as the Uniblocker. It contains a permanent bend near the tip and can be angled into either bronchus. A fiberscope should be available throughout cases using blockers because there is a greater tendency for blockers to become dislocated compared with DLTs.

VAT may be performed to evaluate or treat pleural disease, such as pneumothorax or pleural effusion. Pleural biopsy and pleurodesis may be planned. In these cases, epidural anesthesia or intercostal blocks are alternatives to general anesthesia. Surgery performed under regional block with spontaneous respiration allows for a pneumothorax when the chest (pleural cavity) is opened.

### 4. How can hypoxemia from shunting during one-lung ventilation be treated?

During open thoracotomy, the most effective treatment for hypoxemia during OLV is administration of continuous positive airway pressure (CPAP) with oxygen to the nondependent (collapsed) lung. CPAP leads to some distention of the lung, which is not usually a problem during open thoracotomy if the amount of CPAP is small (e.g., 5 cm $H_2O$). During VAT, however, even a small amount of CPAP can make it difficult for the surgeon to operate.

An alternative to CPAP for the nondependent lung is positive end expiratory pressure (PEEP) to the dependent ventilated lung. PEEP helps to prevent atelectasis that may exacerbate shunting, especially with smaller volumes for lung ventilation. Smaller tidal volumes (5–8 mL/kg) are typically used for OLV to decrease the likelihood of acute lung injury.

During OLV, 100% oxygen is administered. In some cases, the patient may have received chemotherapeutic agents, such as bleomycin, that predispose to pulmonary oxygen toxicity. In these cases, 100% oxygen is administered at the onset of OLV, and then the fraction of inspired oxygen ($FiO_2$) is decreased, as tolerated, according to pulse oximetry ($SpO_2$) monitoring.

It may be necessary to accept a lower $SpO_2$ value during VAT because of limited ability to treat the hypoxemia. A balance must be struck between the surgeon's need for a deflated lung and the oxygenation needs of the patient.

**BOX 13-1 Complications of Video-Assisted Thoracoscopy**

- Arrhythmias
  - Sinus tachycardia
  - Atrial fibrillation
  - Supraventricular tachycardia
- Respiratory failure
- Bleeding
- Infection
- Air leak
- Chronic pain

### 5. What complications can occur with video-assisted thoracoscopy?

There is a high incidence of arrhythmias after thoracic surgery via open thoracotomy. Arrhythmias may also occur after VAT and may include sinus tachycardia, atrial fibrillation, and supraventricular tachycardia (SVT). The incidence of arrhythmias has been reported to range from 10%–25%. Elderly patients and patients who are receiving digoxin preoperatively may be at greater risk. Risk factors for postoperative SVT are significant surgical bleeding and increased tricuspid valve regurgitation as seen on echocardiography. The use of epidural analgesia for treatment of postoperative pain may be associated with a decrease in the incidence of arrhythmias.

Patients may also experience respiratory failure after VAT, although this is usually more common after thoracotomy with a more extensive resection. Patients with significant preexisting pulmonary dysfunction, which can be identified with preoperative pulmonary function testing, are particularly at risk. There is usually less pain and respiratory impairment after VAT compared with thoracotomy.

Other potential complications include bleeding, infection, and air leak. There may be chronic pain after VAT, although it is not as common as after thoracotomy. Postoperative pain may be myofascial or neuropathic in origin and may lead to central sensitization and chronic pain (Box 13-1).

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SECTION 3

# CENTRAL NERVOUS SYSTEM

CASE 14

# Intracranial Mass, Intracranial Pressure, Venous Air Embolism, and Autoregulation

**Irene P. Osborn, MD**

## QUESTIONS

1. What is cerebral autoregulation?
2. What factors contribute to increased intracranial pressure?
3. How do anesthetic agents and vasoactive drugs affect cerebral blood flow and intracranial pressure?
4. What are the signs and symptoms of increased intracranial pressure?
5. How is intracranial pressure monitored?
6. How is increased intracranial pressure treated?
7. How is venous air embolism detected and treated?
8. What are contraindications to the sitting position?
9. How would you induce and maintain anesthesia in this patient?
10. What is an awake craniotomy, and why is it performed?

A 63-year-old woman with a brain tumor presents for bifrontal craniotomy in the supine position. She is neurologically intact but recently experienced headaches, nausea, and blurred vision. Magnetic resonance imaging (MRI) revealed a large meningioma near the sagittal sinus. After induction of anesthesia and the start of surgery, the surgeon begins drilling a burr hole in the skull. End-tidal carbon dioxide ($ETCO_2$) starts to decrease within 5 minutes, and the patient becomes hypotensive.

### 1. What is cerebral autoregulation?

Cerebral autoregulation is the control process by which cerebral blood flow (CBF) is maintained constant over a wide range of cerebral perfusion pressure (CPP) (Figure 14-1). CPP represents the difference between mean arterial pressure (MAP) and intracranial pressure (ICP). Autoregulation adjusts cerebral vessel caliber as CPP changes. Normal CBF is 45–65 mL/100 g of brain tissue per minute. It is coupled to alterations in cerebral metabolic rate, which is linked to oxygen consumption ($CMRO_2$). CBF parallels the changes in $CMRO_2$. Several parameters affect CBF (Box 14-1).

Autoregulation maintains CBF at a CPP of approximately 50–150 mm Hg. At CPP <50 mm Hg, cerebral blood vessels achieve maximal dilation (i.e., resistance to flow is low), and CBF decreases in direct proportion to CPP. Chronically hypertensive patients undergo an upward shift of autoregulation to higher perfusion pressures. Consequently, these patients require higher CPP to maintain normal CBF. At the upper level of autoregulation, cerebral blood vessels are maximally constricted (i.e., resistance to flow is high), and CBF increases linearly with increasing CPP. Integrity of the blood-brain barrier (BBB) is lost at these high pressures, and transudation of fluid occurs resulting in cerebral edema. Autoregulatory compensation generally occurs over 1–3 minutes.

The second parameter affecting CBF is arterial carbon dioxide tension ($PaCO_2$). Increasing levels of $PaCO_2$ produce elevated levels of extracellular hydrogen ions, which induce cerebral vessel smooth muscle relaxation and vasodilation. Consequently, cerebral vascular resistance decreases, increasing CBF by twofold. This effect plateaus at a $PaCO_2$ of approximately 80 mm Hg. Conversely, decreasing $PaCO_2$ increases cerebral vasoconstriction, and CBF decreases. At a $PaCO_2$ of 20 mm Hg, cerebral vasoconstriction is maximal, and CBF decreases by 50%. Further decreases in $PaCO_2$ have no greater vacoconstricting influence. These physiologic changes remain in effect for several hours, after which cerebrospinal fluid (CSF) bicarbonate levels decrease to compensate for induced CSF alkalosis. When CSF pH returns toward normal, respiratory alkalosis no longer provokes cerebral vasoconstriction. The $PaCO_2$ response at the limits of autoregulation can be blunted. If CPP is low and cerebral vessels are maximally dilated, lowering $PaCO_2$ would have little beneficial effect on cerebrovascular resistance.

The third parameter affecting CBF is arterial oxygen tension ($PaO_2$). At a $PaO_2$ <50 mm Hg, CBF increases

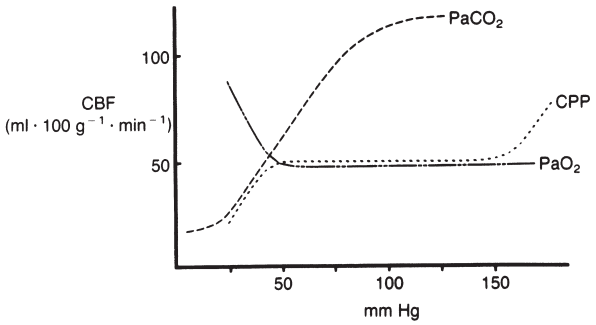


**FIGURE 14-1** ■ Effects of $PaCO_2$, $PaO_2$, and CPP on CBF. (From Bode ET: Neurointensive care. In Cuchiara RF, Michenfelder JD [eds.]: Clinical Neuroanesthesia. Churchill Livingstone, New York, 1990, p 438. Copyright Mayo Foundation.)

**BOX 14-1 Major Determinants of Cerebral Blood Flow**

Cerebral autoregulation
CPP
Cerebral metabolic rate
$PaCO_2$
$PaO_2$

*CPP*, Cerebral perfusion pressure; *$PaCO_2$*, arterial carbon dioxide tension; *$PaO_2$*, arterial oxygen tension.

linearly with decreasing $PaO_2$. Local accumulation of acidic metabolites (e.g., lactate) results in cerebral vasodilation. In contradistinction, hyperoxia has no effect on cerebrovascular tone.

## 2. What factors contribute to increased intracranial pressure?

The cranial vault contains brain tissue, blood, and CSF. It has a fixed volume with one exit, the foramen magnum. A small increase in the contents of the cranial vault alters intracranial pressure (ICP) minimally because compensation occurs by decreasing CSF and blood volumes. However, when compensatory mechanisms have been exhausted, intracranial compliance decreases dramatically, and ICP increases above its normal range of 5–13 mm Hg. At this point, any increase in the volume of the three intracranial components has a profound effect on increasing ICP.

Brain tissue volume increases by two mechanisms. Tumors enlarge the parenchymal tissue volume, and surrounding edema increases brain water content. Both contribute to expanding total intracranial mass, which can be compounded by hemorrhage into or around the neoplasm. Surrounding edema may be decreased by administration of steroids, usually dexamethasone, which reduces the activity of sodium-potassium pumps at the choroid plexus epithelial membrane. Improvement of symptoms may occur in hours to days.

CSF is contained in the subarachnoid space of the central nervous system and in the ventricles within the brain. In adults, total CSF volume approximates 150 mL, and daily production is about 600 mL. Enough CSF is synthesized to replace itself three to four times a day. CSF is formed in the choroid plexus and the ventricles within the brain. Production is reduced by decreased CPP and increased ICP, but the latter effect is minimal. Absorption of CSF occurs at the microscopic villi of the subarachnoid membrane. The rate of absorption is a balance between two interrelated factors: CSF pressure and resistance to absorption. Resistance to absorption decreases dramatically as CSF pressure increases to >30 mm Hg; this appears to represent a closed loop venting mechanism to prevent excessive increases in ICP. The amount of CSF present is determined by the balance between production and reabsorption.

Changes in cerebral blood volume usually have little effect on ICP. However, when intracranial compliance is low and intracranial volume has increased to critical levels, these changes may have dramatic consequences.

## 3. How do anesthetic agents and vasoactive drugs affect cerebral blood flow and intracranial pressure?

The effects of anesthetic agents and vasoactive drugs are multifactorial (Table 14-1). They are described assuming normal brain anatomy and physiology, which is not commonly the situation for neurosurgical patients. Potent inhaled anesthetics are generally cerebral vasodilators, which attenuate cerebral autoregulation. Inhalation anesthetics produce increases in CBF in a dose-dependent manner, while producing progressive depression of cerebral metabolism. The mechanism by which inhalation anesthetics produce vasodilation is not clearly understood. Mechanisms that partially explain the vasodilation include effects on nitric oxide and adenosine triphosphate–dependent potassium channels.

Isoflurane increases CBF in a dose-dependent fashion but increases in subcortical CBF are greater than neocortical CBF increases. Carbon dioxide ($CO_2$) reactivity is maintained but is greater in the awake state. Autoregulation is adequately maintained at 1 minimum alveolar concentration (MAC) but is progressively impaired by higher concentrations. Sevoflurane has very similar CBF effects, although it appears to produce slightly less vasodilation, and autoregulation in humans is maintained up to 1.5 MAC. Desflurane produces an increase in CBF similar to that seen with isoflurane but greater than that seen with sevoflurane at >1 MAC. Autoregulation is progressively abolished as the dose increases. Nitrous oxide ($N_2O$) produces cerebral stimulation, increasing CBF, $CMRO_2$, and sometimes ICP. $N_2O$ is used infrequently for intracranial anesthetics because of these reasons. Although it is a cerebral vasodilator, this effect is diminished by hyperventilation, hypnotic agents, and low concentrations of potent inhalation agents. When administered on its own, $N_2O$ increases both CBF and metabolism. However, when added to the background of another anesthetic, it increases CBF without changing metabolism.

Most intravenous anesthetics are cerebral vasoconstrictors and maintain the relationship between $CMRO_2$

TABLE 14-1 **Central Nervous System Effects of Anesthetic Agents and Adjuvants**

| Agent | Effect | Agent | Effect |
|---|---|---|---|
| Potent inhalation agents | Lowers $CMRO_2$<br>Increases cerebral blood flow by vasodilation; this effect is prevented by prior hyperventilation | Curare | Decreases MAP<br>Cerebral vasodilator |
| Desflurane | Similar to isoflurane, rapid uptake | Pancuronium | Increases heart rate<br>Increases MAP |
| Enflurane | Increases CSF production<br>Decreases CSF reabsorption | Vecuronium* | No significant effects |
| Halothane | Decreases CSF production<br>Decreases CSF reabsorption | Atracurium | Large bolus doses may release histamine, predisposing to decreased MAP and cerebral vasodilation |
| Isoflurane* | No effect on CSF production<br>Increases CSF reabsorption<br>May protect from ischemia | Alfentanil | Decreases MAP<br>Decreases CPP |
| Sevoflurane | Autoregulation maintained at 1.5 MAC | Fentanyl* | With normal or low $PaCO_2$ plus $N_2O$, decreases $CMRO_2$, decreases CBF<br>With increased $PaCO_2$, cerebral vasodilator |
| Nitrous oxide | No change in $CMRO_2$, CSF production, or CSF reabsorption<br>Cerebral vasodilating effects inhibited by hyperventilation<br>Expands intradural air<br>Expands venous air emboli | Remifentanil | Decrease in MAP<br>No change in ICP<br>Very short-acting<br>Increases CSF reabsorption |
| Barbiturates* | Decreases $CMRO_2$<br>Decreases CBF<br>Cerebral vasoconstrictor<br>Decreases CSF production<br>Increases CSF reabsorption | Sufentanil | Decreases CVR<br>Increases CBF |
| Ketamine | Increases ICP<br>Increases CBF<br>Increases MAP<br>No change in $CMRO_2$<br>No change in CSF production<br>Decreases CSF reabsorption | Lidocaine | Low dose: Decreases CBF, and decreases $CMRO_2$<br>High dose: Increases CBF, and increases $CMRO_2$ |
| Etomidate* | Similar to barbiturates<br>Myoclonus indistinguishable from seizures | Sodium nitroprusside | No effect on CBF despite cerebral vasodilatation<br>Decreases MAP<br>Increases CBV |
| Benzodiazepines* | Decreases CBF<br>Decreases $CMRO_2$ | Nitroglycerin | Increases CBF<br>Increases CBV<br>Decreases MAP |
| Propofol | Decreases MAP | Hydralazine | Increases CBF<br>Increases CBV<br>Decreases MAP<br>Onset 10–20 minutes |
| Succinylcholine | Increases $CMRO_2$<br>Increases CBF<br>Increases muscle spindle activity; diminished by pretreatment with nondepolarizing neuromuscular blocker | Labetalol* | Decreases MAP<br>No effect on CBV |

*CBF,* Cerebral blood flow; *CBV,* cerebral blood volume; *$CMRO_2$,* cerebral metabolic rate of oxygen consumption; *CPP,* cerebral perfusion pressure; *CSF,* cerebrospinal fluid; *CVR,* cerebrovascular resistance; *ICP,* intracranial pressure; *MAC,* minimum alveolar concentration; *MAP,* mean arterial pressure.

*Recommended for patients with increased ICP.

and CBF. Barbiturates, notably thiopental, reduce $CMRO_2$ primarily and CBF secondarily. Thiopental acts as a cerebral vasoconstrictor. $CO_2$ reactivity is maintained but is quantitatively reduced compared with the awake state. Cerebral autoregulation is also maintained intact. Thiopental is an excellent drug to reduce ICP acutely; however, amounts sufficient to induce an isoelectric electroencephalogram can produce significant hemodynamic side effects.

Ketamine can cause a significant increase in CBF without an important effect on metabolic rate. It is not considered a wise choice in most neurosurgical settings. However, small to moderate doses in a background of volatile anesthetic or intravenous infusion have not been shown to be significantly harmful. Trauma patients with hypovolemia and concurrent injuries may be suitable candidates for ketamine because blood pressure and CPP may be more easily maintained. Etomidate behaves similarly to thiopental and is an appropriate induction agent for patients who cannot tolerate the hemodynamic effects seen with thiopental. Myoclonus, which occurs after etomidate administration, may be difficult to differentiate from seizure activity. Benzodiazepines offer beneficial effects on elevated ICP by reducing CBF and $CMRO_2$, without meaningful effects on CSF dynamics.

Propofol, a short-acting intravenous agent used for induction and maintenance of anesthesia, appears to maintain the relationship between CBF and $CMRO_2$. Propofol does not cause cerebral vasodilation and does not interfere with the normal response to $PaCO_2$. It is often used to supplement volatile agents during craniotomies or as part of total intravenous anesthesia (TIVA) techniques. It is particularly useful for procedures in which neurophysiologic monitoring is used, but it must be kept in mind that it produces dose-dependent decreases in blood pressure. Propofol has become the mainstay for TIVA and has essentially replaced sodium thiopental as an induction agent for most neurosurgical cases.

Muscle relaxants have no direct intracerebral effects because they do not cross the BBB. Nevertheless, they possess indirect effects because of their actions in the periphery, which are sometimes significant. There is clear evidence from both experimental animals and humans that succinylcholine can increase ICP under conditions of intracranial hypertension. The magnitude of the increase is typically small and transient. It has been shown in humans that ICP changes caused by succinylcholine can be blocked by preadministration of a defasciculating dose of a nondepolarizing relaxant. A probable mechanism is the massive fasciculation-induced afferent barrage from muscle spindles to the brain that causes transient increases in metabolic rate and coupled increases in CBF. The decision to use this agent is determined by the need to secure the airway rapidly. Pretreatment with a small dose of a nondepolarizing agent is helpful and recommended.

Nondepolarizing agents, such as vecuronium, rocuronium, and cisatracurium, have no significant hemodynamic or ICP effects. There is clear evidence that the duration of action of nondepolarizing muscle relaxants is reduced by various anticonvulsant medications. However, the mechanism is unclear. Most patients requiring craniotomy are treated with anticonvulsants, and the nondepolarizing muscle relaxant dosing regimen requires alteration. Atracurium and cisatracurium seem to be largely resistant to these effects, most likely because metabolism is achieved by Hoffman elimination.

Opioids are known to produce respiratory depression, which results in an increase in $PaCO_2$. Consequently, opioids are administered sparingly in a spontaneously breathing patient with cerebral disease. Opioids at low doses produce very little effect on CBF, provided that $PaCO_2$ is not allowed to increase. During controlled ventilation with normocapnia or hypocapnia, opioids provide significant advantages. Independently, fentanyl seems to have little effect on CBF or $CMRO_2$, but when combined with $N_2O$, it decreases $CMRO_2$ and CBF, which is due to the hemodynamic changes caused by this combination of anesthetic agents. It increases the rate of CSF reabsorption without affecting its rate of production. There has been controversy about how and whether opioids, such as sufentanil and alfentanil, increase ICP. With cerebral autoregulation intact, a decrease in blood pressure results in compensatory vasodilation to maintain CBF. This vasodilation increases cerebral blood volume and ICP. Interest in remifentanil for neurosurgery has increased because of its rapid onset and offset and titratability to changing stimuli. It is frequently used as a component of TIVA. However, the lack of residual analgesia requires a plan for postoperative pain relief and blood pressure control.

Sodium nitroprusside is a direct-acting smooth muscle relaxant that produces arteriolar and venous dilation. It is sometimes used in neurosurgery for control of arterial blood pressure. Although it acts as a cerebral vasodilator and decreases MAP, it has little effect on CBF. However, cerebral blood volume is increased, and ICP may be elevated. If ICP is increased, use of sodium nitroprusside is best avoided. Thiopental, lidocaine, or labetalol should be used instead. Nitroglycerin is primarily a venodilator and coronary vasodilator that acts by relaxing smooth muscle and works on the intracerebral venous capacitance vessels. Labetalol, a mixed $\alpha/\beta$ blocker, decreases MAP by reducing systemic vascular resistance and depressing cardiac output. It has no direct effect on cerebral blood vessels. Nicardipine, a calcium channel blocker, is a newer option for blood pressure control in the perioperative period and has no deleterious effects on ICP or CBF.

### 4. What are the signs and symptoms of increased intracranial pressure?

Gradual, chronic increases in ICP cause few signs and symptoms. Symptoms of acute intracranial hypertension are likely caused by decreased CPP resulting in cerebral ischemia or mechanical forces on the brainstem, which thrust intracranial contents through

the foramen magnum. These may include headache, nausea, vomiting, and mental status changes. Cushing triad, consisting of Cheyne-Stokes respirations, increased systolic blood pressure (with resultant increase in pulse pressure), and bradycardia, can be seen when intracranial hypertension is associated with a mass effect. Acute increases in ICP can cause loss of consciousness, hypertension, bradycardia, absent brainstem reflexes, cranial nerve dysfunction, decerebrate posturing, apnea, irregular respiration, fixed and dilated pupils, and death as a result of impaired medullary perfusion (Box 14-2).

## 5. How is intracranial pressure monitored?

Ventriculostomy is the most common method of measuring ICP. A catheter is placed through a burr hole and into the anterior horn of a lateral ventricle. Obliteration of the ventricle because of tumor or edema may create technical difficulties inserting the catheter. Subdural bolts also serve to measure ICP. These devices are placed via a twist drill hole in the calvaria and a small hole in the dura. They are less invasive than ventriculostomy but provide only local pressure data instead of global information. Subdural bolts can become infected and lack the potential to withdraw CSF for lowering ICP. Proper positioning requires the bolt head to be aligned in the same plane as underlying brain. Catheters or electronic transducers placed in the epidural space can also be used for ICP monitoring. Lumbar subarachnoid catheters are used occasionally. The patient should be placed in the horizontal position; otherwise, the accuracy of these devices is impaired. Abrupt withdrawal of CSF through lumbar subarachnoid catheters risks brain herniation.

## 6. How is increased intracranial pressure treated?

Treatment of increased ICP may begin by changing the patient's position. More recent studies have shown that a change to the reverse Trendelenburg position in anesthetized patients rapidly reduces ICP. Elevation of the patient's head promotes drainage of venous blood from the brain and is effective at reducing brain bulk. Obstruction of venous outflow (e.g., by improperly placed tape around the neck, improper positioning of the patient) is often an overlooked cause of increased brain volume. Acutely lowering ICP via hyperventilation ($PaCO_2$ reduction) is frequently employed for intubated patients. Hyperventilation is simple to perform and results in rapid and dramatic decreases in ICP. Alteration of $PaCO_2$ within the range of approximately 20–80 mm Hg causes parallel changes in CBF. CBF-reducing and ICP-reducing effects of hyperventilation are acute and most effective during the first 12–24 hours of hyperventilation. A typical value to aim for is $PaCO_2$ of 30–35 mm Hg because there is little benefit to be gained from lower $PaCO_2$ values. The main complication of hyperventilation is reduction of CBF, which gives rise to cerebral ischemia. Until more recently, hyperventilation was implemented in all patients suspected to have increased ICP, but neuronal ischemia caused by hyperventilation has now been demonstrated in humans.

The two other intracranial compartments, CSF and brain parenchyma, are also amenable to volume reduction. CSF withdrawal can occur through a ventriculostomy, and production of CSF can be reduced by acetazolamide, a carbonic anhydrase inhibitor. Brain edema may respond to osmotic or loop diuretics, such as mannitol or furosemide, respectively. The resulting diuresis reduces intravascular volume and cerebral blood volume. The onset of action of mannitol is approximately 30 minutes, and its effect is accelerated by furosemide. Use of osmotic agents requires a globally intact BBB with only minimal areas of disruption.

Struggling or coughing against a tracheal tube should be prevented, and this is best accomplished via administration of sedative agents such as benzodiazepines, barbiturates, propofol, opioids, and muscle relaxants. Systemic hypertension, tachycardia, and straining increase $CMRO_2$ and CBF (Box 14-3).

**BOX 14-2 Signs and Symptoms of Increased Intracranial Pressure**

- Headache
- Nausea/vomiting
- Mental status changes (drowsiness progressing to coma)
- Cushing triad
  - Increased systolic blood pressure
  - Bradycardia
  - Cheyne-Stokes respiratory pattern
- Absent brainstem reflexes
- Cranial nerve dysfunction
- Decerebrate posturing
- Respiratory rhythm changes
- Fixed and dilated pupils

**BOX 14-3 Treatment of Increased Intracranial Pressure**

- Reduce cerebral blood volume
  - Raise head
  - Hyperventilate to $ETCO_2$ = 27–30 mm Hg
  - Prevent straining and coughing on endotracheal tube with sedatives (propofol, thiopental), opioids, or muscle relaxants
- Reduce CSF volume
  - Drain through ventriculostomy or lumbar subarachnoid catheter
- Reduce brain water
  - Osmotic diuretics (mannitol)
  - Loop diuretics (furosemide)
  - Steroids (dexamethasone)

*CSF*, Cerebrospinal fluid; *$ETCO_2$*, end-tidal carbon dioxide; *$PaCO_2$*, arterial carbon dioxide tension.

## 7. How is venous air embolism detected and treated?

Venous air embolism (VAE) is a potentially life-threatening event that must be detected and treated promptly. It is often associated with cases performed in the sitting position, but it can occur under certain physiologic circumstances. In neurosurgical procedures, air may enter the venous system via noncollapsible venous channels, such as dural sinuses and diploic veins. When the head is elevated above the heart, a pressure gradient can exist, which facilitates air entrainment. In the sitting position, the incidence of VAE is almost four times higher than the incidence in other positions (45% versus 12%). Air can also be entrained from pin sites during a stereotactic biopsy in the semisitting position.

Monitoring for VAE (Box 14-4) generally includes a precordial Doppler, capnometer, pulse oximeter, and esophageal stethoscope. When placed properly, precordial Dopplers can detect 0.1 mL of air. Transesophageal echocardiography is also sensitive for detecting and recognizing intracardiac air but is not generally used in this setting because of technical difficulty and cost. Air collects at the superior vena cava and the right atrium junction.

Pulmonary artery catheters may provide valuable information because pulmonary artery pressures increase during VAE. Pulmonary artery catheters and central venous pressure catheters are inefficient means of VAE aspiration. Continuous $ETCO_2$ monitoring demonstrates rapid decline as VAE ensues. Arterial $PaCO_2$ increases as $ETCO_2$ decreases, increasing the gradient between these two measurements. The difference increases as alveolar dead space increases. If minute ventilation remains constant, the divergence between $PaCO_2$ and $ETCO_2$ may represent a useful marker for the severity of VAE. Sensitive mass spectrometry can show increases in expired nitrogen as the VAE is eliminated through the lung. However, the sensitivity of current nitrogen monitoring technology may be insufficient to detect subclinical VAE. Classically, the "mill wheel" murmur heard through an esophageal stethoscope is associated with intracardiac air.

When detected, VAE requires rapid treatment (Box 14-5). The surgeon must be alerted immediately when VAE is suspected so that open sinuses may be identified and flooded with saline or closed surgically to halt air entrainment. In the absence of an obvious source of air entrainment, venous pressure in the head should be increased in an attempt to force blood through the concealed opening; this is accomplished by lowering the head relative to the heart or occluding venous outflow from the head with jugular compression. If $N_2O$ is being used, administration should cease immediately. Rapid diffusion of $N_2O$ into air bubbles expands their volume, creating mechanical obstruction to flow, and hemodynamic compromise. Volume, inotropes, and vasopressor administration contribute to hemodynamic support, churning large air pockets into smaller ones to be carried out to the pulmonary peripheral blood vessels.

The application of positive end expiratory pressure (PEEP) in an attempt to increase central venous pressure and decrease the magnitude of VAE is controversial. High levels of PEEP greatly increase the risk of hypotension in patients who are already intravascularly depleted. Right atrial pressure may be increased in the face of lowered left atrial pressure, predisposing the patient to paradoxical air embolism through a patent foramen ovale. Application of PEEP probably should be limited to situations in which all other attempts at preventing continuous VAE have failed.

Even moderate amounts of VAE may result in decreased $PaO_2$. Initial treatment should be supportive with enhanced inspired oxygen concentrations guided by pulse oximetry and arterial blood gas determinations. Postoperatively, patients may develop an interstitial pulmonary process that usually resolves in 24–48 hours.

**BOX 14-4 Monitors for Detection of Venous Air Embolism**

Precordial Doppler
Transesophageal echocardiography
Mass spectrometry (end-tidal nitrogen)
Capnography ($ETCO_2$)
Pulse oximetry
Pulmonary artery pressure
Esophageal stethoscope

*$ETCO_2$*, End-tidal carbon dioxide.

**BOX 14-5 Acute Treatment of Venous Air Embolism**

Notify surgeons to identify open sinuses
  Close sinuses surgically or flood field with saline and apply bone wax
Increase venous pressure in head
  Lower head relative to heart
  Place table in Trendelenburg position
  Jugular vein compression
  Positive end expiratory pressure*
Discontinue $N_2O$ administration
Support cardiovascular system
  Volume
  Inotropes
  Vasopressors

*$N_2O$*, Nitrous oxide.
*Controversial.

## 8. What are contraindications to the sitting position?

There are no absolute contraindications to the sitting position; however, each patient requires careful evaluation to determine the feasibility of the sitting position and risks for complications. Specific contraindications involve the presence of a patent foramen ovale or suspected intracardiac shunt. Other conditions that may predispose to development of complications are hemodynamic instability or noted cerebral compromise

when sitting upright preoperatively. Other concerns involve positioning of the neck, which may impair spinal cord perfusion in the patient with severe cervical arthritis. The sitting position is used infrequently today, to avoid its inherent problems. Many surgeons now employ the lateral, prone, or supine position with the head turned.

### 9. How would you induce and maintain anesthesia in this patient?

The preoperative assessment of this patient includes evaluation of mental status and determination of acute increased ICP. Coexisting diseases optimally should be treated before arrival in the operating room. MRI reveals a large mass that has slowly increased in size. This patient can be induced in the typical manner with caution to avoid additional increases in ICP. Intravenous anesthetic induction is followed by moderate hyperventilation until neuromuscular blockade is achieved. Thiopental and propofol are commonly used for induction with an opioid, such as fentanyl, to blunt hemodynamic response to laryngoscopy and intubation. Moderate hyperventilation is achieved to an $ETCO_2$ of 28–30 mm Hg. A radial artery catheter and additional intravenous lines may be placed after endotracheal intubation. The potential for blood loss may be considerable, and large-bore intravenous catheters are recommended. Mannitol is commonly administered at a dose of 0.5–1.0 g/kg.

Maintenance of anesthesia may proceed with low doses of volatile agent (i.e., <1 MAC) and continuous infusion or bolus doses of opioids and muscle relaxants. $N_2O$ may be administered at a concentration of 50%, if surgical conditions do not indicate a "tight brain." Intravenous fluid administration generally requires isotonic crystalloid solutions; colloids are also useful for maintenance of intravascular volume. Extensive blood loss is replaced with packed red blood cells. Hypotonic solutions exacerbate cerebral edema and are generally contraindicated, and glucose-containing solutions are avoided unless truly necessary to treat diagnosed hypoglycemia.

Neurosurgery is characterized by periods of intense stimulation followed by minimal pain during brain resection. Hypertension may occur and is treated promptly to prevent bleeding and potential cerebral swelling. The use of β-adrenergic blockers in addition to adequate anesthesia is recommended throughout. Blood pressure control is especially important on closure and emergence. Patients who have had an uneventful procedure are expected to emerge promptly at the end of surgery for neurologic evaluation. Extubation is managed carefully, after assurance of airway reflexes and stable hemodynamics. Postoperative respiratory insufficiency adversely affects cerebral physiology.

### 10. What is an awake craniotomy, and why is it performed?

Awake craniotomy for tumor surgery is an accepted procedure that provides an opportunity for mapping of eloquent brain functions such as speech, motor, and sensory to minimize neurologic resection. Craniotomy in the awake state has been performed since ancient times. Present-day indications include resection of a lesion in the eloquent or speech center of the brain. Surgical procedures for the treatment of epilepsy, tumors, or arteriovenous malformation are sometimes performed in an awake patient. With refinement of neurophysiologic monitoring techniques, awake craniotomies are necessary in only a small percentage of patients. However, surgery for movement disorders has increased the use of this technique.

Intraoperative complications of awake craniotomy include restlessness and agitation. These complications may occur when the patient is overly sedated yet experiences discomfort. More serious complications are hypoventilation, nausea, and seizures. A change in the level of sedation often resolves these problems. It is important to maintain good rapport with the patient, which should have been established preoperatively. Positioning of the patient to avoid discomfort, allowing surgical access and avoidance of a claustrophobic atmosphere, is essential and requires cooperation of the entire operating room staff. The evolution of anesthetic techniques has progressed from fentanyl and droperidol to the current use of propofol infusion with alfentanil or remifentanil. Intraoperative nausea is rare with the use of propofol infusions. Dexmedetomidine (Precedex), a selective $\alpha_2$-adrenergic agonist, is a newer agent used for continuous intravenous sedation. Dexmedetomidine has been shown to produce sedation and analgesia without respiratory depression. The onset is slower than propofol, and it must be administered by infusion; this may be beneficial for older patients, pediatric patients, or potentially debilitated patients and has been used throughout intraoperative testing. Seizure control is sometimes necessary and can be managed effectively with thiopental (1 mg/kg) or a benzodiazepine (midazolam). Terminating the seizure requires careful titration of sedatives to avoid apnea.

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CASE 15

# Intracranial Aneurysm

**Arthur E. Schwartz, MD**

QUESTIONS



A 55-year-old woman was admitted with severe headache and decreased consciousness. A subarachnoid hemorrhage (SAH) from a ruptured intracranial aneurysm was diagnosed.

## 1. How are patients graded after subarachnoid hemorrhage from a ruptured aneurysm?

The incidence of SAH is about 10–15 per 100,000 person-years. Angiography shows that 80%–85% of cases of SAH are due to an intracranial aneurysm. Cerebral aneurysms are most often found at bifurcations near the circle of Willis, and the risk of rupture is increased with increasing size. SAH almost always manifests with rapid onset of severe headache. The presence of other signs and symptoms is used for clinical grading of patients. The Hunt-Hess clinical grade classification is widely used (Table 15-1). The World Federation of Neurologic Surgeons Grading System has also gained acceptance.

## 2. What are the most serious complications after subarachnoid hemorrhage from aneurysm rupture?

The most serious sequela of SAH is rebleeding. The incidence of rebleeding after aneurysm rupture is approximately 15% in the first week and about 10% in the second week. Morbidity and mortality after rebleed are great and have motivated the trend toward early intervention after aneurysm rupture.

Cerebral vasospasm is also a major cause of morbidity and mortality after SAH. Symptomatic brain ischemia from vasospasm occurs in 15%–35% of patients. Angiographic evidence of vasospasm occurs in 70% of patients. Vasospasm may lead to cerebral infarction. SAH often leads to hydrocephalus and may result in dangerously elevated intracranial pressure.

## 3. What are treatment options?

Treatment of intracranial aneurysm is by either craniotomy or endovascular therapy. After angiography, endovascular treatment most often consists of packing the aneurysm with detachable coils. In many centers, endovascular embolization is the preferred treatment. There may be a preference for craniotomy in younger patients. The most common complication of endovascular treatment is ischemic injury. The second most common complication is vascular perforation. Aneurysms without a sufficiently narrow neck may require complex techniques for endovascular embolization. Some cases require balloon-assisted coiling. Sometimes a stent is initially placed in the artery whose lumen feeds the aneurysm. Thereafter, coils are introduced across the stent wall into the aneurysm cavity.

Classic treatment consists of craniotomy and clipping of the aneurysm. Most centers attempt early clipping after SAH to prevent rebleeding and permit safe induction of hypertension and hypervolemia as treatment of vasospasm.

## 4. Which monitors are indicated for patients undergoing intracranial aneurysm clipping?

In addition to routine monitoring for general anesthesia, patients with aneurysm should have intraarterial measurement of blood pressure. The intraarterial catheter is best inserted before anesthetic induction because hypertension associated with laryngoscopy increases the risk of rupture. A urinary catheter is also indicated as in all craniotomies.

Many centers use electrophysiologic monitoring for aneurysm surgery when temporary arterial occlusion is anticipated during surgical dissection of the aneurysm. In these cases, arterial branches feeding the aneurysm may be temporarily occluded with surgical clips to

TABLE 15-1 **Hunt-Hess Clinical Grade Classification**

| Grade | Clinical Manifestations |
|---|---|
| 0 | Unruptured |
| I | Minimal headache or nuchal rigidity |
| II | Moderate to severe headache<br>Nuchal rigidity with or without cranial nerve play |
| III | Drowsiness<br>Confusion or mild focal deficit |
| IV | Stupor<br>Hemiparesis<br>Early decerebrate rigidity<br>Moribund |

reduce the risk of rupture. However, temporary arterial occlusion may lead to cerebral ischemia. This ischemic risk depends on the duration of arterial occlusion, collateral cerebral circulation, and brain temperature. Electroencephalogram (EEG) electrodes may be placed directly on the cerebral cortex over regions supplied by the arteries in question. Routine scalp electrodes for EEG may also be placed. In some centers, somatosensory evoked potentials are monitored for detection of ischemia. Motor evoked potentials are highly sensitive to ischemia. Although hypothermia is believed to improve the safety of temporary arterial occlusion in these patients, a large randomized trial of mild hypothermia for aneurysm surgery showed no clear clinical benefit over normothermia.

## 5. How is arterial blood pressure controlled?

Careful control of arterial blood pressure is critical in the management of these patients. Aneurysmal rebleed and its consequent high morbidity and mortality may be triggered by arterial hypertension; this has been reported to occur commonly during tracheal intubation. Risk of aneurysm rupture is also great during surgical manipulation of tissue adjoining the aneurysm sac. For this reason, it may be advisable to decrease systemic arterial pressure during aneurysm dissection. However, this decision depends on whether temporary arterial clips are effectively placed. During temporary clipping, mild induced hypertension may be indicated to reduce cerebral ischemia. The absence of normal cerebral blood flow autoregulation after SAH makes these interventions highly critical. Induced hypotension should be limited in duration and magnitude. The effect on intracranial dynamics of agents used to decrease arterial pressure should be taken into account.

## 6. What is cerebral vasospasm, and how is it treated?

Cerebral vasospasm is arterial narrowing and decreased blood flow after SAH. The incidence of vasospasm after surgical treatment of ruptured aneurysms is approximately 30%, with the overall incidence of severe cerebral infarct approximately 10%. The occurrence of vasospasm after endovascular coiling may be higher and is presumed to be due to the continued presence of subarachnoid blood, which is normally evacuated during craniotomy. The mechanism leading to vasospasm is poorly understood but appears to result from the presence of blood degradation products in the subarachnoid space. Therapy encompasses calcium channel blockers, such as nimodipine, and "triple H therapy." Triple H therapy includes deliberate hypertension, hypervolemia, and hemodilution. However, hemodilution is rarely employed. Angioplasty and injection of endovascular papaverine or verapamil have gained popularity. Papaverine therapy is usually applied on day 8 after SAH. Its effect persists for <24 hours, and the magnitude of its effect is greater when vasospasm is severe. Angioplasty, by balloon dilation of the arterial narrowing, has a longer lasting effect than papaverine but presents a greater risk of vessel rupture. In some patients, multiple interventions of papaverine or angioplasty are performed, as guided by repeat angiography. The patient's clinical condition also guides therapy.

## 7. How is aneurysm rupture during aneurysm clipping managed?

Intraoperative aneurysm rupture may be catastrophic if not properly managed by the surgeon and anesthesiologist in a coordinated effort. Unless bleeding is controlled, the outcome is inevitably fatal. The first priority is to permit the surgeon to visualize the rupture site and clip it. If the arteries feeding the aneurysm have been previously dissected and exposed, the surgeon may need only to apply temporary clips to these vessels. Thereafter, permanent aneurysm clips can be placed, and the temporary ones can be removed.

Under challenging circumstances, the anesthesiologist is required to induce hypotension very rapidly and profoundly to permit surgical visualization of the ruptured aneurysm. Typically, a large bolus of intravenous thiopental or propofol is administered. Usually mean arterial blood pressure needs to be lowered to <50 mm Hg before adequate reduction in hemorrhage is achieved. In extreme circumstances with aneurysms of the anterior circulation, it may be helpful to occlude both carotid arteries manually by reaching under the drapes and applying direct pressure on the patient's neck. Another option is to administer intravenous adenosine to induce reversible complete circulatory arrest after aneurysm rupture. As one would expect, administration of adenosine provides a completely bloodless field until cardiac activity resumes. In these situations, one must balance the risks of cerebral ischemia against the surgical need to visualize the cerebrovascular anatomy.

The most frequent complications of endovascular treatment of intracranial aneurysms are thromboembolism and aneurysmal rupture. If aneurysm rupture occurs during endovascular treatment, balloon inflation is used to control bleeding, followed by dense packing of aneurysm coils.

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CASE 16

# Carotid Endarterectomy

**Arthur E. Schwartz, MD**

## QUESTIONS

1. What are indications for carotid endarterectomy?
2. What is the alternative to carotid endarterectomy?
3. What are the most serious perioperative complications associated with carotid endarterectomy?
4. Intraoperatively, how is the patient's neurologic status monitored?
5. What interventions may reduce the risk of neurologic injury?
6. Explain the risks of postoperative blood pressure instability.

A 68-year-old man with a history of transient ischemic attacks presented for carotid endarterectomy (CEA).

### 1. What are indications for carotid endarterectomy?

CEA reduces the risk of stroke in symptomatic patients with significant carotid artery stenosis. Symptomatic patients with >70% luminal narrowing of the carotid artery had improved outcome after surgery compared with patients receiving medical treatment alone. Symptoms include transient ischemic attack, reversible ischemic neurologic deficit, and nondisabling stroke. Asymptomatic patients with significant luminal narrowing are considered for CEA if the risk of perioperative morbidity and mortality is low.

### 2. What is the alternative to carotid endarterectomy?

Carotid artery angioplasty with placement of an arterial stent is a reasonable alternative treatment for carotid artery stenosis. This technique involves placing an endovascular catheter, usually from the femoral artery, with fluoroscopic guidance, through the great arteries and heart to the carotid artery. Balloon dilation of the stenosis is performed. A filter or other device may be temporarily positioned distal to the lesion to limit embolization of material to the brain. After angioplasty, a stent is positioned at the site to maintain arterial patency. The safety and efficacy of angioplasty with stent placement compare favorably with surgical treatment. It may be the only practical treatment for cases of high-grade carotid stenosis in which the lesion is located distally and poorly accessible to surgery.

### 3. What are the most serious perioperative complications associated with carotid endarterectomy?

The most serious perioperative complications of carotid surgery are neurologic and cardiac. Neurologic complications include cerebral infarction, transient ischemia, and cognitive dysfunction. Cardiovascular complications include cardiac ischemia, dysrhythmia, hypotension, hypertension, and myocardial infarction. Ischemic cerebral injury may result from embolization of thrombus or air during surgical manipulation. It may also result from decreased cerebral perfusion during temporary carotid artery occlusion. Arterial stenosis or occlusion after CEA may also produce an ischemic insult. Patients with atherosclerotic disease of the carotid arteries often have similar pathology of coronary vessels.

### 4. Intraoperatively, how is the patient's neurologic status monitored?

The choice of techniques for assessing neurologic status depends on whether regional or general anesthesia is used. With regional anesthesia, intermittent evaluation of motor strength, sensation, and language is performed. This evaluation should be timed to coincide with interventions of relatively high risk. High-risk periods include carotid artery manipulation, arterial occlusion, and reperfusion. The choice and timing of sedation may markedly interfere with proper evaluation. For example, administration of a benzodiazepine may elicit reemergence of a focal deficit that was observed during an ischemic event and subsequently resolved.

With general anesthesia, neurologic status is most often assessed by electroencephalogram (EEG), somatosensory evoked potentials (SSEPs), motor evoked potential (MEPs), or transcranial Doppler (TCD). EEG is the most widely used and considered the "gold standard" for monitoring neurologic function during general anesthesia. It is the most sensitive method for detecting cerebral ischemia in unconscious patients. Sensitivity depends on the number of electrode channels monitored and the experience of the person evaluating the EEG. EEG changes indicative of ischemia are most likely to be observed from

electrodes positioned near the anatomic site of brain with ischemia. Unilateral changes, especially changes observed in regions dependent on the operative artery, are more likely to reflect ischemic insult. EEG changes most indicative of ischemia are decreased amplitude (voltage), slowing (decreased frequency), or burst suppression. It is useful to maintain a steady state of anesthetic agent during monitoring to appreciate EEG changes that are not confounded by altered anesthetic dose.

SSEPs depend on processing of signals from stimulation of a peripheral nerve. Because the response is described by latency and amplitude alone, analysis of SSEPs may require less experience or training than EEGs. SSEPs are probably less sensitive than EEGs for detecting ischemia. Ischemia is indicated by an increase in latency or a decrease in amplitude of the SSEP waveform. This change is of greatest concern when it is unilateral and on the operative side.

MEPs involve stimulation of the motor cortex by electromagnetic signal. Motor response is measured in the corresponding extremity. Muscle relaxants decrease or eliminate the response. Inhalation anesthetics also diminish the response. MEPs are very sensitive to cerebral ischemia.

TCD is used to measure middle cerebral artery blood flow velocity on the ipsilateral side. It does so by assessing the Doppler shift of sound waves reflected by moving red blood cells in the artery. It is also extremely sensitive for the detection of embolic material. Embolization is common during carotid surgery and depends on surgical technique and the presence of atherosclerotic plaque or entrained air. Positioning of detector probes may be quite cumbersome, and readings markedly depend on the probe direction (angle of insonation). Any movement of the Doppler probe may result in diminished or lost waveforms.

Cerebral oximetry may be useful. Less common is cerebral blood flow measurement by washout of intraarterial or intravenous xenon-133.

## 5. What interventions may reduce the risk of neurologic injury?

Ischemic neurologic insult from carotid artery surgery may result from arterial embolization during surgical manipulation, decreased cerebral perfusion during temporary arterial occlusion, reperfusion injury, or unintentional arterial occlusion after surgery. Arterial embolization during surgery is very common and often depends on surgical technique and the presence of atherosclerosis. Surgical placement of a shunt may increase the incidence of embolization. In many centers, shunts are inserted only if indicated by ischemic changes after carotid artery occlusion or other evidence of poor cerebral collateral circulation. Although thiopental may improve outcome after focal ischemia, it is not widely employed for maintenance of general anesthesia because of dose-dependent delayed awakening and its hemodynamic effects. Hypothermia also improves outcome after focal cerebral ischemia. However, it has not gained wide acceptance for carotid artery surgery. Hypothermia has numerous adverse myocardial effects.

Decreased cerebral perfusion during temporary arterial occlusion is most often treated with deliberate hypertension. In many centers, systemic arterial pressure is increased by 10%–20% during temporary arterial occlusion. Intravenous phenylephrine is most often employed for this purpose. Surgical placement of a temporary vascular shunt during carotid artery occlusion also improves cerebral blood flow. However, this shunt may prolong surgical time, obscure surgical exposure, and promote embolization.

After reperfusion, ischemic and infarcted brain may be at risk for reperfusion injury. Usually arterial blood pressure is reduced to near normal before reperfusion.

The choice of anesthetic agent for CEA is controversial. In a randomized study comparing potent inhalation anesthetics, EEG evidence of ischemia occurred at higher cerebral blood flows in patients anesthetized with halothane compared with isoflurane; this may support the use of isoflurane in these patients. There is no widely accepted preference for either a primarily opioid-based or inhalation anesthetic technique. In any case, rapid emergence from general anesthesia, permitting timely assessment of neurologic function, facilitates diagnosis of neurologic deficit resulting from cerebrovascular occlusion. Rapid emergence allows for more rapid intervention, such as therapeutic surgical reexploration, cerebral thrombolysis, or angioplasty, if indicated.

Control of arterial carbon dioxide tension also is controversial. Mild hypocapnia may reduce cerebral blood flow but may also preferentially shunt blood from normal brain to ischemic brain. Most practitioners maintain arterial carbon dioxide tension near normal.

## 6. Explain the risks of postoperative blood pressure instability.

CEA in proximity to the carotid sinus may result in arterial blood pressure fluctuations postoperatively. Carotid artery angioplasty and stent placement may alter carotid wall mechanical properties, increasing baroreflex sensitivity. Heightened baroreceptor responsiveness may lead to impaired cardiovascular autonomic activity and may contribute to postoperative morbidity and mortality. Increased baroreceptor responsiveness results in an increased incidence of hypotension and bradycardia after CEA. These conditions are most often successfully treated with intravenous phenylephrine and atropine. In contrast to conventional CEA, surgical techniques that include transection of the carotid sinus nerve are likely to increase the incidence of postoperative hypertension. This hypertension is usually treated with β-adrenergic blockers, calcium-channel blockers, or peripheral vasodilators. Hemodynamic dysfunction after carotid surgery is most often transient and is best managed in an intensive care unit setting.

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CASE 17

# Electroconvulsive Therapy

**Ethan O. Bryson, MD • Charles H. Kellner, MD**

QUESTIONS

1. What is electroconvulsive therapy?
2. Do you have enough information to proceed with general anesthesia?
3. Are there any relative or absolute contraindications to electroconvulsive therapy?
4. How are implanted cardioverter-defibrillators and pacemakers managed for electroconvulsive therapy?
5. What are the physiologic effects of electroconvulsive therapy?
6. What is an appropriate anesthetic for electroconvulsive therapy?
7. What concerns exist for the immediate postictal period?
8. Describe the events that lead to pulmonary edema after electroconvulsive therapy.
9. What causes prolonged paralysis after electroconvulsive therapy?

An 88-year-old, 72-kg man with a history of treatment-refractory major depressive disorder was referred for electroconvulsive therapy (ECT). He received a successful course of ECT during an episode of depression in 1968 and was in remission until about 2 years ago. He did not recall any problems with either the treatment or the anesthesia. This episode was characterized by depressed mood, poor sleep, thoughts to join his deceased parents, feelings of guilt about burdening his wife, and passive suicidal ideation. His medical history was significant for hypertension, treated with amlodipine and metoprolol. Additional medications included daily famotidine, finasteride, levothyroxine, lorazepam, mirtazapine, quetiapine, rosuvastatin, docusate sodium (Colace), Senna, and tamsulosin.

## 1. What is electroconvulsive therapy?

ECT is the application of electrical stimuli to the brain to induce a therapeutic seizure. ECT is an effective treatment for major depressive disorder, bipolar disorder, catatonia, and schizophrenia. Most patients referred for ECT are seriously depressed, often suicidal or psychotic and unable to function because of their psychiatric illness. These patients have typically failed medical treatment. ECT has been a safe and effective therapy for refractory depression and other mental illnesses since its introduction. Most treatment-associated morbidity and mortality have been attributed to cardiovascular sequelae related to the physiologic response to treatment.

ECT can be administered with either bilateral or unilateral electrode placement. Bilateral electrode placement is associated with more rapid improvement but also portends increased risk of short-term and long-term memory impairment. Unilateral electrode placement is associated with less risk for memory-associated problems, but the clinical response may be slower and the patient may require a greater number of treatments. In addition, the period of asystole during stimulus application is typically longer with unilateral electrode placement. For patients who are at increased risk for a cardiovascular event during treatment, the risks associated with an increased number of treatments needs to be evaluated if unilateral electrode placement is considered.

## 2. Do you have enough information to proceed with general anesthesia?

The tasks of the anesthesiologist are to determine if the patient is an acceptable anesthetic candidate for ECT, to create a humane and safe anesthetic without suppressing the therapeutic seizure, to mitigate or manage the physiologic effects of the treatment, and to manage the transient effects of the anesthetics including management of the airway. General anesthesia is required, and patients receiving ECT should have the same quality of anesthetic evaluation as patients undergoing anesthesia for a surgical procedure. A thorough history should be taken.

A complete list of current medications should be obtained because some medications are known to interact with either the treatment or the anesthetic (Box 17-1). Patients presenting for ECT are usually taking multiple psychotropic medications. These medications may include tricyclic antidepressants (TCAs), lithium carbonate, monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs), antipsychotics, benzodiazepines, and miscellaneous second-generation antidepressants such as bupropion.

TCAs block the reuptake of norepinephrine at the postganglionic sympathetic nerve endings, resulting in increased baseline sympathetic tone. In these patients, direct-acting sympathetic agents are preferred to indirect-acting agents that increase the release of norepinephrine. Several categories of drugs must be used cautiously with

**BOX 17-1 Anesthetic Implications of Selected Psychotropic Agents**

*TCAs* block reuptake of norepinephrine at postganglionic sympathetic nerve endings
- Drug levels of certain *SSRIs* (i.e., fluoxetine) may increase two to five times when used with TCAs

*MAOIs* block the metabolism of catecholamines
- Baseline sympathetic tone is increased
- Interaction with meperidine or indirect-acting sympathomimetic agents may lead to hypertensive crises, seizures, and hyperpyrexia

*SSRIs* block serotonin reuptake pump via the 5-hydroxytryptamine 1A receptor
- Serotonin release is inhibited
- 5-Hydroxytryptamine 1A receptors may be downregulated
- There is little effect on norepinephrine reuptake
- An association with "serotonin syndrome" (restlessness, chills, ataxia, and insomnia), in combination with lithium or carbamazepine, may be fatal

*Lithium carbonate* prolongs neuromuscular blockade

*Benzodiazepines* may increase resistance to ECT by increasing the seizure threshold

TCAs, antihypertensives, potent volatile agents, and anticholinergics.

MAOIs block the metabolism of catecholamines, increasing baseline sympathetic tone as well. The interaction between MAOIs and meperidine or indirect-acting sympathomimetic agents has been shown to lead to hypertensive crises, seizures, and hyperpyrexia.

Patients who have a history of pseudocholinesterase deficiency or who are at risk for malignant hyperthermia present special problems. Both of these issues relate to succinylcholine, a depolarizing muscle relaxant. Patients with pseudocholinesterase deficiency are at risk for prolonged neuromuscular blockade if given succinylcholine, so an alternative agent such as rocuronium should be administered. Succinylcholine is contraindicated in patients with malignant hyperthermia because it is a known trigger for the disease.

In the present case, none of the medications the patient is taking appears to present a problem, but his blood pressure is elevated. Because ECT is associated with acute but transient elevations in blood pressure, one needs to confirm that the patient has received his antihypertensive medications according to schedule and that his blood pressure is within the expected range given his history before proceeding. Additional antihypertensive medications may be administered immediately before the procedure or on an "as-needed" basis to keep the systolic pressure less than 200 mm Hg. The patient's blood pressure should be measured frequently throughout the perioperative period (every 1 to 2 minutes).

### 3. Are there any relative or absolute contraindications to electroconvulsive therapy?

ECT is generally a low-risk procedure, but many patients who receive ECT fall into the "high-risk" category. Some patients referred for ECT have life-threatening psychiatric illnesses and may have no other treatment options. Consequently, the risk of death with no treatment can be high enough to trump other concerns. Relative contraindications that may make anesthetic management more complicated include the following:
- Increased intracranial pressure (may be exacerbated during treatment)
- Recent hemorrhagic stroke (<1 month) (increased risk for rebleed)
- Retinal detachment (may be exacerbated during treatment)

A history of a recent myocardial infarction (<1 month) and unstable angina are not contraindications to ECT as long as the patient is managed appropriately. Tachycardia and hypertension occur frequently during ECT; either one can predispose to repeat infarction. Cardiology consultation is important to assess risk and plan for appropriate treatment. Severe coronary artery disease is a common life-threatening problem that can be exacerbated by ECT. The likelihood that further myocardial injury may occur as a result of treatment should be weighed against the risks of withholding ECT. It could be helpful to know the location of lesions for which stent implantation is contraindicated, the amount of myocardium at risk, and the results of postinfarction stress tests because adverse hemodynamic conditions could occur during ECT. Patients should be given adequate β blockers and be normotensive before treatment. Short-acting β blockers, such as esmolol, may be administered during treatment along with nitroglycerin or other short-acting agents to maintain blood pressure within the acceptable range. Clopidogrel and warfarin, if indicated, may be continued.

### 4. How are implanted cardioverter-defibrillators and pacemakers managed for electroconvulsive therapy?

Artifacts produced by fasciculations from succinylcholine or interference from ECT might be misinterpreted by a pacemaker or implantable cardioverter-defibrillator (ICD). Two approaches exist. One school of thought suggests deactivating ICDs before ECT. The other school of thought recommends allowing ICDs to function normally. The rationale for deactivating ICDs before ECT is based on concern that artifacts generated during treatment could be interpreted as a treatable rhythm by the internal device, resulting in discharge. Theoretically, such artifacts could result from fasciculations in close proximity to sensing leads or from electromagnetic interference produced by ECT devices. Unnecessary defibrillation from ICDs risks an electrical shock delivered during repolarization, R on T phenomenon, and real ventricular arrhythmias. Proponents of allowing ICDs to function normally point out that even an induced ventricular arrhythmia would be best treated by the ICD. Because most treatment-associated morbidity and mortality have been attributed to cardiovascular sequelae of ECT, the benefit of allowing ICDs to remain active most likely outweighs the small risk of erroneous activation owing to artifact or interference. Deactivation of ICDs is generally simple. A magnet placed over most modern devices prevents defibrillation

but allows the pacemaker function to continue. Reactivation of most modern ICDs is achieved by removing the magnet (Chapter 7).

For a patient who has an implanted pacemaker, it is important to know why the device was placed. Although modern pacemakers are resistant to electromagnetic interference associated with ECT, there is a small risk of malfunction related to the treatment. Consequently, it is prudent to have external pacing equipment available for pacemaker-dependent patients. Theoretically, interference could either inhibit pacemaker output or reset the device to a committed pacing mode (DOO or VOO). Applying a doughnut magnet to the pacemaker converts it to a committed mode. Placing the doughnut magnet prevents inhibition of the device should interference occur, and normal pacemaker function is restored on magnet removal. Magnet application is not always required. It is reasonable to have the magnet available for application if inhibition of pacemaker output is noted coincident with treatment. Even if the device has been placed into magnet mode, posttreatment interrogation is not routinely required, but it should be performed by a trained individual when there is evidence of pacemaker reset (i.e., asynchronous pacing). If there is any question, a 12-lead electrocardiogram (ECG) should be obtained after the procedure (Chapter 7).

### 5. What are the physiologic effects of electroconvulsive therapy?

The stimulus applied to the brain during ECT initially results in a profound parasympathetic surge. Asystole during this period is common and may persist throughout the stimulus application. After stimulus termination, the resulting seizure is accompanied by a profound sympathetic surge, commonly with associated tachycardia and hypertension. The elevation in blood pressure is significant, and systolic blood pressure may increase by 40% over baseline secondary to the increase in sympathetic activity. If the patient does not have a seizure and asystole persists, treatment with atropine coupled with one or two rounds of chest compressions may be necessary. In cases in which the risk of prolonged asystole is high, pretreatment with an anticholinergic, such as glycopyrrolate, is often indicated. One example is stimulus dose titration. Dose titration involves administration of increasing electrical stimuli until a seizure is produced.

Elevated serum creatine phosphokinase has been reported after ECT. Elevations of isoenzymes specific for myocardial infarction (CK-MB) are not observed without damage to the myocardium, even in patients with documented coronary artery disease and prior infarction.

### 6. What is an appropriate anesthetic for electroconvulsive therapy?

Anesthesia for ECT can directly influence the efficacy of treatment. The goals are to induce general anesthesia without increasing the seizure threshold, provide adequate muscle relaxation to prevent patient injury during motor seizures, and manage the patient until recovery from both the anesthetic and the neuromuscular blockade. In the United States, the drug of choice for induction of general anesthesia is the ultra-short-acting barbiturate methohexital, although propofol and ketamine can also be used. The advantage of using methohexital is rapid induction of general anesthesia without adversely altering therapeutic seizures. Additionally, methohexital is rapidly redistributed out of the brain so that the patient awakens soon after the treatment has been performed. Propofol is not the first-choice anesthetic for these procedures because it is potently anticonvulsant and may raise seizure threshold or decrease seizure threshold. However, propofol has been shown to be beneficial in patients with a history of prolonged ECT-induced seizures and patients with a history of nausea and vomiting after ECT.

Succinylcholine is the drug of choice for neuromuscular blockade because of the short duration of these treatments. For patients in whom use of succinylcholine is contraindicated, rocuronium is an acceptable alternative.

### 7. What concerns exist for the immediate postictal period?

Return of spontaneous respiration generally occurs within 3 to 5 minutes after succinylcholine administration, which is usually before emergence from general anesthesia. Ventilatory support via bag-valve-mask devices is indicated until patients have adequate tidal volumes and are able to support their own airways without assistance. During this period, it is important to look for signs of light anesthesia and residual paralysis, which may suggest prolonged succinylcholine action requiring further ventilatory support and either a reduction in succinylcholine dose on subsequent treatments or the use of a different neuromuscular blocking agent altogether. Hemodynamic instability is common during this time, and patients who require tight blood pressure control should have their blood pressure checked frequently in the postictal period and receive medications as needed. Agitation after a seizure can result from hypoxia or hypercarbia as well as from the effects of treatment. It is important to ensure appropriate oxygenation and ventilation before administering posttreatment sedation.

### 8. Describe the events that lead to pulmonary edema after electroconvulsive therapy.

Although very rare, pulmonary edema associated with ECT has been reported and may be due to numerous causes, including negative pressure and neurogenic pulmonary edema. Negative pressure pulmonary edema results when the patient attempts to inspire against a closed glottis. Lax pharyngeal muscles are unable to lift soft tissues out of the airway, allowing for upper airway collapse and obstruction. Simultaneously, strong diaphragm and intercostal muscles generate substantial negative intrathoracic pressures. Negative intrapleural pressures created in this way can overcome the Starling forces that keep plasma within capillaries. Fluid is drawn into alveoli, resulting in pulmonary edema. Prevention is aimed at restoring pharyngeal muscle tone, maintaining airway

support, using an oral airway to provide airway patency if necessary, and using positive pressure ventilation until neuromuscular blockade has completely dissipated.

Neurogenic pulmonary edema can occur secondary to significant perturbations in the autonomic nervous system related to ECT. It typically develops within a few hours after treatment. The diagnosis requires exclusion of other causes of pulmonary edema. Most patients do not develop this complication even with exceedingly elevated blood pressures.

The tachycardia and hypertension that result from sympathetic activity associated with therapeutic seizures significantly increases myocardial oxygen demand. Changes in the ECG suggestive of ischemia have been reported during this period, along with ventricular hypokinesia and wall motion abnormalities. In patients with subclinical coronary disease, this situation may lead to acute heart failure and flash pulmonary edema. Tight control of blood pressure can be achieved in patients thought to be at risk (patients with known coronary artery disease, recent myocardial infarction, or stable angina) through frequent dosing of short-acting agents such as esmolol or nitroglycerin.

Regardless of the cause, treatment of pulmonary edema after ECT is founded on specific principles. In addition to aggressive treatment of elevated systolic blood pressure and diuretic therapy, supplemental oxygen via facemask should be instituted for decreased oxygen saturation. Intubation with positive pressure ventilation is indicated for patients who do not respond to facemask oxygen.

### 9. What causes prolonged paralysis after electroconvulsive therapy?

Succinylcholine is rapidly degraded by ester hydrolysis involving butyrylcholinesterase (plasma cholinesterase or pseudocholinesterase); because of this, the relative amount of normal butyrylcholinesterase determines the duration of action of succinylcholine. Patients with atypical pseudocholinesterase metabolize succinylcholine at a slower rate and present with prolonged neuromuscular blockade that can last 70 to 120 minutes. Acquired pseudocholinesterase deficiency has been associated with many disease states and with the administration of numerous different classes of drugs (Box 17-2). In most cases of acquired pseudocholinesterase deficiency, the enzyme works well, but there is a small amount of it. For most surgical cases, this situation is not clinically significant because the prolongation of neuromuscular blockade secondary to acquired deficiency lasts only 10 to 25 minutes. However, ECT presents a unique clinical situation because the procedure usually lasts no more than 10 minutes. Because the treatment itself is so brief, it is important that the duration of anesthesia and muscle relaxant is matched to the time required for ECT.

**BOX 17-2 Etiologies of Acquired Pseudocholinesterase Deficiency**

**Disease Related**

- Liver disease (owing to decreased pseudocholinesterase synthesis)
- Renal disease (unclear etiology)
- Malnutrition (decreased protein synthesis)
- Pregnancy (decreased after the 10th week)
- Malignancy (liver > lung > gastrointestinal > genitourinary > breast)
- Burns (decreased activity for 4 months after injury)

**Medication Related**

- Echothiophate eye drops (contraindicated)
- Organophosphate insecticides (temporary acquired deficiency with acute exposure)
- Neostigmine, physostigmine, pyridostigmine, edrophonium (all are competitive inhibitors)
- Phenelzine (MAOI associated with decreased activity with therapeutic levels)
- Metoclopramide (may prolong block 2 to 3 minutes if administered directly before succinylcholine)
- Chemotherapy (cyclophosphamide, cytarabine, vincristine, and rituximab may prolong block 10 minutes for 2 to 3 weeks after treatment)

Prolonged neuromuscular blockade in this setting can result in a patient who is awake but remains paralyzed. These patients are at risk for hypoventilation, hypoxia, and aspiration. They require an extended period of ventilator support after treatment.

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CASE 18

# Spine Surgery

**Stacie G. Deiner, MD**

## QUESTIONS

1. Does severe cervical stenosis necessitate awake fiberoptic intubation?
2. How is chronic pain managed during major spine surgery?
3. Explain the mechanism by which intraoperative neurophysiologic monitoring helps detect evolving spinal injury; are there any contraindications to its use?
4. How would you alter your anesthetic plan to facilitate neurophysiologic monitoring?
5. What are the concerns for prone positioning in this patient?
6. Is there a safe range for mean arterial pressure during spine surgery; what are the risks of induced hypotension?
7. How would you use your knowledge of propofol pharmacology to ensure a rapid but safe emergence?

A 73-year-old man with spinal cord compression presented for posterior cervical fusion (C3-6). For the past year, he has experienced neck pain and increasing weakness and "tingling" in his right arm. His medications included sustained-release oxycodone, 40 mg twice a day, and oxycodone 5 mg/acetaminophen 650 mg, 2 tablets every 4 hours, although he did not take his medication the morning of surgery. Radiology studies showed severe cervical spinal cord compression. The neurophysiologic monitoring team monitored somatosensory evoked potentials (SSEPs), motor evoked potentials (MEPs), and electromyography (EMG) beginning after induction to obtain a baseline before positioning.

### 1. Does severe cervical stenosis necessitate awake fiberoptic intubation?

The decision to perform an awake fiberoptic intubation for patients with cervical spine disease depends on the location of the injury or disease, the risk of aspiration (full stomach), the anticipated relative ease of mask ventilation, and the patient's ability to cooperate with airway anesthesia. Awake fiberoptic intubation is the "gold standard" to minimize neck movement caused by mask ventilation and direct laryngoscopy. Additionally, any patient who has risk factors for difficult mask ventilation (i.e., obesity, >55 years old, history of snoring, lack of teeth, the presence of a beard, Mallampati class III or IV, abnormal mandibular protrusion test) should be considered for awake intubation. In an uncooperative patient, one must weigh the risk of induction versus movement from agitation or inadequate airway anesthesia. Induction before tracheal intubation is an option for patients who are not at increased risk for aspiration and for whom mask ventilation is not predicted to be difficult.

Videolaryngoscopes may be useful to secure the airway in patients with limited mobility, although they can cause more movement of the cervical spine than a well-executed fiberoptic intubation. Some channel-type videolaryngoscopes (e.g., Airway Scope (AWS) S-100; [Pentax-AWS system]; AWS; Pentax, Tokyo, Japan, and AirTraq [ATQ; Prodol Meditec, Vizcaya, Spain]) have been shown to produce less cervical spine movement relative to direct laryngoscopy. Glidescopes (Glidescope® videolaryngoscope (Verathon, Bothell, WA) have been shown to cause less cervical spine movement at C2-5 but similar movement to direct laryngoscopy at other levels, which means that Glidescopes are not a better choice for cases with more rostral cervical instability. However, the Glidescope does produce improved views, even with a cervical immobilization collar in place. The advantage of these alternative devices is their larger field of view, making them better choices for an airway with a large amount of secretions or blood or debris, such as in a trauma patient.

### 2. How is chronic pain managed during major spine surgery?

#### *Preoperative*

Although transdermal systems (e.g., fentanyl patch) should not be initiated, they should be continued if already in use. Patients should be instructed to take their oral medications, with the exception of nonsteroidal antiinflammatory drugs, which should be discussed with the surgeon. For opioid-tolerant patients who refrain from pain medication on the morning of surgery, the daily opioid consumption can be calculated and converted to the equivalent intravenous morphine dosage. This calculation provides an approximation of the daily opioid intake, some of which should be administered intravenously during surgery. Converting oral opioids to an intravenous dose is controversial; however, the

underlying principle is that surgical patients who are opioid-tolerant require opioid dosing based on their usual consumption.

Oral gabapentin can reduce morphine consumption and pain scores in the first 12 hours after surgery. The optimal preoperative dose to maximize pain control and minimize side effects ranges from 600 to 900 mg. The most common side effects are nausea and vomiting, lightheadedness, and ataxia. Because many patients with chronic pain have experience with gabapentin, it is prudent to ascertain effective dosing for each individual patient. In some cases, side effects limit use of gabapentin. Based on this information, a decision can be made for or against administering gabapentin preoperatively and at what dose.

### *Intraoperative*

Methadone can be an important part of the intraoperative opioid regimen in opioid-tolerant patients undergoing major spine surgery. A single bolus dose of methadone (0.2 mg/kg) may reduce postoperative opioid use and visual analog scale scores for 48 hours postoperatively. Ketamine can also be a useful adjunct during spine surgery because it is profoundly analgesic and may improve the quality of intraoperative monitoring. Especially for opioid-dependent patients, the use of intraoperative ketamine (0.5 mg/kg on induction of anesthesia, with continuous infusion at 10 μg/kg/min terminated at wound closure) can reduce opioid requirements and pain scores up to 48 hours to 6 weeks later without an increase in side effects. The mechanism of action of ketamine includes *N*-methyl-D-aspartate receptor antagonism.

## 3. Explain the mechanism by which intraoperative neurophysiologic monitoring helps detect evolving spinal injury; are there any contraindications to its use?

Three major categories of neurophysiologic monitoring are routinely performed for spine surgery: SSEPs, MEPs, and EMG.

- *SSEPs* monitor the integrity of the dorsal columns of the spinal cord. An electrical or magnetic impulse is delivered to the periphery, producing electrical potentials that propagate through the spinal cord to the brain. The waveform that is generated can be measured at the level of the spinal cord proximal to the surgical field or at the brain (Figure 18-1).
- *MEPs* monitor the integrity of the anteriorly located motor tracts of the spinal cord. An electrical or magnetic impulse is delivered to the brain or spinal cord proximal to the surgical site and measured as D and I waves with epidural electrodes on the surgical field (less common) or as compound muscle action potentials measured by pairs of needles over the muscle corresponding to the monitored nerve (more common).
- *EMG* is a measurement of electrical activity generated by muscle contraction, monitored by two electrodes in or near a muscle. Two major types of EMG are recorded during surgery:
  - Passive or free run—continual monitoring of a muscle for spontaneous activity
  - Stimulated EMG—an electrical stimulus is applied near or to a nerve, and the response is recorded over the muscle

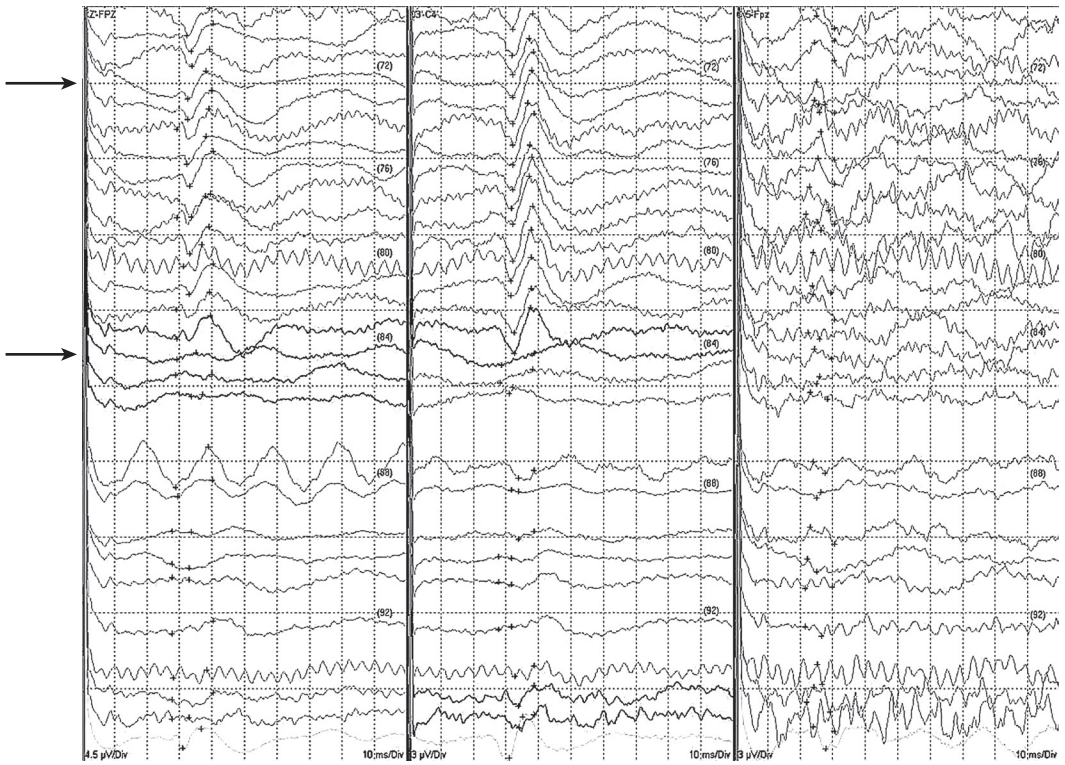

**FIGURE 18-1** ■ Signal loss in SSEP trace. *Top arrow* indicates normal; *bottom arrow* indicates loss.

Neuromonitoring is sensitive for spinal cord injury from any etiology. Surgical causes include ischemia from trauma, compression, or transection. In addition to surgical causes, there have been many reports of loss of signals from malpositioning during surgery. A classic example would be an impending brachial plexus injury. Loss of signal in an area where the surgeon is not working and not associated with a prior deficit should alert the anesthesiologist to recheck the positioning of the affected limb. A more global loss of signal could be associated with a change in the anesthetic depth (e.g., introduction of potent inhalation agent, bolus of an intravenous agent, or muscle relaxant) or a significant physiologic change such as hypotension or severe anemia.

Although SSEPs and MEPs monitor the integrity of a tract, they may be unable to detect injury of a single nerve root. EMG allows the identification of a single nerve, especially in cases where the anatomy is abnormal (e.g., scar tissue, tumor). EMG is extremely sensitive and can detect activation of only 1% to 2% of a muscle's fibers. Commonly monitored nerves include the following:

- Cervical nerve roots during spine surgery (C2-7)
- Lumbosacral (L2-S2) during spine surgery
- Facial nerve during acoustic neuroma surgery or parotid surgery
- Recurrent laryngeal nerve during anterior cervical surgery
- Cranial nerves during brainstem surgery

Relative contraindications for evoked potential monitoring include the following:

- Implanted pacemaker
- Functioning implantable cardioverter-defibrillator—in high-risk cases may need to disable antitachyarrhythmia function
- Implanted metal in the cranial vault (e.g., aneurysm clips)
- Epilepsy
- Increased intracranial pressure
- Convexity defects of the skull

In all cases, the risks of surgery without neurophysiologic monitoring must be weighed against the risk of arrhythmia, seizure, or thermal injury.

### 4. How would you alter your anesthetic plan to facilitate neurophysiologic monitoring?

Both MEP and SSEP monitoring are affected to some degree by all anesthetics. The goal is to create a constant depth of anesthesia during acquisition of baseline signals that would be maintained throughout surgery. This approach avoids introducing an anesthetic or a physiologic change that could be confused with surgical injury to the spinal cord.

Inhalation anesthetics cause a decrease in waveform amplitude and an increase in latency. Intravenous anesthetics with two exceptions, etomidate and ketamine, to varying degrees cause a decrease in waveform amplitude and an increase in latency. Etomidate and ketamine may increase waveform amplitude. Dexmedetomidine infusion appears to have no deleterious effects on neuromonitoring.

During MEP monitoring, muscle relaxants should not be administered. If MEP monitoring is instituted before patient positioning, the effects of muscle relaxants used for intubation should have dissipated or been antagonized. The intravenous anesthetic infusion should be immediately available to avoid having to readminister a bolus to restore adequate blood levels.

The components of an anesthetic for spine surgery involving neurophysiologic monitoring include the following:

- For amnesia, propofol infusion is most commonly used, sometimes in combination with ketamine, dexmedetomidine, or less than 0.5 minimum alveolar concentration (MAC) of a potent inhalation agent.
- For analgesia, an opioid infusion is used.

The choice of which particular agent is administered depends on the patient's underlying medical conditions and whether the patient is opioid-tolerant. Administration of potent inhalation anesthetics depends on which neurophysiologic monitoring is used during the surgery. Compared with SSEPs, MEPs are more sensitive to the effects of inhalation agents. Studies suggest that a relatively low-dose volatile agent (i.e., 0.25 to 0.5 MAC) is enough to suppress single pulse transcranial stimuli. Although more aggressive stimulation patterns can produce compound muscle action potential responses in some patients, others are entirely unattainable. Patient factors that may contribute to volatile agent sensitivity include myelopathy secondary to chronic spinal cord compression and diabetic neuropathy.

Similarly, muscle relaxant infusion is controversial because the relationship between MEPs and train-of-four responses is not linear. It is possible for a patient to have one or two twitches with train-of-four monitoring but absent MEPs.

Stimulation of the cervical motor tracts causes jaw contractions and may result in bite-related patient injury. These injuries range from lingual hematoma to mandibular fracture. Tracheal extubation may be precluded if hematoma formation is significant. Bite-blocks are recommended during cervical tract motor stimulation. However, it is still possible to sustain oral injuries even with a bite-block in place. Compression of the rear portion of the tongue (usually on the opposite side of the tracheal tube) can occur.

### 5. What are the concerns for prone positioning in this patient?

Most spine surgeries are performed in the prone position, which may improve ventilation in many cases. However, malpositioning may lead to significant morbidity. In osteoporotic patients and patients with cervical instability, particular attention should be given to positioning. Before induction, patients should be allowed to position themselves for comfort in the supine position. After induction and tracheal intubation, it is important to log roll the patient safely with in-line stabilization of the neck. Whether a commercially available table and frame or a regular operating table with bolsters and padding is used, the overall goals are the same. The patient's neck should be maintained in neutral position with a foam headrest or cervical traction device. Horseshoe headrests

have fallen out of favor for prone positioning because of an association with postoperative blindness when they impinge on the lateral canthus of the eye. Every effort should be made to avoid positioning the patient with the face turned to one side because this is associated with postoperative blindness and stroke.

Arm positioning may be challenging in patients who had previous shoulder surgery or traumatic injury. Positioning is often dictated by the need for intraoperative fluoroscopy or x-ray. Most often, patients undergoing cervical spine surgery have their arms secured at their sides. The surgeon may tape the patient's shoulders down to improve visualization of the lower cervical and upper thoracic spine during routine fluoroscopy or to help contour a wound for incision and closure. Care must be taken to avoid overaggressive traction on the shoulders and brachial plexus because this can lead to neurologic injuries. Occasionally, traction on the shoulders may need to be released during surgery based on neurophysiologic monitoring changes suggestive of undue stretch on the brachial plexus.

Patients undergoing lumbar surgery have their arms positioned at 90 degrees in all planes, supported by arm boards. Typically, the shoulder is abducted, with minimal shoulder flexion and 5 to 10 degrees of internal rotation. Neuromonitoring can help assess neck and brachial plexus position throughout surgery.

Finally, lengthwise bolsters should be placed to support the patient from the tip of the shoulders to the iliac crests allowing the abdomen to hang freely; this provides for venous return and diaphragmatic excursion during ventilation. Legs should be bent at the knees. The hips may be extended to create lordosis of the lumbar spine for fusion or flexed for decompression procedures without fusion. All pressure points and areas where peripheral nerves are subject to compression (e.g., ulnar nerve at the elbow, peroneal nerve at the fibular head) should be padded with foam, and the wrist should be in a neutral position to protect the median nerve.

## 6. Is there a safe range for mean arterial pressure during spine surgery; what are the risks of induced hypotension?

"Adequate" intraoperative blood pressure during spine surgery is a complicated issue. Both the brain and the spinal cord autoregulate blood flow within physiologic ranges of mean arterial blood pressures between 50 and 150 mm Hg. Local factors (e.g., spinal stenosis) may contribute to acute or chronic decreased blood flow. In some patients, this decreased blood flow may result in greater susceptibility to regional ischemia, even at a "safe" systemic blood pressure. During spinal distraction, the effects of hypotension may be exacerbated. Acceptable minimal systemic blood pressure should be determined in concert with information from the neuromonitoring team.

Induced hypotension is a strategy employed to prevent blood loss. However, studies examining this technique have noted complications including reactionary hemorrhage, persistent hypotension, cardiac ischemic injury, and ischemic optic neuropathy. Consequently, induced hypotension is generally avoided. An alternative strategy to decrease intraoperative blood loss is administration of antifibrinolytics such as aminocaproic acid. Aminocaproic acid has been shown to decrease intraoperative requirements for transfusion, although there is a small risk of thrombosis. Generally, a loading dose is followed by an infusion continued throughout the case.

## 7. How would you use your knowledge of propofol pharmacology to ensure a rapid but safe emergence?

Rapid awakening after long surgery using total intravenous anesthesia (TIVA) requires advanced planning because the time required for drug elimination is dependent on the infusion duration. Context-sensitive half-life is the time required for the plasma concentration of a drug to decrease by 50% after cessation of an infusion designed to maintain a constant concentration. Based on pharmacologic studies, a 50% reduction in plasma drug concentration is necessary for recovery after a steady-state infusion of most intravenous hypnotics (Figure 18-2). Based on these findings, cessation of the intravenous anesthetic after a prolonged procedure may be necessary 40 minutes before surgical finish. Commonly, during closure of the incision, neuromonitoring is discontinued, and if necessary, a potent inhalation agent can be added.

Processed electroencephalography (EEG) monitoring may give some insight into tapering anesthetic infusions with respect to amnesia, although it is not helpful as an index of immobility. Sevoflurane and propofol affect movement to noxious stimuli differently at equivalent levels of consciousness. At an equivalent depression of the processed EEG, sevoflurane suppresses the blink reflex more than propofol, indicating different pharmacodynamic properties of these anesthetics at the brainstem level. The differential level of immobility at similar levels of hypnosis can make titration of TIVA during spine surgery without the use of muscle relaxants complex.

Although an immediate postoperative neurologic examination is desirable, extubation of the trachea should not be attempted unless accepted extubation criteria are met. Caution should be exercised if the patient is extremely edematous or there is evidence of hemodynamic instability.

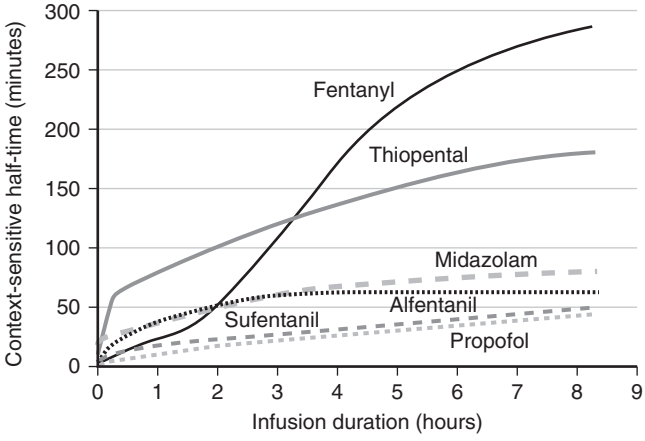


**FIGURE 18-2** ■ **Context-sensitive half-lives of intravenous anesthetics.** (From Hughes MA, Glass PSA, Jacobs JR. Context-sensitive half-time in multicompartment pharmacokinetic models for intravenous anesthetic drugs. Anesthesiology 1992;76:334.)

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CASE 19

# Transsphenoidal Hypophysectomy

Irene P. Osborn, MD

## QUESTIONS

1. What is acromegaly?
2. What symptoms are typical of acromegaly?
3. How is acromegaly treated?
4. What are the anesthetic considerations for patients with acromegaly?
5. Describe the airway management concerns for patients with acromegaly.
6. What structures lie within the transsphenoidal surgical field?
7. What is diabetes insipidus?
8. What are the postoperative concerns for patients with acromegaly?

A 44-year-old man with marked features of acromegaly presents for transsphenoidal hypophysectomy. The patient reports increasing shoe size, glove size, and worsening sleep apnea. Magnetic resonance imaging revealed a pituitary mass. Laboratory findings are within normal limits with the exception of serum glucose, which is 170 mg/dL. The patient does not have any allergies and does not take medications at home. Past surgical history includes carpal tunnel release bilaterally. He denies other medical problems.

### 1. What is acromegaly?

Acromegaly was previously considered a rare disease. However, more recent European studies and improved screening suggest that clinically significant pituitary adenomas occur in 1 per 1064 people. Growth hormone (GH)–secreting tumors of the pituitary constitute at least 10% of benign pituitary tumors. The pituitary gland is anatomically and functionally separated into the anterior pituitary (adenohypophysis) and posterior pituitary (neurohypophysis). In children, GH-secreting tumors cause gigantism; acromegaly occurs in adults whose epiphyses have fused. Acromegaly is most common in patients 20–60 years old, with equal distribution between the genders. The diagnosis is generally made 10–15 years after the onset of pathologic GH secretion. There is a twofold to fourfold increase in mortality versus the general population. If untreated, 50% of patients with acromegaly die before age 50 years. The most common cause of death is cardiac and may be the result of hypertension, coronary artery disease, compensatory hypertrophy as a result of generalized somatomegaly, or the direct effects of GH on the heart.

Acromegaly results from excess secretion of GH and subsequent elevation of circulating and locally produced insulin-like growth factor I (IGF-I). GH and IGF-I levels are controlled via several interactions rather than stimulating growth directly. GH induces the release of IGF-I, which promotes DNA, RNA, and protein synthesis as well as cell and tissue growth.

### 2. What symptoms are typical of acromegaly?

The structural changes of acromegaly cause chronic pain and discomfort. These symptoms reduce quality of life and life expectancy. Changes include skeletal overgrowth deformities (particularly of the hands, feet, and face), cardiovascular disease (hypertension, enlarged heart), arthropathy, neuropathy, and respiratory obstruction (Boxes 19-1 and 19-2).

### 3. How is acromegaly treated?

Acromegaly is a severe, often chronic disease with increased mortality rates if it is not treated appropriately. Treatment options include surgery, medical therapy, and radiation. Each modality has specific advantages and disadvantages.

Surgical therapy is the primary treatment for most symptomatic adenomas. There are several surgical approaches to pituitary masses. Most pituitary masses can be removed adequately via a transsphenoidal approach. This approach is associated with less morbidity (e.g., hypopituitarism, diabetes insipidus) and mortality than transcranial resections and radiation. Larger lesions with extensive growth outside the sella are best approached through craniotomy.

Oral medical therapy includes bromocriptine, a dopamine agonist, and levodopa, a dopamine precursor. These agents suppress hypothalamic-mediated GH levels and decrease tumor size. In addition to somatostatin analogues, these agents may offer alternatives to surgery in debilitated or elderly patients.

**BOX 19-1 Airway Changes in Acromegaly**

**Anatomic**

Hypertrophy
- Facial bones—large bulbous nose
- Nasal turbinates
- Soft palate
- Tonsils
- Epiglottis

Glottic stenosis
Impaired mobility of cricoarytenoid joints
Compression of recurrent laryngeal nerves
Limitation in head and neck mobility

**Physiologic**

Development or exacerbation of sleep apnea
Hoarseness
Dyspnea

**BOX 19-2 Peripheral Effects of Excess Growth Hormone**

**Anatomic**

Skeletal overgrowth
- Gigantism
- Enlarged hands and feet
- Distortion of facial features
- Prognathism

Soft tissue overgrowth
- Enlarged lips, tongue, epiglottis, and vocal cords
- Visceromegaly

Connective tissue overgrowth
- Recurrent laryngeal nerve paralysis

Peripheral neuropathy
- Carpal tunnel syndrome

**Physiologic**

Glucose intolerance
Hypertension
Osteoarthritis
Osteoporosis
Skeletal muscle weakness

### 4. What are the anesthetic considerations for patients with acromegaly?

The constellation of physical manifestations of acromegaly, especially heart and lung disease, combined with upper airway involvement, presents particular concern to the anesthesiologist. Cardiac complications in patients with acromegaly have been described, and cardiomegaly can occur with or without coexisting hypertension. Many typical acromegalic features suggest difficult airway management in these patients (see Question 5). An anesthetic technique appropriate for most patients with acromegaly focuses on opioids, volatile agent, nitrous oxide, and muscle relaxants. Many surgeons use intranasal epinephrine-containing local anesthetics and cocaine as part of their presurgical preparation. The use of these solutions reduces bleeding but also may lead to arrhythmias in the presence or absence of volatile agents. Hypertension and bleeding during intrasellar exploration may be controlled effectively with appropriate anesthetic depth and intravenous administration of β-adrenergic blockers or vasodilators. Practical considerations include difficulty in positioning of large extremities and placement (if needed) of intraarterial catheters. Also, a throat pack is inserted to prevent aspiration of blood from oropharyngeal pooling. The throat pack is removed at the end of surgery, before extubation.

### 5. Describe the airway management concerns for patients with acromegaly.

Airway assessment begins with careful history taking and physical examination. Airway obstruction is one of several mechanisms that are associated with difficult airway management in these patients. Compared with patients without acromegaly, this group of patients presents a higher incidence of predicted and unpredicted difficult intubations and problematic mask ventilation. A recent history of an uneventful intubation may be reassuring; however, anatomic and physiologic changes over the course of 1–5 years may change that. Typical features, such as large tongue, large epiglottis, distortion of the larynx, and soft tissue swelling, complicate visualization of the larynx in patients with acromegaly. Patients without hoarseness or dyspnea and with adequate mouth opening may be cautiously approached in the routine manner. Only oral intubation or tracheostomy can be considered for transsphenoidal surgery because nasal intubation would obstruct the surgical field. Patients are instructed preoperatively that mouth breathing will be required in the postoperative period because of bilateral nasal packs.

The American Society of Anesthesiologists Difficult Airway Algorithm is a good framework to treat failed intubation and difficult ventilation. Although it may be prudent to secure the airway with the patient awake, fiberoptic-guided intubation is often challenging because of excessive soft tissue in the oropharynx. Minimizing mechanical trauma to the upper airway and vocal cords is an important consideration because additional edema can result in airway obstruction after tracheal extubation. An awake and responsive patient is needed for safe removal of the tracheal tube.

### 6. What structures lie within the transsphenoidal surgical field?

The sella turcica, within the body of the sphenoid, provides bony protection for the pituitary gland. The diaphragma sella is a roof of dura pierced by the pituitary stalk with its arachnoid, which extends to the hypothalamus. The cavernous sinus surrounds the walls of the sella and contains the cavernous portion of the internal carotid artery and cranial nerves III, IV, and VI. The fifth cranial nerve, which provides facial and eye sensation, is in the outside wall of the cavernous sinus. The optic nerves converge above the diaphragm to form the chiasm. Arterial bleeding during transsphenoidal hypophysectomy may be from the carotid artery or its branches, and

venous bleeding arises from the cavernous sinus. If excessive bleeding from the cavernous sinus occurs, it may be difficult to control. Temporary or permanent packing of the sinus may be necessary.

## 7. What is diabetes insipidus?

The most common endocrine dysfunction postoperatively is diabetes insipidus (DI). The dilute polyuria of central DI is caused by diminished or absent antidiuretic hormone synthesis or release. Neurosurgical procedures in the region of the sella result in DI for various reasons, including direct hypothalamic injury or ischemia, stalk edema, or high pituitary stalk dissection. DI may be permanent or transient and rarely occurs intraoperatively in previously asymptomatic patients. Classic manifestations of DI are polydipsia and high output of poorly concentrated urine despite increased serum osmolarity. DI that develops during or immediately after pituitary surgery is generally due to reversible trauma to the posterior pituitary and is transient.

The differential diagnosis includes diuresis from mannitol, glucose, or excessive crystalloid administration. Initial treatment of DI consists of oral fluid intake to replace urine loss. If oral intake is inadequate and hypernatremia is present, losses should be replaced with dextrose and water or an intravenous solution that is hypoosmolar with regard to the patient's serum such as half-normal saline. When urinary volumes are excessive and the patient is unable to drink water, administration of exogenous vasopressin is indicated. Aqueous vasopressin, 5–10 U, can be given subcutaneously every 4 hours. Alternatively, desmopressin can be administered intravenously while the nasal packing is in place and intranasally after the nasal packing is removed. Desmopressin therapy can be prescribed in patients with permanent, partial, or complete DI (Box 19-3).

**BOX 19-3 Diabetes Insipidus**

**Etiology**

Direct hypothalamic injury
Pituitary stalk edema
High pituitary stalk dissection

**Symptoms**

Polydipsia
Poorly concentrated polyuria
High serum osmolarity

**Differential Diagnosis**

Diuresis from mannitol, hyperglycemia, or excessive crystalloid administration

**Treatment**

Increase oral intake
Intravenous infusion if oral intake inadequate or impossible
Aqueous vasopressin or desmopressin

## 8. What are the postoperative concerns for patients with acromegaly?

Surgical considerations include cerebrospinal fluid (CSF) rhinorrhea and bleeding. Intraoperatively, after tumor resection, the sinus is occasionally packed with autologous fat. If a CSF leak occurs intraoperatively, a lumbar drain can be placed postoperatively to divert CSF until the diaphragma sella has healed. A rare complication is copious bleeding from the carotid artery or cavernous sinus requiring excessive pressure and packing for control. Such pressure may result in partial or complete occlusion of the intracavernous portion of the internal carotid artery and pressure on cranial nerves III, IV, V, and VI. Postoperative ophthalmoplegia, facial anesthesia, and contralateral hemiparesis or hemiplegia may result from direct pressure or vasospasm.

Although intact airway reflexes are essential before extubation, emergence from anesthesia should proceed smoothly to avoid excessive coughing, bucking, and hypertension. Suctioning of the oropharynx commonly reveals blood as the throat pack is removed. Adequate tidal volume is confirmed, and the head should be elevated to facilitate ventilation. Application of the facemask must be performed gently because one or both of the nares will be packed. The patient is asked to breathe via the mouth and is evaluated for return of consciousness and assessment of vision. Prolonged mouth breathing requires airway humidification, which improves oxygenation if an elevated fraction of inspired oxygen is used. Postoperative pain is generally mild and limited to headache. Small doses of opioids and oral analgesics with a sip of water as soon as tolerated may help.

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SECTION 4

# NEUROMUSCULAR SYSTEM

CASE 20

# Depolarizing Neuromuscular Blockade

**Michael T. Bialos, MD • James B. Eisenkraft, MD**

## QUESTIONS

1. What is the differential diagnosis for a healthy patient whose vital signs are stable but who is not "waking up" after general anesthesia?
2. How is normal neuromuscular transmission accomplished?
3. Describe the mechanism of action of succinylcholine.
4. How is the action of succinylcholine terminated?
5. Explain the potential side effects of succinylcholine administration.
6. What are the contraindications to succinylcholine administration?
7. What is the best and safest neuromuscular blocking drug for rapid-sequence induction?
8. Are there any drugs that could replace succinylcholine in the future?

An otherwise healthy, 16-year-old boy weighing 60 kg is scheduled for urgent appendectomy. Following preoxygenation, rapid-sequence induction is carried out with propofol 130 mg, fentanyl 150 μg, and succinylcholine 80 mg intravenously. Cricoid pressure is maintained throughout induction. Direct laryngoscopy and tracheal intubation are easily accomplished. Ventilation is controlled and anesthesia is maintained with 2% sevoflurane in 80% oxygen with air. During surgery, the patient receives 500 mL of 0.9% saline and 1 g of cefazolin. Vital signs are stable throughout, and the procedure is completed 35 minutes after induction of anesthesia. As the skin is being closed, sevoflurane is discontinued, and 100% oxygen is administered. At 20 minutes after the end of the procedure, the end-tidal concentration of sevoflurane is 0.0%, heart rate and blood pressure are increasing, end-tidal carbon dioxide ($ETCO_2$) is 35 mm Hg, and there is no spontaneous respiration.

### 1. What is in the differential diagnosis for a healthy patient whose vital signs are stable but who is not "waking up" after general anesthesia?

Assuming stable and appropriate blood pressure, heart rate, arterial oxygen saturation, core temperature, and $ETCO_2$, the differential diagnosis can be divided into three main categories: anesthetic drugs, metabolic disturbances, and neurologic problems.

It is important to consider every drug administered during the perioperative course, including opioids, benzodiazepines, potent inhaled anesthetics, neuromuscular blocking agents, and other drugs such as ketamine and dexmedetomidine. Did an opiate-naïve patient receive enough fentanyl to produce apnea after a short procedure? Was a long-acting neuromuscular blocking drug administered shortly before the end of a procedure? The metabolism of each drug must be considered as well. Is there something interfering with the metabolism of one or more agents? Are small amounts of many agents working additively to produce unconsciousness and apnea?

Metabolic disturbances in a patient with normal vital signs can also produce prolonged unconsciousness and apnea. Hyponatremia, which can be produced by plasma dilution during transurethral prostate surgery, can lead to severe mental status changes. Hypoglycemia, which may follow insulin administration in a fasting patient, can also produce unconsciousness. Hypocalcemia, which may follow administration of multiple units of banked blood products, can lead to such profound weakness as to produce apnea, especially in malnourished and frail patients.

Finally, prolonged hypotension and hypoperfusion can result in global neurologic sequelae. Misuse and misinterpretation of blood pressure monitoring devices can lead to this type of disaster. Documented cases exist of a patient undergoing surgery and general anesthesia in the sitting position, with a noninvasive blood pressure cuff on the calf. The pressure gradient between the brain and the lower extremities can be significant. Prolonged hypoperfusion of the brain has resulted in adverse outcomes despite "normal" blood pressure readings that were measured in a dependent lower extremity.

### 2. How is normal neuromuscular transmission accomplished?

As the action potential of a motor neuron depolarizes its terminal, an influx of calcium ions causes vesicles containing acetylcholine to fuse with the terminal membrane, releasing acetylcholine into the synaptic cleft. Acetylcholine molecules diffuse across the synaptic cleft

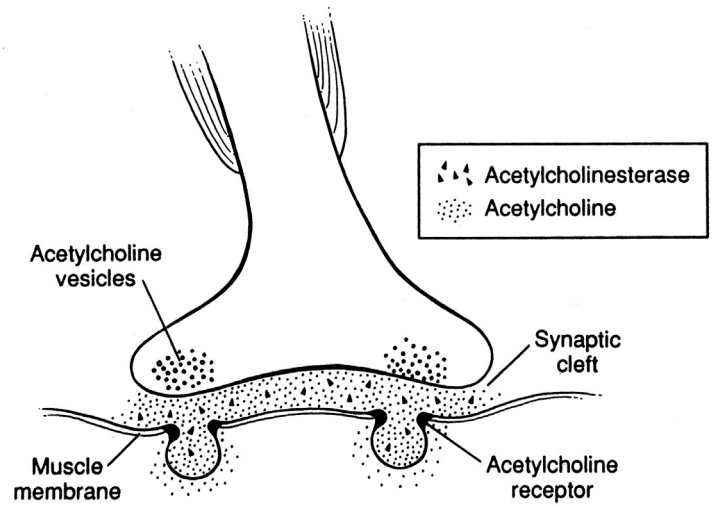


**FIGURE 20-1** ■ Anatomy of the neuromuscular junction. (From Abel M: Depolarizing neuromuscular blockade. In Reed AP, Yudkowitz FS [eds.]: Clinical Cases in Anesthesia, 3rd edition. Churchill Livingstone, Philadelphia, 2005.)

and bind to nicotinic cholinergic receptors on the motor end plate (Figure 20-1). The binding of acetylcholine to these receptors produces conformational changes in transmembrane ion channels that allow sodium and calcium ions to flow into the muscle cell, generating an end plate potential. If enough receptors are bound by acetylcholine, the motor end plate potential will be strong enough to depolarize the perijunctional membrane of the muscle fiber, and voltage-controlled sodium channels within this portion of the muscle membrane will open, producing the beginning of an action potential, which is propagated along the muscle fiber.

### 3. Describe the mechanism of action of succinylcholine.

Succinylcholine is the only depolarizing neuromuscular blocking drug in clinical use. Its blocking properties are due to the chemical mimicry of acetylcholine. Succinylcholine acts as an agonist at the nicotinic cholinergic receptors at the motor end plate, producing a muscle action potential and the muscle fasciculations associated with succinylcholine administration. However, in contrast to acetylcholine, succinylcholine is not metabolized by acetylcholinesterase, and the concentration of succinylcholine in the synaptic cleft remains relatively high for a period of time. As long as succinylcholine remains in the synaptic cleft, it binds to nicotinic cholinergic receptors there. The result is continuous motor end plate depolarization and neuromuscular blockade.

### 4. How is the action of succinylcholine terminated?

In normal subjects, succinylcholine is very rapidly metabolized by plasma pseudocholinesterase. The metabolism of succinylcholine by this enzyme is normally so efficient that only a fraction of the drug injected in a peripheral vein ever reaches the nicotinic cholinergic receptors in the synaptic cleft. As plasma succinylcholine levels decrease with metabolism, succinylcholine molecules diffuse away from the neuromuscular junction, restoring normal neuromuscular transmission.

For normal intubating doses of 0.6–2 mg/kg intravenously, succinylcholine has a duration of action of roughly 5–10 minutes. Several abnormalities can prolong the duration of action of succinylcholine. Hypothermia can slow the action of pseudocholinesterase. Low plasma pseudocholinesterase levels, as found in pregnancy, renal failure, and hepatic failure, can prolong the action of succinylcholine. However, because normal pseudocholinesterase breaks down succinylcholine so efficiently, even low plasma levels of this enzyme usually do not prolong the duration of action of succinylcholine to >30 minutes. Some patients may have genetically determined abnormal pseudocholinesterase that does not break down succinylcholine. Approximately 1 in 50 patients has one normal and one abnormal gene (heterozygous) coding for pseudocholinesterase, which results in a moderately prolonged drug action of 20–30 minutes. Approximately 1 in 3000 patients are homozygous for the gene coding that produces atypical pseudocholinesterase. These patients have virtually no working pseudocholinesterase enzyme and have very prolonged neuromuscular block after administration of a normal intubating dose of succinylcholine, possibly up to 8 hours. In these cases, patients must remain sedated, intubated, and supported with mechanical ventilation until the drug has been metabolized by other pathways. There is presently no clinically approved reversal agent for succinylcholine-induced neuromuscular blockade.

### 5. Explain the potential side effects of succinylcholine administration.

Succinylcholine is the only depolarizing neuromuscular blocking agent available to practicing clinicians. The drug has a host of potentially lethal side effects. With so many nondepolarizing neuromuscular blocking agents available today, why is it still in such widespread clinical use? The answer is its rapid onset of action (30–45 seconds) and superior skeletal muscle relaxation. It is faster and more efficacious than any other paralytic agent given in a reasonable, safe, and effective dose; this may be due to the relative "overdose" that clinicians routinely administer

before laryngoscopy (1.5 mg/kg is four to five times the 95% effective dose [$ED_{95}$] of this drug). In normal metabolizers, the offset of succinylcholine, without pharmacologic antagonism, is reliably faster than that of any other neuromuscular blocking drug. Succinylcholine generally produces optimum relaxation for laryngoscopy, which is extremely important for obtaining adequate laryngeal views. Should intubation and mask ventilation prove to be difficult or impossible, succinylcholine's short duration of action offers the greatest likelihood that patients will recover spontaneous ventilation before hypoxemia ensues. There is no other neuromuscular blocking agent currently available that can provide this type of "fast on, fast off" performance.

So why not use succinylcholine routinely? Many practitioners still do, but it is imperative to understand the potential pitfalls and side effects.

The greatest hazard in the use of succinylcholine is the potential for sudden and severe hyperkalemia, possibly leading to cardiac arrest. In normal patients, serum potassium levels increase approximately 0.5 mEq/L after an intubating dose. Patients with spinal cord injuries, severe burns, crush injuries, intraabdominal sepsis, or prolonged immobilization commonly have proliferation of extrajunctional nicotinic cholinergic receptors. These receptors are the result of upregulation after a relative loss of motor neuron function, and if they are stimulated by succinylcholine, a sudden increase of potassium (several mEq/L) may result. A similar clinical scenario can result from the administration of succinylcholine to young male patients with undiagnosed myopathy. In the early 1970s, the United States Food and Drug Administration (FDA) issued a "black box" warning concerning the use of succinylcholine in young and adolescent boys because of the possibility of hyperkalemic cardiac arrest in patients with undiagnosed myopathy. When the need to secure an airway as quickly as possible arises in a young male patient, the practitioner must use his or her best judgment when weighing the risks and benefits of the airway emergency against the rare, but potentially fatal, possibility of undiagnosed myopathy and hyperkalemia.

Another remote but potentially deadly problem with succinylcholine is that it is a recognized malignant hyperthermia trigger. It must be avoided in any patient who may be susceptible to malignant hyperthermia. Likewise, in any facility where succinylcholine is being used, there must be adequate supplies of malignant hyperthermia rescue drugs, including dantrolene, and medical staff trained to recognize and treat an episode of malignant hyperthermia.

Other complications associated with the administration of succinylcholine include masseter muscle spasm, myalgias, increased intraocular and intracranial pressures, and allergic reactions.

Although not technically a side effect, prolonged administration of succinylcholine as an infusion, especially without neuromuscular monitoring, can lead to phase II neuromuscular blockade. A phase II block is characterized by fade on train-of-four stimulation, the pattern of response typical of nondepolarizing muscle relaxants. Patients in phase II blockade must receive positive pressure ventilation. A phase II block typically resolves within 60 minutes of discontinuing succinylcholine infusion in normal metabolizers. Neostigmine may speed the recovery from a phase II block, although the response to anticholinesterases is unpredictable.

## 6. What are the contraindications to succinylcholine administration?

The contraindications to succinylcholine administration are listed in Box 20-1.

## 7. What is the best and safest neuromuscular blocking drug for rapid-sequence induction?

Rapid-sequence induction and intubation is a technique designed to facilitate expeditious tracheal intubation and protect from aspiration of gastric contents. The objective is to minimize the time between loss of protective airway reflexes and tracheal intubation with a cuffed tracheal tube. The concept of rapid-sequence induction and intubation has evolved slowly starting with the introduction of succinylcholine in the early 1950s and the description of cricoid pressure a decade after that. Much controversy surrounds the current understanding of what constitutes the best set of drugs and techniques to perform the safest rapid-sequence induction and intubation.

The FDA approves only two neuromuscular blocking drugs for this purpose at the present time: succinylcholine and rocuronium. The choice of drug depends on the particular patient and the clinical scenario. Most practicing clinicians agree that succinylcholine produces the most profound relaxation of jaw muscles and laryngeal muscles in the shortest period of time, and it remains the best option in otherwise healthy patients. In addition, the relaxant effect of succinylcholine is almost always limited to 5–10 minutes in normal metabolizers, providing a good possibility for the early return of spontaneous ventilations should intubation or ventilation be more difficult than anticipated. This property of succinylcholine provides a distinct safety advantage over long-acting nondepolarizing neuromuscular blocking drugs in patients who are

**BOX 20-1 Contraindications to Succinylcholine Administration**

Allergy to succinylcholine
Known or suspected malignant hyperthermia
Pseudocholinesterase deficiency or abnormality
Spinal cord transection
Stroke >72 hours old
Prolonged immobilization
Crush injury
Intraabdominal sepsis
Burn injury >72 hours old
Muscular dystrophy
Multiple sclerosis
Amyotrophic lateral sclerosis
Rhabdomyolysis
Significant hyperkalemia

super obese (and may be impossible to ventilate) or have other airway abnormalities that could make laryngoscopy challenging.

As described earlier, succinylcholine has many hidden dangers. A patient in need of rapid-sequence induction and intubation often has sustained trauma, spinal cord injury, prolonged immobilization, or severe infection. In such cases, the risk of extrajunctional cholinergic receptor proliferation is high. Using succinylcholine in these patients poses a risk of severe hyperkalemia. Succinylcholine must be avoided in patients with a known malignant hyperthermia risk, allergy to the drug, or known myopathy. In patients for whom succinylcholine is considered possibly harmful, clinicians must weigh the risks and benefits and consider inducing neuromuscular blockade with rocuronium.

Although succinylcholine 1 mg/kg intravenously usually produces excellent intubating conditions within 45–60 seconds, a "double dose" of rocuronium 1.2 mg/kg must be used to meet the FDA-approved standard for rapid-sequence induction (note that 1.2 mg/kg is four times the $ED_{95}$ dose). Even then, good intubating conditions may not be achieved for 90 seconds in most patients. In terms of unanticipated reactions, rocuronium is a very safe drug. The only significant contraindication to its use is known allergy to steroid-type neuromuscular blocking drugs. So why not use rocuronium routinely for rapid-sequence induction and intubation? Antagonism of neuromuscular blockade with rocuronium 1.2 mg/kg intravenously cannot be accomplished for at least 30 to 60 minutes. Should the patient be impossible to intubate and impossible to ventilate, there is no chance for recovery of spontaneous ventilation before hypoxemia develops. In cases where the patient is at risk for aspiration of gastric contents, and the use of succinylcholine is contraindicated, clinicians must carefully evaluate the patient and consider the potential for impossible ventilation. Prediction of impossible supraglottic ventilation is an indication for awake intubation or awake tracheostomy.

### 8. Are there any drugs that could replace succinylcholine in the future?

Succinylcholine is an old drug that has been available to clinicians for 6 decades. Given all of the potential side effects of this drug, some of them fatal, how come it is still in widespread clinical use? The search is ongoing for nondepolarizing neuromuscular blockers with a succinylcholine-like onset-offset profile; to date, no acceptable substitute has been found. Ultra-short-acting nondepolarizers have been developed but failed clinical trials because of toxicity or other safety concerns. Some of these new drugs await clinical trials in humans and may prove to be useful additions to our armamentarium. However, it is not easy to find a nondepolarizer with an onset of action similar to that of succinylcholine, and any new depolarizing drug developed would almost certainly have the same side-effect profile as succinylcholine owing to its action as a depolarizing agent.

Sugammadex is a novel drug designed to encapsulate rocuronium (and vecuronium) molecules, effectively terminating their bioavailability. Sugammadex may offer a major breakthrough in the antagonism of nondepolarizing neuromuscular blocking drugs. It is more efficacious than neostigmine in antagonizing profound rocuronium-induced and vecuronium-induced blockade. By itself, sugammadex does not affect neuromuscular function, and, in contrast to neostigmine and other anticholinesterases, it does not create cholinergic excess. Sugammadex would effectively allow clinicians to use large overdoses of rocuronium to produce profound relaxation rapidly for however brief a time period desired, followed by complete antagonism within 1–2 minutes. Use of sugammadex could end the need for development of ultra-short-acting nondepolarizers to replace succinylcholine. Although sugammadex is approved and widely used in Europe, it has not yet gained FDA approval for use in the United States. In rare cases, a hypersensitivity reaction may occur shortly after administration of sugammadex.

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CASE 21

# Nondepolarizing Neuromuscular Blockade

**Barbara M. Dilos, DO • James B. Eisenkraft, MD**

## QUESTIONS

1. Describe how nondepolarizing neuromuscular blocking drugs produce skeletal muscle relaxation.
2. How do nondepolarizing neuromuscular blocking drugs differ from one another?
3. How do potent inhaled anesthetics, local anesthetics, and antibiotics affect nondepolarizing neuromuscular blockade?
4. Describe the effects of metabolic derangements on nondepolarizing neuromuscular blockade.
5. How do burns affect the use of nondepolarizing neuromuscular blocking drugs?
6. How do other drugs and certain disease states affect nondepolarizing neuromuscular blockade?

A 22-year-old woman presented for abdominoplasty. Her weight was 75 kg and her height was 160 cm. Past medical history was significant for seizure disorder treated with phenytoin 100 mg twice daily. She had been seizure-free for the past 6 years. She had never received anesthesia before. Her plasma phenytoin level was within therapeutic range. After placement of monitors, fentanyl 100 μg and midazolam 2 mg were administered. General anesthesia was induced with propofol 200 mg, followed by vecuronium 8 mg for neuromuscular blockade. Intubating conditions were excellent. Anesthesia was maintained with isoflurane 2% in 70% oxygen/30% nitrous oxide. The end-tidal isoflurane concentration was 1.2%. During preparation of the abdomen 10 minutes later, she moved. Bispectral index was 45. Train-of-four stimulation of the ulnar nerve at the wrist demonstrated four twitches of the adductor pollicis brevis muscle.

### 1. Describe how nondepolarizing neuromuscular blocking drugs produce skeletal muscle relaxation.

Nondepolarizing neuromuscular blocking drugs (NMBDs) produce relaxation of voluntary (skeletal or striated) muscles by the following mechanisms:

- Inhibit the effect of acetylcholine by competing with it as they bind to the alpha subunit of the nicotinic acetylcholine receptor at the postjunctional membrane
- Block prejunctional acetylcholine receptors at the motor nerve terminal, decreasing acetylcholine release in response to motor nerve stimulation
- Noncompetitively block open postjunctional acetylcholine channels

### 2. How do nondepolarizing neuromuscular blocking drugs differ from one another?

Although numerous NMBDs are available for clinical use, structurally they fall into one of two types: steroid-based or benzylisoquinolinium compounds. Steroidal NMBDs include rocuronium, vecuronium, pancuronium, and pipecuronium. Benzylisoquinolinium compounds include atracurium, cisatracurium, mivacurium (no longer available in the United States), and doxacurium. NMBDs are usually classified according to their durations of action as short-acting, intermediate-acting, or long-acting (Table 21-1). The choice of NMBDs depends on several factors, including onset time, duration of action, elimination time, potency, and route or routes of elimination. In addition, some NMBDs may have desirable or undesirable effects on the cardiovascular and respiratory systems. These effects may be mediated by the autonomic nervous system or histamine receptors or both.

Clinical factors that potentially affect the responses to nondepolarizing NMBDs include age, gender, weight, body composition, hepatic reserves, renal function, cardiac status, acid-base balance, hypothermia, anesthetic agents, and depth of anesthesia.

### 3. How do potent inhaled anesthetics, local anesthetics, and antibiotics affect nondepolarizing neuromuscular blockade?

Many drugs and conditions influence NMBD pharmacology, some potentiating and others inhibiting (Table 21-2). Certain medications have direct effects on neuromuscular transmission, whereas others interact at different sites. Some have more than one mechanism of action, which

TABLE 21-1 **Properties of Nondepolarizing Neuromuscular Blocking Drugs**

| Drug | $ED_{95}$ (mg/kg) | Onset Time/ Clinical $RI_{25–75}$ (min) | Elimination Half-Life* (min) | Route(s) of Elimination | Cardiovascular Effects | Histamine Release | Autonomic Ganglion Block | Intubating Dose (mg/kg) |
|---|---|---|---|---|---|---|---|---|
| Atracurium | 0.2 | Slow/11–23 | 20 | Nonenzymatic ester hydrolysis<br>Hoffman elimination | None | Skin flushing<br>Hypotension<br>Bronchospasm | None | 0.5–0.6 |
| Cisatracurium | 0.05 | Slow/11–23 | 20 | Nonenzymatic ester hydrolysis<br>Hoffman elimination | None | None | None | 0.15–0.2 |
| Mivacurium | 0.07 | Slow/6–8 | 18 | Hydrolysis by plasma cholinesterase | None | Yes | None | 0.2–0.25 |
| Pancuronium | 0.07 | Slow/24 | 145 | Renal; some hepatic | Tachycardia | None | None | 0.08–0.12 |
| Rocuronium | 0.3 | Rapid/10–15 | 60–75 | Hepatic; some renal | None | None | None | 0.6–1; 1.2 (RSI) |
| d-Tubocurarine | 0.5 | Slow/25–35 | 80 | Renal; minimal hepatic | Hypotension<br>Bradycardia | Skin flushing | Yes | 0.5–0.6 |
| Vecuronium | 0.05 | Slow/10–15 | 62 | Hepatic; some renal | None | None | None | 0.1–0.2 |

*$ED_{95}$*, Mean effective dose producing 95% twitch height depression; *$RI_{25–75}$*, time interval between recovery from 25%–75% twitch height; *RSI*, rapid-sequence induction.
*Time for plasma concentration to decrease by 50%.

TABLE 21-2 **Interactions with Nondepolarizing Neuromuscular Blocking Drugs**

| Potentiation | Resistance |
|---|---|
| All potent inhaled agents | Methylxanthines (e.g., theophylline, aminophylline) |
| Local anesthetics | Phenytoin |
| β-adrenergic blockers | Carbamazepine (e.g., Tegretol) |
| Calcium-channel blockers | Burns |
| Aminoglycosides | Steroids |
| Polymyxin | |
| Lincosamides (e.g., clindamycin) | |
| Dantrolene | |
| Class IA antiarrhythmics | |
| Cyclosporine | |
| Lithium | |
| Hypermagnesemia | |
| Hypocalcemia | |
| Hypokalemia | |
| Metabolic or respiratory acidosis | |
| Myasthenia gravis | |
| Eaton-Lambert syndrome | |

results in potentiation or reduction in effect of NMBDs. Sites where interference occurs include presynaptic motor end plates, nerve terminals, nicotinic receptors, postsynaptic muscle membranes, central nervous system, and intracellular excitation-contraction coupling. Dantrolene and calcium also affect intracellular excitation-contraction coupling, affecting activity of NMBDs. Although dantrolene does not block neuromuscular transmission, neuromuscular blockade is potentiated because it depresses mechanical responses to stimulation. Calcium enhances excitation-contraction coupling, decreasing sensitivity to NMBDs.

Potent inhaled anesthetics potentiate neuromuscular blocking effects by direct action on the central nervous system and inhibition of postsynaptic nicotinic acetylcholine receptors. Isoflurane and sevoflurane inhibit neuromuscular transmission at nicotinic receptors of the neuromuscular junction. This influence is dose-dependent so that at deeper levels of anesthesia (greater minimum alveolar concentration equivalents), the 95% effective dose ($ED_{95}$) of NMBDs is decreased. Among the older agents, isoflurane has a greater potentiating effect than enflurane and halothane. Of the newer agents, desflurane has a greater effect than sevoflurane. Desflurane and sevoflurane have a greater effect than isoflurane (i.e., desflurane > sevoflurane > isoflurane > halothane > enflurane).

Local anesthetics and class IA antiarrhythmic drugs potentiate nondepolarizing NMBDs by blocking sodium channels. They decrease end plate and muscle membrane ion conductance, decreasing propagation of the action potential. Ester-type local anesthetics have a greater effect than amide local anesthetics on sodium channels.

Some antibiotics potentiate nondepolarizing neuromuscular blockade. Older drugs such as neomycin, streptomycin, and polymyxin are less of a problem because they are so infrequently used. Aminoglycosides such as gentamicin and tobramycin potentiate nondepolarizing NMBDs by decreasing release of acetylcholine at the motor nerve terminal and by decreasing the sensitivity of the acetylcholine receptor to acetylcholine. The steroidal nondepolarizing NMBDs are affected to a greater extent than the benzylisoquinolinium compounds. Lincosamides such as clindamycin, which also have local anesthetic properties, exert a potentiating effect only when used in very large doses. Penicillins, cephalosporins, tetracyclines, erythromycin, and metronidazole do not affect nondepolarizing blockade in doses used clinically.

### 4. Describe the effects of metabolic derangements on nondepolarizing neuromuscular blockade.

Acidosis, both respiratory and metabolic, potentiates blockade, whereas alkalosis decreases it. Hypokalemia, hypocalcemia, and hypermagnesemia also potentiate the effect of nondepolarizing NMBDs.

### 5. How do burns affect the use of nondepolarizing neuromuscular blocking drugs?

Burn injury can alter both the pharmacokinetic and the pharmacodynamic properties of nondepolarizing NMBDs. Succinylcholine is contraindicated in burn patients from about 24 hours after injury until the burn has healed because it may cause hyperkalemic cardiac arrest. Nondepolarizing NMBDs are the muscle relaxants of choice for burn care and skin grafting. In these patients, owing to proliferation of extrajunctional nicotinic cholinergic receptors, there is resistance to NMBDs (i.e., the $ED_{95}$ is increased). Some patients may require two to five times the usual intubating dose. Despite the increased $ED_{95}$, the duration of action does not appear to be increased.

### 6. How do other drugs and certain disease states affect nondepolarizing neuromuscular blockade?

β-adrenergic and calcium-channel blockers potentiate neuromuscular blockade in vitro but not in vivo. Magnesium, through its interaction with calcium, enhances neuromuscular blockade. Dantrolene directly suppresses calcium release in skeletal muscle, acting as a muscle relaxant. Cyclosporine, an immunosuppressant, also potentiates the effects of vecuronium and atracurium.

Some drugs inhibit the action of nondepolarizing NMBDs. Phenytoin induces increased liver enzyme activity, affecting relaxants that are eliminated by the hepatic route. Patients receiving long-term therapy with phenytoin develop resistance to pancuronium, vecuronium, and rocuronium (i.e., $ED_{95}$ is increased). Proposed mechanisms for this resistance include increased metabolism, decreased sensitivity at the receptor site, increased receptor number, and increased end plate anticholinesterase activity. Steroids antagonize the effects of nondepolarizing neuromuscular blockers, possibly because of facilitation of acetylcholine release at the presynaptic motor nerve terminal. Prolonged administration of steroids and NMBDs in the critical care setting may result in myopathy.

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CASE 22

# Antagonism of Nondepolarizing Neuromuscular Blockade

**Barbara M. Dilos, DO • James B. Eisenkraft, MD**

QUESTIONS

1. Describe the principles underlying antagonism of residual nondepolarizing neuromuscular blockade.
2. How is acetylcholinesterase inhibited?
3. Name clinically relevant acetylcholinesterase inhibitors and their onsets of action.
4. What are the usual doses and expected durations of action for acetylcholinesterase inhibitors?
5. Why is it necessary to administer an anticholinergic drug with an acetylcholinesterase inhibitor?
6. What other class of drugs is under investigation for antagonism of nondepolarizing neuromuscular blockade?

A 36-year-old woman underwent laparoscopic bilateral tubal ligation. She was otherwise in good general health. Tracheal intubation was facilitated with rocuronium, 0.6 mg/kg. No additional neuromuscular blocking drug (NMBD) was administered. On completion of surgery, train-of-four (TOF) monitoring demonstrated two twitches. The decision was made to antagonize the residual neuromuscular blockade.

## 1. Describe the principles underlying antagonism of residual nondepolarizing neuromuscular blockade.

Residual neuromuscular blockade can have serious consequences in the postoperative period. A study of patients during the first 15 minutes after admission to the postanesthesia care unit found that 0.8% developed critical respiratory events. Mean TOF ratio was 0.62 in patients who experienced these events compared with TOF ratios of 0.98 in patients who experienced no event. Complete recovery from neuromuscular blockade should be the goal for every anesthetic. TOF monitoring is an excellent way to assess neuromuscular blockade. Using a peripheral nerve stimulator, one can assess residual blockade by the ratio of the fourth to first twitch amplitude. A TOF ratio greater 0.9 should be achieved before tracheal extubation.

A competitive nondepolarizing neuromuscular block can be terminated spontaneously or pharmacologically. Over time, spontaneous recovery occurs as the NMBD diffuses away from receptor sites and is eliminated by metabolism or excretion. As the concentration of NMBD in plasma and at effect sites decreases, acetylcholine molecules gain greater access to nicotinic cholinergic receptors at the motor end plates.

Pharmacologic agents may be used to increase the amount of acetylcholine at the neuromuscular junction by inhibiting the enzyme acetylcholinesterase. Inhibition of acetylcholinesterase produces a competitive inhibition of the NMBD at receptors. The neuromuscular block can be partially or fully antagonized, depending on the relative amounts of acetylcholine and NMBD molecules present.

## 2. How is acetylcholinesterase inhibited?

Acetylcholinesterase hydrolyzes acetylcholine at the neuromuscular junction. By inhibiting the action of acetylcholinesterase, increased concentrations of acetylcholine accumulate at the neuromuscular junction. Acetylcholine competes with NMBDs for nicotinic receptor sites at the postjunctional membrane. Acetylcholinesterase inhibition also results in presynaptic generation of an action potential that may spread retrograde up the axon and cause other nerves in the same motor unit to discharge.

Acetylcholinesterase molecules possess an esteratic and an anionic binding site. Anticholinesterases inactivate the enzyme by reversibly binding to one or both of these sites. The stability of the bond determines the duration of the inhibition. Edrophonium binds electrostatically at the anionic site, forming a bond that is weak and resulting in a relatively short duration of action. It also has prejunctional effects, which promote the release of acetylcholine from the motor nerve terminal. Neostigmine and pyridostigmine form covalent bonds at the esteratic site to form a carbamyl ester, which leads to a more prolonged duration of effect.

Organophosphate compounds (e.g., parathion, malathion) inhibit acetylcholinesterase by the formation of irreversible bonds. These compounds are normally used as pesticides but have been used as chemical weapons because they are absorbed by ingestion, inhalation, and transdermally. Occasionally, a patient may present with a cholinergic crisis (see Chapter 24) because of organophosphate poisoning.

### 3. Name clinically relevant acetylcholinesterase inhibitors and their onsets of action.

Edrophonium, neostigmine, and pyridostigmine are the acetylcholinesterase inhibitors used clinically. They are all quaternary ammonium compounds; they do not penetrate the blood-brain barrier. Although in theory, these agents have the ability to affect cholinergic function in the central nervous system, in practice, they do not reach a high enough concentration to do so. However, physostigmine is a tertiary ammonium compound that readily penetrates the blood-brain barrier. For this reason, it is not used for antagonism of neuromuscular blockade. Edrophonium does not inhibit plasma (pseudo-) cholinesterase, whereas neostigmine does.

The onsets of action of the anticholinesterase drugs are as follows:

- Edrophonium—1 to 2 minutes
- Neostigmine—7 to 11 minutes
- Pyridostigmine—15 minutes

### 4. What are the usual doses and expected durations of action for acetylcholinesterase inhibitors?

Dose recommendations depend on the particular NMBD to be antagonized and the intensity of neuromuscular blockade. The more intense the block, the longer the time for adequate antagonism. When the spontaneous recovery of T1 is 25% or more or when four twitches are present at a ratio of less than 0.3 to 0.4 to TOF stimulation, a full antagonism dose is recommended. If only two twitches are present, recovery to a TOF ratio of 0.9 would take much longer. To antagonize lesser degrees of blockade, smaller doses of anticholinesterase may be administered. If the anticholinesterase is given too early (i.e., when no twitches can be elicited), the duration to recovery is unknown, and attempts to antagonize the block are likely to be unsuccessful.

Neostigmine appears to be a better antagonist than edrophonium when a profound neuromuscular block is present, such as produced by long-acting nondepolarizing NMBDs. The degree of reversal depends directly on the dose of anticholinesterase administered. If spontaneous recovery of T1 is 50%, a full dose of anticholinesterase would not speed recovery significantly. A smaller dose would be adequate and help protect from side effects. The recommended dose range for neostigmine is 0.04 to 0.07 mg/kg and for edrophonium is 0.5 to 1 mg/kg. A ceiling effect is observed so that additional doses are ineffective. On a weight (mg) basis, neostigmine is 5 times more potent than pyridostigmine and about 12 times more potent than edrophonium. Their durations of action range from 60 to 120 minutes (Table 22-1).

Neostigmine and pyridostigmine bind to anionic and esteratic sites of acetylcholinesterase molecules. This binding accounts for their longer duration of action. Edrophonium interacts with the anionic site of the molecule by hydrogen and electrostatic bonding, resulting in a shorter duration of action. Edrophonium is excreted via the kidneys intact. In contrast, neostigmine is broken down to a carbamyl ester.

### 5. Why is it necessary to administer an anticholinergic drug with an acetylcholinesterase inhibitor?

Acetylcholine has both nicotinic and muscarinic agonist effects. Increasing acetylcholine concentrations at nicotinic receptors of the neuromuscular junction is the goal for reversal, but many muscarinic effects are undesirable. These effects include profound bradycardia, junctional rhythm, asystole, salivation, increased gastrointestinal motility, increased bronchopulmonary secretions, and bronchospasm. An increased risk of postoperative nausea and vomiting has been implicated, but this is controversial.

When an anticholinesterase drug is administered, coadministration of an antimuscarinic agent, such as atropine or glycopyrrolate, is necessary to prevent potentially

TABLE 22-1 **Commonly Used Acetylcholinesterase Inhibitors and Antimuscarinic Agents**

| | Edrophonium | Neostigmine | Pyridostigmine |
|---|---|---|---|
| Dose (mg/kg) | 0.5-1 | 0.04-0.07 | 0.2 |
| Onset (min) | 1-2 | 7-11 | 15 |
| Duration (min) | 60-120 | 60-120 | 60-120 |
| Atropine | | | |
| Dose (mg/kg) | 0.01 | 0.02 | 0.02 |
| Onset (min) | 1 | 1 | 1 |
| Duration (min) | 30 | 30 | 30 |
| Glycopyrrolate | | | |
| Dose (mg/kg) | | 0.01 | 0.01 |
| Onset (min) | | 2-3 | 2-3 |
| Duration (min) | | 60 | 60 |

serious side effects. The time to onset of action is much shorter for atropine than for glycopyrrolate. Consequently, atropine is a better pairing with edrophonium, which also has a more rapid onset of action than neostigmine. However, atropine must be administered before edrophonium, and edrophonium should be administered only after the effects of atropine have been observed. This timing of administration ensures the vagolytic effect of atropine has taken place before the bradycardic effect of edrophonium. Glycopyrrolate has a slower onset and may be mixed with neostigmine because they possess similar delays to onset.

### 6. What other class of drugs is under investigation for antagonism of nondepolarizing neuromuscular blockade?

A novel approach to reversal of nondepolarizing block is the use of sugammadex, a gamma cyclodextrin molecule designed specifically to bind steroidal nondepolarizing muscle relaxants. Administered intravenously, sugammadex molecules encapsulate steroidal NMBD molecules, rocuronium and vecuronium, to form a stable complex that has no neuromuscular blocking properties. Rocuronium and vecuronium molecules dissociate from receptors at the motor end plates and diffuse down their concentration gradient to become bound to sugammadex in the plasma. The time to complete recovery from a profound rocuronium or vecuronium block (i.e., with no response to TOF stimulation) occurs within 2 to 3 minutes. Sugammadex appears to have few side effects, in contrast to neostigmine and edrophonium, and does not require the concomitant administration of an antimuscarinic. Although sugammadex has been used widely in Europe and elsewhere, at the time of this writing it is not approved for clinical use in the United States by the Food and Drug Administration because of concerns for allergic reactions.

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CASE 23

# Monitoring the Neuromuscular Junction

**Barbara M. Dilos, DO • James B. Eisenkraft, MD**

## QUESTIONS

1. Why is monitoring of neuromuscular blockade important whenever a neuromuscular blocking drug is administered?
2. What are the basic principles of neuromuscular blockade monitoring?
3. Why is a supramaximal stimulus used for neuromuscular blockade monitoring?
4. Describe the clinically available devices used to monitor neuromuscular blockade.
5. Describe patterns of stimulation used to monitor neuromuscular blockade and implications of evoked responses.
6. How can you evaluate this patient who has no response to train-of-four stimulation?

A 50-year-old, healthy, 70-kg man (body mass index 24 kg/m$^2$) is undergoing an inguinal hernia repair. He is tracheally intubated after administration of 70 mg of rocuronium (1 mg/kg) and is receiving sevoflurane in oxygen/air and fentanyl. At 30 minutes into the procedure, the surgeon complains that the patient is "tight," and an additional rocuronium dose of 20 mg (approximately 0.3 mg/kg) is administered. The surgeon announces 5 minutes later that he is finished. You apply train-of-four (TOF) stimulation over the ulnar nerve at the wrist, but no twitch responses are elicited.

### 1. Why is monitoring of neuromuscular blockade important whenever a neuromuscular blocking drug is administered?

Neuromuscular blocking drugs (NMBDs) are widely used to facilitate tracheal intubation and to provide and maintain optimal operating conditions. In the past, neuromuscular blockade was commonly evaluated on the basis of clinical criteria alone, such as a surgeon's assessment of inadequate relaxation, patient movement, attempts at breathing "against the ventilator," or observation of "curare clefts" in the capnograph tracing. For certain procedures, excessive doses of an NMBD may be administered. Because there is considerable variability among patients' sensitivities to NMBDs, clinical criteria alone cannot be used to accurately asses depth of, or recovery from, neuromuscular blockade. A quantitative and documentable method of assessment is necessary. Monitoring neuromuscular blockade in response to administration of a NMBD allows titration of doses to the desired effect. Adequate relaxation can be achieved without administering unnecessary doses of a NMBD and recovery from relaxation becomes more predictable. Monitoring to ensure adequate recovery from neuromuscular blockade is important to prevent respiratory failure after tracheal extubation, which may occur as a problem in the postanesthesia care unit.

### 2. What are the basic principles of neuromuscular blockade monitoring?

Monitoring of neuromuscular transmission requires supramaximal stimulation of a motor nerve and measurement of the response evoked in the innervated muscle. NMBDs have no direct effect on muscle; if stimulation is applied directly over a muscle, that muscle contracts despite complete blockade at the neuromuscular junction. It is important to stimulate a motor nerve in a location where direct muscle stimulation cannot occur and only the indirectly evoked response (i.e., via the neuromuscular junction) is assessed.

It is essential to know which muscle to observe in response to indirect stimulation. When the ulnar nerve is stimulated, thumb adduction by the adductor pollicis brevis muscle is the appropriate site to monitor. Finger and wrist flexion should be ignored because they are likely due to direct stimulation if electrodes are placed over the forearm muscles.

During recovery from anesthesia, the most important muscles are the muscles of respiration and airway patency, but these muscles (e.g., diaphragm, laryngeal) cannot be monitored during clinical anesthesia. The ulnar nerve–adductor pollicis brevis combination is easily monitored and is used as a surrogate.

### 3. Why is a supramaximal stimulus used for neuromuscular blockade monitoring?

Motor nerves consist of numerous nerve fibers, each of which innervates a motor unit in the muscle. Because the muscle's total response is required to assess neuromuscular blockade, all of the nerve fibers must be reliably stimulated. In this way, any decrement in muscle contraction is due to neuromuscular junction blockade and not due to a failure to stimulate all of the fibers in the motor nerve.

In a normal unparalyzed patient who has surface electrodes placed over the ulnar nerve, as the intensity (mA) of nerve stimulation is gradually increased, the force of contraction of the muscle increases until all of the nerve fibers are stimulated. Further increase in stimulus intensity does not result in further increase in evoked response. The stimulus producing a maximal muscle response is called the maximal stimulus. Stimuli of greater intensity are termed supramaximal. During neuromuscular blockade monitoring, supramaximal stimuli (usually 120% of maximal stimulus current) are used to ensure that all nerve fibers are stimulated. The maximal (and supramaximal) stimulus varies among individual patients, depending on the amount of tissue between the skin and the nerve. The negative stimulating electrode should always be placed distal to the positive one because this configuration results in the greatest muscle response.

### 4. Describe the clinically available devices used to monitor neuromuscular blockade.

In principle, neuromuscular blockade monitoring requires two devices: a peripheral nerve stimulator to deliver the supramaximal stimulus and a device, which may be mechanical or electrical, to measure the response evoked in the muscle.

#### *Peripheral Nerve Stimulators*

Stimulation of a nerve fiber is a function of the amount and duration of current applied. Modern peripheral nerve stimulators are designed to deliver a constant current, despite changes in resistance that may develop over time between the surface electrodes and the nerve. The current is delivered in square wave pulses of 200 μsec (0.2 msec) duration. At this pulse width, motor nerves but not sensory nerves are stimulated; this is because stimulation of sensory nerves requires a longer pulse duration (approximately 1 msec).

Peripheral nerve stimulators are the devices most commonly used to facilitate assessment of neuromuscular blockade in clinical settings. With only a peripheral nerve stimulator, the clinician must evaluate the force of contraction by observing or palpating thumb adduction. Such observations are difficult to quantify and are subject to considerable interobserver variability.

The following devices may be used to quantify evoked response.

#### *Mechanomyography*

Historically, mechanomyography (MMG) has been the "gold standard" for objective monitoring of a muscle's evoked response. Stimulation of a motor nerve produces isometric contraction of the innervated muscle, commonly the adductor pollicis brevis. The mechanical force developed is measured using a force transducer connected to the thumb. For accurate measurements, such as for research purposes, it is necessary to preload the muscle with 200–300 g of tension, and the force vector (i.e., the direction of thumb movement) must be perpendicular to the force transducer. The force transducer is calibrated in kg-force, and the output of the force transducer is displayed graphically or digitally on a monitor. In an unparalyzed patient, delivery of supramaximal stimuli to the nerve results in a maximal (100%) response in the muscle. This response is considered to represent 100% and is used as a reference for subsequent evoked responses after the patient has received an NMBD.

Although a purpose-designed arm board with built-in force transducer has been commercially available, MMG is not practical for routine clinical use. The force transducer is bulky, the muscle must be preloaded with a specific tension, and the arm must be abducted and kept immobile so that there is no interference with movement of the thumb.

#### *Electromyography*

Electromyography (EMG) records the compound muscle action potential in response to peripheral motor nerve stimulation. Stimulating electrodes are placed over the peripheral motor nerve, and recording electrodes are placed over the innervated muscle. The magnitude of the evoked response is measured. Clinically, EMG is easier to use than MMG because muscle preloading and precise force vector measurements are unnecessary; both arms can be adducted at the patient's side. As a result, EMG has replaced MMG in neuromuscular studies conducted more recently. Integrated EMG monitoring is commercially available only as a modality in the Neuromuscular Transmission Module of the GE S/5 monitoring system (GE Healthcare, Datex-Ohmeda S/5 NMT Module (Datex-Ohmeda Inc. P.O.Box 7550, Madison, Wisconsin, 53707. USA)). Similar to MMG, the EMG response is first calibrated to 100% in an unparalyzed patient, and subsequent responses are displayed as a percentage of the initial response.

#### *Accelerography*

Accelerography is based on the principle that force is the product of mass times acceleration ($F = ma$). If mass is kept constant, force (of contraction) is directly proportional to acceleration. Accelerography uses a piezoelectric transducer attached to the thumb (the mass of which remains constant) to determine the rate of angular acceleration in response to nerve stimulation. The size of the acceleration output signal is displayed digitally and graphically. Accelerography requires unobstructed thumb movement, similar to MMG. This technology is commercially available for clinical use and has been widely employed in clinical research studies. It provides a simple and objective method of assessing neuromuscular blockade. It eliminates interobserver variability associated with subjective clinical observation of evoked responses, on which peripheral nerve stimulators rely.

### Kinemyography

Kinemyography (KMG) is clinically available as a modality in the Neuromuscular Transmission Module of the GE S/5 monitoring system. KMG uses a piezoelectric strip incorporated into a flexible U-shaped ("boomerang") device that is placed between the thumb and index finger. The U-shaped device, mechanosensor, is designed to mimic a MMG-like preload. Movement of the thumb produces a redistribution of electrical charge across the piezoelectric membrane. The voltage produced by movement of the thumb is measured, processed, and displayed digitally and graphically on the monitor screen. Results have been shown to correspond closely with MMG, making it a reasonable option for clinical use.

## 5. Describe patterns of stimulation used to monitor neuromuscular blockade and implications of evoked responses.

Several patterns of motor nerve stimulation are used to monitor the neuromuscular junction.

### Single Twitch

Single twitch is the simplest form of monitoring the neuromuscular junction. A single supramaximal stimulus is applied for 0.2 msec. The size ("height") of the twitch response remains at baseline until 75% of neuromuscular junction receptors are occupied by NMBD and disappears completely when 90%–95% of the receptors are occupied. The single stimulus (twitch) is mostly used in research where relative potencies of NMBDs can be measured and rates of recovery can be quantified. NMBDs are compared by their $ED_{95}$, which is the effective dose that produces a 95% decrease in twitch height.

Before administration of NMBDs, a control twitch response is required for later comparison, which makes this modality impractical for clinical use. Application of a single stimulus at a rate of 1/sec (1 Hz) results in no decrement in twitch height in an unparalyzed patient. In the presence of a depolarizing neuromuscular block, the twitch response is uniformly smaller and increases as recovery occurs. In the presence of an incomplete nondepolarizing neuromuscular block, there is progressive decrease (fade) in twitch height with each subsequent stimulus. Return to the control twitch height after administration of NMBDs does not mean that 100% of neuromuscular receptors are unoccupied; 75% of neuromuscular junction receptors may still be occupied because of the large margin of safety in normal neuromuscular transmission.

### Tetanic Stimulation

Tetanic stimulation (Figure 23-1) is usually applied at a frequency of 50 Hz, (i.e., 50 stimuli/sec) for 5 seconds. In unparalyzed patients, stimulation of a motor nerve at 50 Hz results in sustained muscle contraction with a force greater than that achieved by a single stimulus. In the presence of depolarizing neuromuscular blockade, tetanic stimulation produces sustained contraction of smaller force (i.e., no fade in muscle response). In the presence of incomplete nondepolarizing neuromuscular blockade, the response is not sustained (i.e., there is fade).

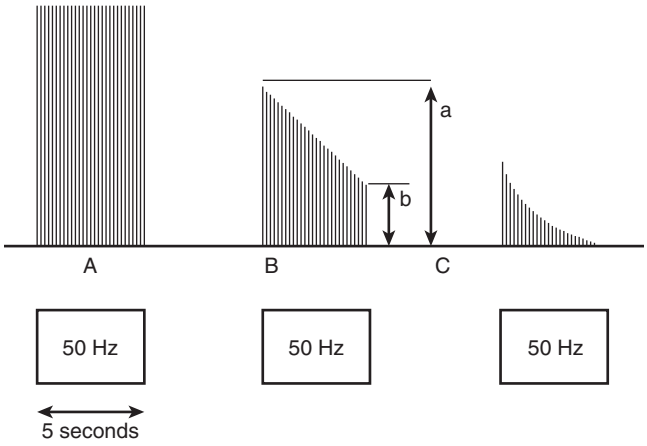


**FIGURE 23-1** ■ Tetanic stimulation. **A,** In the absence of a neuromuscular blocker, a 50-Hz tetanic train for 5 seconds produces a muscular response of constant intensity. **B,** In the presence of increasing nondepolarizing neuromuscular block, there is depression of the initial contraction but also fade with subsequent pulses. The fade ratio is equal to the amplitude of the final contraction (the end of the tetanus) divided by the amplitude of the first contraction (the start of the tetanus) and is represented by *b/a*. **C,** As nondepolarizing neuromuscular block increases, fade increases, and if the block were deep enough, the response ultimately would disappear altogether. (Redrawn from Pollard BJ: Neuromuscular imaging. Curr Anesth Crit Care 15:383, 2004.)

### Train of Four

As mentioned earlier, monitoring twitch response to single stimuli is impractical clinically because it requires a control twitch (Tc) measurement before the onset of neuromuscular blockade. The answer to this problem is the TOF pattern of stimulation. The motor nerve is stimulated with four successive supramaximal 0.2-msec stimuli delivered at 2 Hz, and the ratio of the size of the fourth twitch to the first twitch (T4/T1 or fade ratio) is measured (Figure 23-2). It has been shown that the T4/T1 ratio is equivalent to the

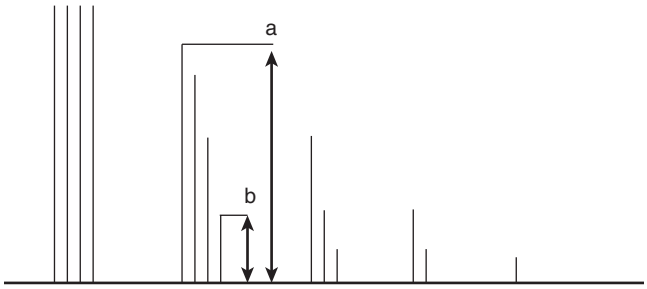


**FIGURE 23-2** ■ Responses to a TOF stimulation pattern. The four stimuli are separated by 0.5 second each. The height of each bar represents strength of muscular contraction. Initially, all four responses are equal. As nondepolarizing neuromuscular blockade increases, the fourth twitch is depressed earliest, and the ratio b/a is known as a TOF ratio. As the block deepens, the four responses decrease further, disappearing in the following order: fourth, third, second, first. (Redrawn from Pollard BJ: Neuromuscular imaging. Curr Anesth Crit Care 15:383, 2004.

T1/Tc ratio measured by MMG, and because TOF measurements do not require a control twitch measurement, TOF has become the modality of choice in clinical practice.

In the absence of nondepolarizing neuromuscular blockade, the TOF ratio is approximately 1. When 70%–75% of neuromuscular junction receptors are occupied by NMBD, the fourth response (T4) is lost. When 95% of neuromuscular junction receptors are occupied, all the twitches disappear.

TOF stimulation is very useful in assessing neuromuscular blockade. A T4/T1 ratio greater than 0.9 is generally considered a good indicator of adequate: respiratory muscle function, laryngeal muscle function (i.e., airway patency and protection), vital capacity, and maximum expiratory force. It also correlates with a strong handgrip and ability to perform a 5-second head lift. When monitoring TOF by manual palpation, the degree of fade might be easily underestimated.

### *Double-Burst Stimulation*

The accuracy of manual TOF assessment by clinicians is poor, and it is frequently difficult to detect the presence of fade. Double-burst stimulation (DBS) was suggested as a method to improve manual detection of fade. Instead of four stimuli (TOF), two bursts, each consisting of three brief 50-Hz tetanic stimuli, are used. They are separated by an interval long enough to permit muscle relaxation, usually 750 msec (Figure 23-3). The DBS is repeated every 12–15 seconds. Fade is more easily appreciated with DBS than with TOF because only two responses, one to each burst, are compared.

### *Posttetanic Facilitation and Posttetanic Count*

Posttetanic facilitation (PTF) is characteristic of nondepolarizing NMBDs. If a patient receives a nondepolarizing NMBD, the response to single stimuli (1 Hz) decreases, TOF ratio decreases, and there is fade in response to 5 seconds of 50-Hz tetanic stimulation. If single stimuli are applied (and evoke a small twitch response), then 50-Hz stimulation is delivered for 5 seconds (producing fade), followed by a hiatus in stimulation for 3 seconds, followed by 20 single stimuli at 1 Hz; the responses to these posttetanic stimuli are greater than the pretetanic ones (i.e., they are potentiated), and then gradually decrease in size (i.e., they fade). The degree and duration of the PTF depend on the degree of neuromuscular blockade.

Posttetanic count (PTC) is the application of the phenomenon of PTF to assess deeper levels of neuromuscular blockade, when there is no response to stimulation at 1 Hz, to TOF, or to 50 Hz. In this case, the above-described sequence of stimulation is applied, and the number of posttetanic twitch responses is counted (Figure 23-4). The number of evoked twitch responses is called the PTC and is related to the depth of neuromuscular blockade. Initially, there may be a PTC of 0 or 1 indicating profound neuromuscular blockade. The PTC increases as recovery occurs and correlates with the time to initial recovery of the twitch response to a single stimulus or reappearance of the first twitch (T1) in the TOF. If the PTC is zero, the time to recovery is indeterminate.

## 6. How can you evaluate this patient who has no response to train-of-four stimulation?

Ideally, neuromuscular monitoring will have been used throughout the case with a control TOF at the beginning and intermittently thereafter; this ensures that the nerve stimulator is functioning. If the stimulator is applied only at the end of the case and there appears to be no elicited twitch response, the functionality of the nerve stimulator should be checked. One way is to test it on oneself, using a small current. Some peripheral nerve stimulators display the current flowing (in mA), which ensures that the electrodes and contacts are adequate and that there is a completed electrical circuit. A recorded current of zero

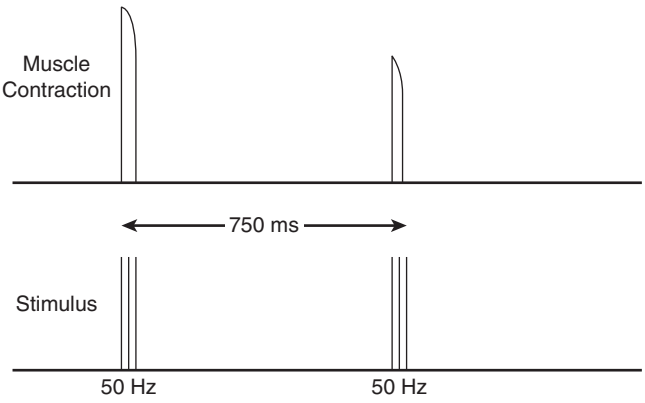


**FIGURE 23-3** ■ Double burst stimulation (DBS). Three discrete stimuli at a base frequency of 50 Hz each produce a muscle contraction that is essentially a small, fused tetanus. The double-burst ratio is the height of the second response divided by the height of the first response. (Redrawn from Pollard BJ: Neuromuscular imaging. Curr Anesth Crit Care 15:383, 2004.)

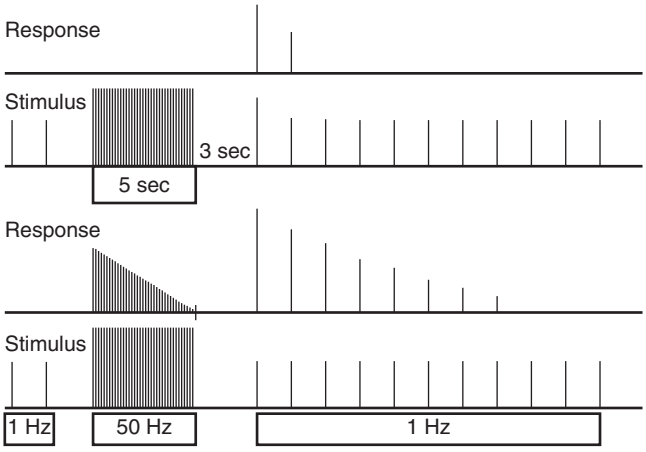


**FIGURE 23-4** ■ Posttetanic count (PTC). In the upper two recordings, there is no response to single stimuli at 1 Hz or to a 5-second tetanic train of 50 Hz. Following a 3-second hiatus in stimulation, stimulation at 1 Hz results in two contractions; the rest are missing. This would represent a PTC of 2. In the lower two recordings, there is a weak response to the tetanic train, and the following PTC is 8. (Redrawn from Pollard BJ: Neuromuscular imaging. Curr Anesth Crit Care 15:383, 2004.)

from a stimulator equipped with a charged battery suggests problems such as desiccated skin electrodes or broken wire between the stimulator and electrodes.

If the peripheral nerve stimulator is working properly and there is no response to TOF or single twitch stimulation, PTC can be used to assess neuromuscular blockade. If the PTC is zero, neuromuscular blockade is profound and cannot be reversed at this time. The patient should be kept sedated, intubated, and ventilated until sufficient spontaneous neuromuscular blockade recovery has occurred to allow for adequate antagonism of neuromuscular blockade.

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CASE 24

# Myasthenia Gravis

**Jason H. Epstein, MD • James B. Eisenkraft, MD**

## QUESTIONS

1. What is myasthenia gravis?
2. How is myasthenia gravis diagnosed, and how is it classified?
3. What are the treatment alternatives for a patient with myasthenia gravis?
4. Explain why patients with myasthenia gravis are resistant to succinylcholine but sensitive to nondepolarizing muscle relaxants.
5. How is a patient with myasthenia gravis optimized for surgery?
6. Describe an appropriate anesthetic technique for patients with myasthenia gravis undergoing transcervical thymectomy.
7. What are the considerations in a patient with myasthenia gravis who requires a rapid-sequence induction?
8. After emergence from anesthesia and before extubation, how is adequacy of strength assessed?
9. What is a cholinergic crisis, and how is it distinguished from a myasthenic crisis?
10. Can the need for postoperative ventilation be predicted preoperatively?

A 38-year-old woman with a 5-year history of myasthenia gravis (MG) Osserman and Genkins grade IIB presented for transcervical thymectomy. Her medications were pyridostigmine, 240 mg, azathioprine, 100 mg, and prednisone, 15 mg per day in divided doses. She was also taking omeprazole 20 mg per day for reflux esophagitis. Spirometry revealed a vital capacity of 60% predicted and forced expiratory volume in 1 second/forced vital capacity of 80%. After placement of standard monitors and while the patient was breathing 100% oxygen, rapid-sequence induction with cricoid pressure was performed using propofol, 2 mg/kg, and succinylcholine, 1.5 mg/kg. The trachea was intubated uneventfully. Anesthesia was maintained with oxygen, air, fentanyl, and desflurane as required. Ventilation was controlled throughout the procedure. Neuromuscular monitoring with a peripheral nerve stimulator was initiated, and cisatracurium, 0.05 mg/kg, was administered with resulting loss of twitch response to peripheral nerve stimulation. The surgery proceeded uneventfully and lasted 2 hours. Anesthetic agents were discontinued, and the patient demonstrated four equal twitch responses to train-of-four (TOF) stimulation. Neostigmine, 0.06 mg/kg, and glycopyrrolate, 0.01 mg/kg, were administered. When the patient was awake and responded to commands, her trachea was extubated. Soon after extubation, the patient became dyspneic.

### 1. What is myasthenia gravis?

MG is an autoimmune disorder of the neuromuscular junction, the function of which is routinely altered in modern anesthesia practice. Typically, MG manifests as a fluctuating, painless weakness and easy fatigability of voluntary muscles. Weakness resolves with rest. Slow, insidious onset is common, and the condition is associated with relapses and remissions. The incidence of MG is approximately 1 in 30,000 adults and 1 in 200,000 children and adolescents. These figures may underestimate the true incidence because mild cases in elderly adults are commonly misdiagnosed. Peak incidence occurs in the third decade of life for women and fifth decade for men, but any age may be affected.

In MG, antibodies are produced to the acetylcholine (nicotinic) receptor of the neuromuscular junction. Consequently, patients with MG have 70% to 80% fewer usable postsynaptic acetylcholine receptors at the end plates of affected muscles, fewer folds in synaptic clefts, and widened synaptic clefts. The amount of presynaptic acetylcholine released is normal or increased. In a person with a normal number of acetylcholine receptors, only 25% to 30% of the receptors are required for normal neuromuscular transmission; this is termed the "margin of safety" in neuromuscular transmission. In patients with MG, the margin of safety is decreased.

### 2. How is myasthenia gravis diagnosed, and how is it classified?

The diagnosis of MG is suspected from the patient's history and confirmed by clinical, electrophysiologic, immunologic, and pharmacologic testing. Although any muscle group may be affected, the most common onset is ocular, with ptosis or diplopia. If the disease remains localized to the eyes for 2 years, there is a low likelihood

of progression to generalized MG. Involvement of bulbar musculature predisposes to difficulty breathing and swallowing.

Patients with MG cannot sustain or repeat muscle contractions. Electromyography (EMG) studies can highlight this feature when a motor nerve is stimulated three times per second (3 Hz). A decrement of response of at least 10% by the fifth stimulus is usually seen in patients with MG. Although this is the most specific nerve test for MG, it can be performed only on certain muscles, which may not be the muscles affected in the individual patient.

The edrophonium (Tensilon) test may help to differentiate MG when responses to EMG studies are equivocal. An intravenous dose (2 to 10 mg) of the acetylcholinesterase inhibitor edrophonium may elicit improvement in the strength of patients with MG because it inhibits the degradation of acetylcholine. In normal patients, no improvement in strength is seen.

If testing is still equivocal, a regional curare test may be employed. In this test, an arterial tourniquet is applied to isolate the limb and limit the drug's systemic action. EMG is performed before and after administration of very small doses of curare (0.2 mg) into a forearm. Patients with MG show a marked decrease in response to repeated stimulation. In equivocal cases, antibodies to acetylcholine receptors may be detectable; however, antibody titers do not correlate with severity of disease. When MG is diagnosed, the Osserman and Genkins classification system is commonly used to describe the severity of disease (Table 24-1).

### 3. What are the treatment alternatives for a patient with myasthenia gravis?

The mainstay of treatment for MG is to increase the amount of acetylcholine available at the neuromuscular junction, increasing the likelihood of agonist-receptor interaction and successful neuromuscular transmission. Acetylcholinesterase inhibitors such as neostigmine (Prostigmin), edrophonium, and pyridostigmine (Mestinon) have been used for this purpose since 1934. Physostigmine is not used because it crosses the blood-brain barrier producing central nervous system symptoms. Because of its longer duration of action and fewer muscarinic side effects, pyridostigmine has the best treatment profile within the drug class. Dosage requirements can vary from day to day, and patients frequently learn to titrate amounts accordingly. Overdosage can cause cholinergic crisis, and underdosage can cause myasthenic crisis.

Treatment may also be directed at immunomodulation to decrease the amount of circulating antibodies. In the short-term, immunomodulation is managed with steroids; long-term therapy involves other immunosuppressive agents, such as azathioprine, cyclophosphamide, cyclosporine, methotrexate, rituximab, and tacrolimus. Steroids can provide clinical improvement in 80% of patients; however, initiation of steroid therapy often exacerbates symptoms because of direct inhibitory effects on neuromuscular transmission. In addition, prolonged therapy may lead to side effects such as osteoporosis, hypertension, and peptic ulcers.

Plasmapheresis or plasma exchange produces transient but dramatic improvement in clinical symptoms in 45% of patients. Improvement may last days to weeks after the procedure. This treatment is reserved for severe MG. Of significance to the anesthesiologist is that plasmapheresis can decrease levels of plasma cholinesterase, resulting in prolonged effects of drugs, such as succinylcholine, that are metabolized by this enzyme.

Many patients with MG have abnormalities of the thymus gland. Imaging (computed tomography or magnetic resonance imaging) may help confirm the presence of an abnormal thymus. Thymectomy provides significant long-term immunomodulation and improvement in most patients. It is considered the treatment of choice

TABLE 24-1 **Clinical Classification of Myasthenia Gravis (after Osserman and Genkins*)**

| Grade | Name | Description | Testing and Prognosis |
|---|---|---|---|
| I | Ocular | Involvement of ocular muscles only<br>Diplopia and ptosis | Electrophysiologic testing of other musculature negative |
| IA | Ocular + peripheral | Involvement of ocular muscles<br>No clinical symptoms in peripheral musculature | Electrophysiologic testing of other musculature positive |
| IIA | Mild generalized | Involvement of skeletal or bulbar musculature<br>No respiratory involvement | Good response to drug therapy |
| IIB | Moderate generalized | More severe involvement of skeletal and bulbar muscles<br>Dysarthria, dysphagia, difficulty chewing without respiratory involvement | Fair response to drug therapy |
| III | Acute fulminating | Rapid onset of severe bulbar and skeletal weakness with respiratory involvement | Poor response to therapy<br>Low mortality rate |
| IV | Late severe | Severe MG developing >2 years after onset of symptoms | Poor response to therapy<br>Poor prognosis |

*MG,* Myasthenia gravis.

*Osserman KE, Genkins G: Studies in myasthenia gravis: review of a twenty-year experience in over 1200 patients. Mt Sinai J Med 38:497, 1971.

for most patients with MG; the exception is patients with Osserman and Genkins class I MG. Response to thymectomy is best when the procedure is performed within the first 3 years after diagnosis. Clinical outcome is equivalent whether the procedure is performed via video-assisted thoracoscopy or via a median sternotomy.

### 4. Explain why patients with myasthenia gravis are resistant to succinylcholine but sensitive to nondepolarizing muscle relaxants.

Acetylcholine receptors are each activated by two acetylcholine molecules, which causes a small electrical current across the membrane at the motor end plate. When the summation of small currents from multiple receptors reaches a threshold, the end plate depolarizes and muscle contraction occurs. Although only 20% of a normal number of receptors are required for neuromuscular transmission, patients with MG can have 80% fewer receptors, and any factor that even minimally interferes with neuromuscular transmission may cause severe weakness. Small amounts of nondepolarizing neuromuscular relaxants may block enough receptors to interfere with this transmission.

Succinylcholine acts as an agonist at acetylcholine receptors and causes neuromuscular blockade by first depolarizing the motor end plate and then preventing rapid repolarization. Because of the smaller number of receptors available in patients with MG, larger doses of succinylcholine are required to activate sufficient receptors to cause depolarization. The $ED_{95}$ dose (i.e., the mean dose that produces a 95% decrease in the muscle's response to supramaximal nerve stimulation) for succinylcholine in patients with MG is 2.6 times normal (normal being approximately 0.3 mg/kg). In addition to exhibiting resistance to succinylcholine, patients with MG often have prolonged duration of action of the drug. Both anticholinesterase drugs and plasmapheresis may inhibit or decrease the amount of pseudocholinesterase, which is responsible for the metabolism of succinylcholine.

### 5. How is a patient with myasthenia gravis optimized for surgery?

Numerous anesthetic techniques are applicable to patients with MG undergoing thymectomy. No matter which technique is chosen, patients should be admitted in remission when possible. All other medical and emotional states are best optimized before surgery. Patients with a history of respiratory disease or bulbar involvement could benefit from pulmonary function testing. These patients should be informed of the potential for postoperative intubation and ventilation and educated in the use of incentive spirometers. Premedication is best used with caution and avoided in patients with respiratory difficulty.

Although steroids should be continued in the perioperative period, recommendations for preoperative anticholinesterases are controversial. Withholding anticholinesterase medication may reduce or obviate the need for exogenous neuromuscular blockade. Administration of preoperative anticholinesterase medication could prolong succinylcholine effects and could antagonize nondepolarizing muscle relaxant effects. Withholding anticholinesterases may be challenging in patients who are physically or psychologically dependent on them, and some authors argue that these drugs can be given without interfering significantly with perioperative management. Anticholinesterase dosage may be reduced during the relative immobility of hospitalization and surgery.

### 6. Describe an appropriate anesthetic technique for patients with myasthenia gravis undergoing transcervical thymectomy.

Reports of successful anesthetic techniques for thymectomy in patients with MG include balanced anesthesia and total intravenous anesthesia (TIVA) techniques. Some authors advocate TIVA with thoracic epidural anesthesia to reduce the need for neuromuscular blocking agents and systemic opioids. All patients undergoing anesthesia should have American Society of Anesthesiologists standard monitors in place. When muscle relaxants are to be administered, peripheral nerve stimulation and neuromuscular monitoring should also be performed, preferably with a means to quantify responses objectively.

After denitrogenation with 100% oxygen, induction of anesthesia is achieved with propofol, etomidate, or ketamine. In elective cases, relaxation for tracheal intubation is readily achieved with a potent inhaled anesthetic agent. Patients with MG are more sensitive to the neuromuscular depressant effects of these agents. Patients with MG who were anesthetized with isoflurane at a 1.6 minimum alveolar concentration demonstrated a 30% to 50% decrease in response (i.e., twitch height) to single stimuli, and a fade (TOF) ratio of 0.41. Less soluble inhaled agents such as desflurane and sevoflurane produce similar effects and are easily titrated.

Patients who are unable to tolerate the cardiovascular depression associated with potent inhaled agents may require balanced techniques with small incremental doses of intermediate-acting nondepolarizing muscle relaxants. Because the sensitivity of any individual patient with MG may vary widely and because sensitivity to muscle relaxants is increased in the presence of potent inhaled anesthetics, nondepolarizers should be titrated at one tenth the usual dose. Vecuronium and rocuronium have been safely used in patients with MG. Cisatracurium is an alternative choice that offers a short elimination half-life, small volume of distribution, and high clearance by Hofmann elimination.

### 7. What are the considerations in a patient with myasthenia gravis who requires a rapid-sequence induction?

Patients with MG who present for emergent surgery may require rapid-sequence induction if they are at increased risk for aspiration. As described earlier, patients with MG show resistance to the effects of succinylcholine; however, the standard intubating dose of 1 to 1.5 mg/kg represents 3.5 times the $ED_{95}$ in patients without MG. A 1.5-mg/kg dose of succinylcholine has been successfully used to facilitate intubation in a rapid-sequence fashion in patients with MG. Patients with MG frequently do not show fasciculation before paralysis with succinylcholine. Patients who have received recent anticholinesterase

medication or plasmapheresis may have a prolonged response to succinylcholine because of delayed metabolism.

Sugammadex is a cyclodextrin drug that is designed to bind rocuronium with great affinity, providing rapid and effective antagonism of deep rocuronium-induced neuromuscular blockade. Before the introduction of sugammadex, anticholinesterase drugs were the only option for antagonism of residual neuromuscular blockade, which in patients with MG must be administered with caution to avoid myasthenic or cholinergic crises. Sugammadex antagonized deep rocuronium-induced neuromuscular blockade within 210 seconds in patients with MG. Although sugammadex offers potential advantages in the management of patients with MG, as of this writing, the Food and Drug Administration has not approved sugammadex for clinical use in the United States.

Another possible rapid-sequence induction technique is to avoid neuromuscular blocking agents entirely. A rapid-sequence intubation in a 14-year-old patient with MG and a full stomach using lidocaine, propofol, and remifentanil has been described. This technique allows for a case to be managed without the potential adverse effects of neuromuscular blocking agents. This technique seems attractive for use in patients with MG, but intubating conditions are frequently poor when neuromuscular blocking agents are omitted.

### 8. After emergence from anesthesia and before extubation, how is adequacy of strength assessed?

Various techniques are used to assess residual neuromuscular blockade. In normal patients, a sustained response to tetanic stimulation at 50 Hz for 5 seconds or a negative inspiratory force of −20 cm $H_2O$ may be observed when 50% of receptors are still occupied by neuromuscular blocking drugs. Patients can sustain a head lift for 5 seconds when 33% of receptors are occupied. Other, less sensitive measures of strength include maintaining a tidal volume of 6 mL/kg, a TOF fade ratio greater than 0.9, and vital capacity of 15 mL/kg (Table 24-2).

Patients with MG represent a special case because the above-mentioned criteria may not apply. The disease, rather than residual neuromuscular blockade, may prevent a patient with MG from reaching full strength. Because of the variability of debilitation, preoperative measurements of strength are important for postoperative comparisons. Before administration of an anesthetic drug that may interfere with neuromuscular transmission, control EMG or TOF should be recorded. Response to tetanic stimulation may also be assessed after induction of anesthesia but before administration of drugs that interfere with neuromuscular transmission.

It is important that a patient with MG have good muscle function so as to be able to cough and clear secretions. Patients with MG who demonstrate residual weakness on emergence from anesthesia should not automatically be assumed to have residual blockade from a muscle relaxant. Inhaled anesthetics, antibiotics, local anesthetics, anticonvulsants, and β-adrenergic blockers may interfere with neuromuscular transmission (Box 24-1).

### 9. What is a cholinergic crisis, and how is it distinguished from a myasthenic crisis?

Crisis is the acute onset of muscle weakness in a patient with MG. Cholinergic crisis arises from an excess of

TABLE 24-2 **Common Extubation Criteria**

| | |
|---|---|
| Sustained head lift | 5 sec |
| Sustained tetanus at 50 Hz | 5 sec |
| TOF | Ratio of 4th to 1st twitch height >0.9 |
| Central nervous system | Awake and alert |
| Respiratory system | Tidal volume >6 mL/kg<br>Vital capacity >15 mL/kg<br>Negative inspiratory force <−40 cm $H_2O$*<br>Adequate oxygenation with $F_{IO_2}$ ≤0.4<br>Adequate ventilation with $pCO_2$ <55 mm Hg<br>Respiratory rate <25 breaths per minute in adults |
| Cardiovascular system | Adequate blood pressure to perfuse vital organs<br>Absence of new arrhythmias |
| Metabolic | Normothermia<br>Normal glucose and electrolytes |
| Hematologic | Adequate surgical hemostasis<br>Not coagulopathic |

*$FiO_2$*, Fraction of inspired oxygen; *$pCO_2$*, partial pressure of carbon dioxide; *TOF*, train-of-four.
*Negative inspiratory force is measured by inspiring against a gauge and indicator. The greater the force generated, the more the indicator moves from its original set-point. The set-point is arbitrarily labeled 0. Traditionally, the gauge has been calibrated with negative numbers. The more the indicator is displaced from its 0 set-point, the more negative the reading. The important aspect is the amount of indicator displacement. The greater the displacement, the more negative the reading. Consequently, greater displacement is read as a larger absolute number. Because the numbers are designated as negative numbers, confusion has arisen over their meaning. The greater the absolute indicator displacement, the greater the force generated. A reading of −40 cm $H_2O$ represents a greater inspiratory force than a reading of −20 cm $H_2O$.

**BOX 24-1 Factors That Augment Nondepolarizing Neuromuscular Blockade**

- Acid-base alterations
  - Respiratory acidosis
  - Metabolic acidosis
- Electrolyte imbalance
  - Hypocalcemia
  - Hypokalemia
  - Hyponatremia
  - Hypermagnesemia
- Residual potent inhaled anesthetic agents
  - Isoflurane
  - Sevoflurane
  - Desflurane
- Local anesthetics
  - Lidocaine
  - Procaine
- Class IA antiarrhythmics
  - Quinidine
  - Procainamide
- Antibiotics
  - Gentamicin
  - Neomycin
  - Clindamycin
  - Polymyxin B
  - Tetracycline
  - Streptomycin
  - Lincomycin
- Calcium-channel blockers
- Dantrolene
- Hypothermia

acetylcholine at nicotinic and muscarinic receptor sites. Usually occurring as a result of excess anticholinesterase administration, symptoms include weakness, wheezing, increased secretions, fasciculations, nausea, vomiting, diarrhea, lacrimation, bradycardia, and hypotension. Respiratory weakness may progress to respiratory failure, whereas increased secretions and dysphagia predispose to upper airway obstruction and aspiration pneumonitis. Myasthenic crisis occurs when the amount of acetylcholine available is insufficient to stimulate enough postsynaptic receptors at the motor end plates, resulting in failure of neuromuscular transmission.

Both cholinergic crisis and myasthenic crisis manifest with muscle weakness, but because the appropriate treatment of one is the antithesis of the other, correct diagnosis is critical. Two means of differentiating between both states are to check pupillary size and to perform an edrophonium challenge test. A patient in a cholinergic crisis has constricted pupils (miosis), whereas a patient in myasthenic crisis has dilated pupils (mydriasis). In addition, a small dose of intravenous edrophonium (2 to 10 mg) improves strength in a patient in myasthenic crisis (relative dearth of acetylcholine), whereas a patient in cholinergic crisis (excess of acetylcholine) should show no change or an exacerbation of symptoms. The muscarinic side effects of a cholinergic crisis may be treated with atropine or glycopyrrolate.

### 10. Can the need for postoperative ventilation be predicted preoperatively?

Patients with MG are at increased risk for prolonged postoperative ventilation. Attempts have been made to predict preoperatively which patients are at greater risk for postoperative respiratory failure. In 24 patients undergoing transsternal thymectomy under general anesthesia via an endotracheal tube with nitrous oxide and either halothane or enflurane without muscle relaxants, positive predictors included duration of MG greater than 6 years, history of chronic respiratory disease aside from MG, pyridostigmine dose greater than 750 mg/day, and preoperative vital capacity less than 2.9 L. These predictors were not found to be useful when applied to patients with MG having transcervical thymectomy at other centers or to patients with MG undergoing other types of surgery.

The incidence of postoperative respiratory failure is lower after transcervical rather than transsternal thymectomy. The risk of postoperative respiratory failure is more likely in some circumstances than others. For high-risk patients, preoperative plasma exchange and high-dose perioperative steroid therapy, can help reduce the probability of respiratory failure.

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CASE 25

# Malignant Hyperthermia

**Joseph Sebeo, MD, PhD • James B. Eisenkraft, MD**

QUESTIONS

1. What is malignant hyperthermia?
2. What is the pathophysiology of malignant hyperthermia?
3. What are the clinical characteristics of malignant hyperthermia?
4. Discuss masseter muscle rigidity during induction.
5. Explain the known triggering agents for malignant hyperthermia.
6. Describe the pharmacology of dantrolene and its use in malignant hyperthermia.
7. How is a suspected case of malignant hyperthermia treated?
8. What is the preparation for a known case of malignant hyperthermia?
9. What is the "gold standard" for diagnosing malignant hyperthermia?
10. Is genetic testing available for malignant hyperthermia susceptibility?
11. What is neuroleptic malignant syndrome?
12. What are some medicolegal issues in malignant hyperthermia?

A 12-year-old, 40-kg boy was scheduled for strabismus corrective surgery of the right eye. He had no significant past medical history and no family history of anesthetic problems or muscle or nerve disease. He had never received general anesthesia before. Physical examination was normal. The preoperative vital signs were blood pressure 100/60 mm Hg, heart rate 92 beats per minute, and axillary temperature 36.7° C. Because the patient was needle-phobic, an inhalation induction of anesthesia was achieved with sevoflurane 4.0 vol% in a mixture of nitrous oxide and oxygen (fraction of inspired oxygen 0.4). After induction, an intravenous catheter was placed, and rocuronium bromide, 20 mg, and fentanyl, 50 μg, were administered. Direct laryngoscopy was performed, and the trachea was intubated easily with a 6.0-mm cuffed tube. The patient's heart rate suddenly increased 60 minutes after intubation from 130 to 190 beats per minute. Over the next 10 minutes, the end-tidal carbon dioxide ($ETCO_2$) tension increased from 35 to 65 mm Hg, and the axillary temperature increased from 35° C to 38.9° C. An esophageal temperature probe showed a temperature of 39.5° C.

## 1. What is malignant hyperthermia?

Malignant hyperthermia (MH) is a life-threatening familial hypermetabolic disorder of skeletal muscle that can be precipitated by specific anesthetic agents. MH was first reported in the 1960s and is characterized by tachycardia, tachypnea, hyperthermia, generalized muscle rigidity, acidosis, and increasing $ETCO_2$ levels. The incidence of MH is 1 in 15,000 anesthetics in children and 1 in 50,000–100,000 anesthetics in adults. Children <15 years old account for >50% of all reported MH cases, with most cases reported in boys. MH can be described as a spectrum, ranging from the classic life-threatening reaction to mild presentations.

## 2. What is the pathophysiology of malignant hyperthermia?

In the normal state, depolarization of skeletal muscle fiber membranes leads to calcium ion release from the sarcoplasmic reticulum (SR). After calcium diffusion into thin filaments, calcium binds to calcium-regulatory sites on troponin, leading to normal excitation-contraction coupling. In MH, calcium is released from the SR at very high rates, leading to a sustained hypermetabolic state and subsequent loss of cellular integrity. This hypermetabolic state produces increased lactate levels, high adenosine triphosphate (ATP) consumption, increased carbon dioxide release, increased oxygen consumption, and increased muscle heat accumulation secondary to sustained muscle contractions. Later in the clinical course, ATP production ceases, causing failure of intracellular membrane pumps. Cellular leakage of electrolytes follows, including potassium and calcium, enzymes such as creatine phosphokinase, large amounts of metabolic acids, and myoglobin. Fatal arrhythmias, end-organ damage, and eventually death may ensue.

The ryanodine receptor has been implicated in the pathogenesis of MH. Ryanodine receptors are a group of high-conductance SR calcium channels in muscles and endoplasmic reticulum in other cells. Mutations impairing function of ryanodine receptors occur in central core disease, an autosomal dominant congenital myopathy, and King-Denborough syndrome, a congenital myopathy. Both conditions are associated with an increased susceptibility to MH.

### 3. What are the clinical characteristics of malignant hyperthermia?

MH episodes are characterized by sinus tachycardia, muscle contractures, arrhythmias, increased core temperature, increased serum creatine kinase levels, myoglobinuria, and eventually cardiac arrest. All of these changes combine with hypoxemia, hypercapnia, metabolic acidosis, respiratory acidosis, and hyperkalemia. Early recognition and treatment of MH are essential if an adverse outcome is to be avoided. The earliest signs are usually masseter muscle rigidity, tachypnea (if spontaneously breathing), tachycardia, and increasing $ETCO_2$ (but not inspired carbon dioxide). The sequence of clinical events during an episode of MH is summarized in Table 25-1. None of these signs are specific for MH, and a broad differential diagnosis should always be considered (Box 25-1).

**BOX 25-1 Differential Diagnosis of Suspected Malignant Hyperthermia Event**

- Inadequate anesthesia/analgesia
- Insufficient ventilation/fresh gas flow
- Overwarming
- Exothermic reaction in absorber (sevoflurane + Baralyme)
- Anesthesia machine malfunction
- Anaphylactic reaction
- Sepsis
- Antimuscarinics
- Neuromuscular disorders
- Neuroleptic malignant syndrome
- Thyroid crisis
- Pheochromocytoma
- Carcinoid
- Cocaine toxicity
- Laparoscopic associated hypercarbia

### 4. Discuss masseter muscle rigidity during induction.

Children and adults can exhibit decreased mouth-opening and increased jaw stiffness when succinylcholine is administered after exposure to halogenated volatile anesthetics. Masseter muscle rigidity (MMR) is the inability to open the jaw (trismus). The exact incidence of MMR after succinylcholine administration is unknown but has been estimated to range from 1 in 1000 to 1 in 100,000 patients. MMR may be an early indicator of, but is not pathognomonic for, MH. Differential diagnosis for MMR includes inadequate dose of succinylcholine, outdated succinylcholine, rapid succinylcholine hydrolysis, underlying myotonic dystrophy, trismus secondary to facial trauma, and MMR as an early sign of MH.

When MMR occurs, MH could ensue. Consequently, all triggering agents should be discontinued, 100% oxygen should be delivered, monitoring should be continued for evidence of other signs of MH, and an arterial blood gas (ABG) should be drawn. Combined respiratory and metabolic acidosis indicates MH, and if present, the patient should be treated appropriately. If the ABG does not show a combined respiratory and metabolic acidosis, and other signs of MH are absent, the anesthesiologist has two options. One is to postpone surgery, awaken the patient, and continue monitoring in the postanesthesia care unit. The second option is to convert to a nontriggering anesthetic and proceed with surgery, monitoring carefully for any signs of MH. In the case of emergency surgery that cannot be delayed, the only option is to convert to a nontriggering anesthetic while maintaining a heightened vigilance for MH. In all cases, the patient should be referred for further evaluation of MH susceptibility.

### 5. Explain the known triggering agents for malignant hyperthermia.

All potent inhaled volatile anesthetics may trigger an episode of MH, but they may not all be equal in this respect; sevoflurane and isoflurane have been suggested to be more potent triggers than others. Succinylcholine is also a potential trigger. These agents should be avoided in patients with MH susceptibility. Although not directly triggering a MH reaction, ketamine may lead to increased muscle tone, which confounds the diagnosis of MH. Use of ketamine is not contraindicated, but it may not be ideal in patients with a known history of MH. Anesthetic agents believed to be safe to use in a patient with MH susceptibility are listed in Box 25-2.

TABLE 25-1 **Clinical Features of Malignant Hyperthermia**

| | Early Signs | Late Signs |
|---|---|---|
| Musculoskeletal | Sustained jaw rigidity | Generalized muscle rigidity |
| Cardiovascular | Tachycardia<br>PVCs<br>Unstable blood pressure | Severe cardiac arrhythmias<br>Cardiovascular collapse |
| Respiratory | Tachypnea (spontaneously breathing)<br>Rising $ETCO_2$ (despite increased minute ventilation) | |
| Metabolic | Rising temperature<br>Hypoxia (increased oxygen consumption)<br>Acidosis (respiratory and metabolic)<br>Hyperkalemia | Rapidly increasing temperature<br>Life-threatening hyperkalemia<br>Increased CPK<br>DIC<br>Myoglobinemia |

*CPK,* Creatine phosphokinase; *DIC,* disseminated intravascular coagulation; *$ETCO_2$,* end tidal carbon dioxide; *PVCs,* premature ventricular contraction.

**BOX 25-2 Nontriggering Agents**

Volatile anesthetics
- Nitrous oxide

Intravenous anesthetics
- Propofol
- Ketamine
- Barbiturates
- Benzodiazepines

Nondepolarizing muscle relaxants
- Vecuronium
- Rocuronium
- Pancuronium
- Cisatracurium

Analgesics
- All opioids

Local anesthetics
- All local anesthetics

### 6. Describe the pharmacology of dantrolene and its use in malignant hyperthermia.

Dantrolene is a muscle relaxant, originally synthesized in the 1960s, that affects only skeletal muscle. It reverses the hypermetabolic state of MH by causing dissociation of excitation-contraction coupling through inhibition of calcium release from the SR. Chemically, dantrolene is a hydantoin derivative with an onset of action of 2–3 minutes. Its plasma half-life is 5–8 hours in healthy volunteers but increases to 12 hours in patients with MH.

The Malignant Hyperthermia Association of the United States (MHAUS) protocol for treatment of MH recommends an initial dantrolene loading dose of 2.5 mg/kg intravenously. Additional incremental doses up to 10 mg/kg may be used until the signs of MH are reversed. Doses >10 mg/kg may be necessary in some cases. Dantrolene administration in a dose of 1 mg/kg every 4-6 hours is continued for at least 24 hours after the MH episode. Each vial of dantrolene contains a significant amount of mannitol (3 g); volume status should be monitored closely. The goal for urine flow is >2 mL/kg per hour. Prophylactic preoperative administration of dantrolene is not routinely recommended for patients who are susceptible to MH.

The most common side effects of dantrolene include muscle weakness, phlebitis, and respiratory failure. There have been reports of extravascular infiltration leading to tissue necrosis; large peripheral or central venous access sites are preferred for administration. Dizziness, nausea, vomiting, confusion, and postpartum uterine atony are rare complications. A possible future alternative to dantrolene is azumolene, a 30-fold more water-soluble analogue of dantrolene. Azumolene is equipotent to dantrolene for blocking in vitro pharmacologically induced muscle contractures. Further studies may lead to clinical applications in MH.

### 7. How is a suspected case of malignant hyperthermia treated?

Management of a suspected case of MH includes prompt recognition and treatment as summarized in Table 25-2. Increasing $ETCO_2$ is one of the earliest, most specific, and sensitive signs of MH. Immediate ABG analysis at the onset of MH reveals respiratory acidosis, metabolic acidosis, and possibly hyperkalemia. When MH is suspected, volatile inhalation anesthetics are discontinued, the lungs are ventilated with 100% oxygen using high fresh gas flows (>10 L per minute), and minute ventilation is increased. Assistance should be sought promptly. If the MH episode occurs during surgery, anesthesia should be maintained with intravenous agents (total intravenous anesthesia). Prompt and effective communication between the anesthesiologist and surgeon is crucial. In cases where MH occurs, surgery should be terminated if possible, and either surgical closure should be achieved or temporary packing should be placed. Patient safety is the primary goal.

When MH is diagnosed, both MH and crash carts should be brought to the room, and dantrolene should be administered as soon as possible. Each vial of dantrolene contains 20 mg of dantrolene sodium, 3 g of mannitol, and enough bicarbonate to achieve a pH of 9.5. Each 20 mg is dissolved in 60 mL of sterile water. Dissolving 20 mg of dantrolene in water is estimated to take 86 seconds but has improved to 20 seconds with the more rapidly soluble dantrolene products available since November 2009. Dantrolene has a shelf life of 36 months, and MHAUS recommends that a minimum of 36 vials of the drug be kept in every center that administers volatile anesthetics or succinylcholine. A member of the operating room team should be dedicated to mixing the dantrolene and administering it as an intravenous bolus.

Chilled intravenous fluids, cooling blankets, axillary and groin ice packs, and gastric lavage may help treat hyperthermia. Hyperkalemia is managed with hyperventilation and insulin, dextrose, calcium, and sodium bicarbonate administration. Cardiac arrhythmias are managed by treating the underlying cause (i.e., acidosis, hyperkalemia). Calcium-channel blockers are contraindicated in patients with MH. Calcium-channel blockers in the presence of dantrolene may lead to hyperkalemia and cardiovascular collapse. Continuous intensive care unit (ICU) monitoring of $ETCO_2$, ABGs, serum calcium, serum potassium, coagulation parameters, core temperature, and urine output is required until all values return to normal. After treatment of (and recovery from) an acute episode, MHAUS recommends a minimum of 36 hours of observation in an ICU to monitor for signs of MH recurrence and administration of dantrolene (1 mg/kg intravenously every 6 hours for 24–48 hours). If MH symptoms persist or ABG values do not normalize, dantrolene treatment may be continued beyond this period.

Core temperature is estimated with reasonable accuracy using esophageal, axillary, rectal, and bladder temperature probes. Esophageal temperature has been shown to agree most closely with pulmonary artery temperature and is the preferred site for monitoring during a MH episode.

### 8. What is the preparation for a known case of malignant hyperthermia?

Prompt management of MH is crucial to prevent an adverse outcome. An MH cart should be maintained and immediately available. Activated charcoal filters placed in

TABLE 25-2 **Treatment of Suspected Malignant Hyperthermia**

| Acute Treatment | Continued Treatment |
|---|---|
| Call for help, alert surgeon | Monitor in ICU for >24 hours |
| Get MH cart and crash cart | Ensure good urine output |
| Remove vaporizer and switch to TIVA | Continue treatment of hyperkalemia, acidosis, hyperthermia, and arrhythmias |
| Hyperventilate with 100% oxygen | Administer dantrolene 1 mg/kg every 4–6 hours prn for 24–48 hours |
| Obtain adequate venous access | Close monitoring of core temperature |
| Insert arterial catheter | |
| Perform arterial blood gas analysis | |
| Administer dantrolene 2.5 mg/kg, repeat as needed to 10 mg/kg | |
| Treat hyperthermia | |
| Treat arrhythmias | |

**Treatment of Metabolic Disturbances**

**Hyperthermia (stop when <38°C)**
Iced saline
Cooling blankets
Cool irrigation of body cavities
Ice packs (never directly on skin)

**Hyperkalemia**
Hyperventilation
Insulin
  Adult dose: insulin 10 units + dextrose 50% 50 mL
  Pediatric dose: insulin 0.1 unit/kg + dextrose 50% 1 mL/kg
Sodium bicarbonate
  Adult dose: 50 mEq/L over 5 minutes
  Pediatric dose: 1–2 mEq/L
Calcium chloride (life-threatening hyperkalemia): 10 mg/kg

**Arrhythmias**
Usually resolves with treatment of acidosis and hyperkalemia
Standard drug therapy
*Avoid calcium-channel blockers* (hyperkalemia or cardiac arrest with dantrolene)

**Acidosis**
Hyperventilation
Sodium bicarbonate if pH <7.2

**Myoglobinuria**
Hydration to maintain urine output >2 mL/kg per hour
Diuretics: furosemide, mannitol
Urine alkalinization

*ICU,* Intensive care unit; *MH,* malignant hyperthermia, *prn,* pro re nata (as needed); *TIVA,* total intravenous anesthesia.

the inspiratory and expiratory limbs of the breathing system have been shown to remove volatile anesthetics effectively from the anesthesia delivery system, and more recent studies have discussed their potential use in cases of MH. Although no "safe" (i.e., nontriggering) concentration of potent inhaled anesthetics has been established in humans, most studies aim for a level of <5 parts per million (ppm) for a machine to be considered "clean."

Preparation of the anesthesia workstation for a patient susceptible to MH includes removal of vaporizers, replacing the breathing system, substituting a new carbon dioxide absorber, and flushing the machine with oxygen before inserting activated charcoal filters into the breathing system. Next, the circuit is flushed with the charcoal filters in place. The required flushing periods (to reach <5 ppm anesthetic concentrations) vary considerably among machines of different manufacturers. During anesthetic delivery, charcoal filters must remain in the breathing system, and fresh gas flow must be maintained at >10 L per minute for the first 5 minutes and >2 L per minute for the remainder of the case. As summarized in Box 25-3, in addition to the standard American Society

**BOX 25-3 Malignant Hyperthermia Cart**

**Equipment**

- Syringes (60 mL × 5) to dilute dantrolene
- Irrigation tray
- Esophageal and bladder temperature probes
- Cold saline
- Ice packs
- Central venous catheter kit

**Medications**

- Dantrolene vials (36)
- Sterile water vials (100 mL)
- Sodium bicarbonate (2)
- Dextrose 50% (2)
- Furosemide (4)
- Calcium chloride (2)
- Insulin (1 refrigerated)
- Lidocaine (1)

**Laboratory Test Supplies**

- ABG kits (6)
- Blood specimen tubes for:
  - Coagulation studies
  - Myoglobin
  - Creatine phosphokinase
  - Complete blood count
  - Platelets

of Anesthesiologists basic monitors, appropriate equipment, drugs, and laboratory supplies must be available.

### 9. What is the "gold standard" for diagnosing malignant hyperthermia?

The "gold standard" for MH diagnosis is the in vitro halothane-caffeine contracture test (IVCT) that was developed in accordance with the European Group or MHAUS and can define MH phenotypically. The IVCT requires that fresh muscle be taken from the patient under local anesthesia. The muscle is exposed to halothane and caffeine-containing solutions, and the force of contraction is measured as the endpoint. Muscle from a patient with MH susceptibility shows an increased force of contraction.

When using a European MH group protocol, the IVCT has a sensitivity of 99% and specificity of 93.6%. The MHAUS protocol has a sensitivity of 84% and specificity of 78%. The IVCT is an expensive test, requires a surgical (muscle biopsy) procedure, is performed only in specialized centers, and can be equivocal with the mentioned rates of false-positive and false-negative results. This test should be used for susceptible patients (e.g., with personal or family history of MH). In the case of a patient who has just experienced a suspected MH episode, the IVCT should be delayed for 6 months.

### 10. Is genetic testing available for malignant hyperthermia susceptibility?

A mutation of the ryanodine receptor gene (*RYR1*) in skeletal muscle was discovered in the 1990s, and is responsible for a positive MH disposition. This discovery raised hope in establishing noninvasive and more specific procedures than the IVCT for MH diagnosis. However, although genetic testing showed promise, because of the genetic and clinical variability of MH, the IVCT remains the "gold standard" in the diagnosis of MH to date.

### 11. What is neuroleptic malignant syndrome?

Neuroleptic malignant syndrome (NMS) is a rare reaction to traditional (e.g., haloperidol, fluphenazine) and nontraditional (e.g., quetiapine, risperidone) neuroleptics and dopamine receptor antagonists (e.g., prochlorperazine, metoclopramide). NMS is thought to result from an acute dopaminergic blockade in the central nervous system. Clinical manifestations are very similar to MH and include hyperpyrexia, profuse sweating, and severe muscle rigidity. NMS and MH are clinically similar but pharmacologically distinct, with cross-reactivity between triggering agents unlikely. The distinction between NMS and MH is made clinically based on history of exposure to a volatile anesthetic versus neuroleptic medications. NMS is treated with dantrolene or bromocriptine, a dopamine agonist.

### 12. What are some medicolegal issues in malignant hyperthermia?

Even with prompt diagnosis and appropriate management, MH can be an unpredictable catastrophic reaction with a high mortality rate. Departures from the standard of care may include administration of a MH trigger to a patient with a known personal or family history of MH, failure to have appropriately stocked crash and MH carts available, and substandard resuscitative response. Medicolegal implications of MH have made headlines when young, otherwise healthy patients died as a result of MH during office-based procedures. In one case, the anesthesiologist was reported to have failed to administer dantrolene in a timely manner; the lawsuit that ensued was eventually settled out of court. It is imperative that all anesthesiology caregivers, from office-based practitioners to practitioners in tertiary care and academic institutions, have a MH cart readily available with an adequate supply (enough for 10 mg/kg in the average adult) of unexpired dantrolene as well as resuscitation equipment.

A patient who has a history of MH should be strongly encouraged to wear a MedicAlert or equivalent bracelet. Advice on managing a suspected case of MH is available from the MHAUS 24-hour hotline (1-800-644-9737). There is a MH registry on the MHAUS website (http://www.mhaus.org), and all cases of MH should be reported to MHAUS.

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SECTION 5

# ENDOCRINE SYSTEM

CASE 26

# Diabetes Mellitus

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## QUESTIONS

1. Describe the pathophysiology of type 1 and type 2 diabetes mellitus.
2. What are the end-organ effects of diabetes mellitus, and how do they affect the perioperative course?
3. Discuss the oral medications and insulin preparations available to treat diabetes mellitus and how they should be managed perioperatively.
4. What impact does hyperglycemia have on perioperative morbidity and mortality?
5. What is "tight glucose control," and what are its advantages and disadvantages?
6. Describe and contrast diabetic ketoacidosis and hyperglycemic hyperosmolar states.
7. Outline the management of diabetic ketoacidosis and hyperglycemic hyperosmolar states.
8. When should elective surgery be delayed because of hyperglycemia?

A 62-year-old man with type 2 diabetes mellitus (DM) is scheduled for a laparoscopic hemicolectomy. His medications include metformin and glyburide. Preoperative finger stick glucose value on the morning of surgery is 360 mg/dL.

### 1. Describe the pathophysiology of type 1 and type 2 diabetes mellitus.

DM is a metabolic disease arising from defects in insulin secretion, insulin responsiveness, or both. Insulin is normally released from the endocrine pancreas, specifically from pancreatic β cells, in response to increases in blood glucose. Insulin receptors are present on cell membranes of several tissue types. It is responsible for storing excess nutrients as glycogen in the liver, as fat in adipose tissue, and as protein in muscle. These stored nutrients are available during periods of fasting to maintain glucose delivery to the brain, muscle, and other organs.

The diagnostic criteria for DM are listed in Box 26-1. Any of the listed criteria can establish the diagnosis of DM; it is not a requirement to meet all criteria. However, in the absence of hyperglycemia symptoms, the test is repeated before solidifying the diagnosis. In the acute setting, hyperglycemia symptoms include polyuria, polydipsia, weight loss, and blurred vision. The most extreme cases of acute hyperglycemia, diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar state (HHS), can be life-threatening (see Questions 6 and 7). Uncontrolled chronic hyperglycemia is detrimental to multiple organ systems.

Type 1 DM is caused by an absolute deficiency of insulin secretion; this accounts for only 5%–10% of cases. Classically, type 1 DM is caused by cell-mediated autoimmune destruction of pancreatic β cells. Immune-mediated DM commonly occurs in childhood and adolescence but can occur at any age. Individuals with type 1 DM require exogenous insulin administration for survival. In the absence of insulin administration, these individuals rapidly become symptomatic from hyperglycemia. Carbohydrate, fat, and protein metabolism are dramatically disturbed. Frequently, the first clinical presentation of a type 1 diabetic is DKA. As a result of significantly impaired glucose utilization, blood ketoacid concentration is elevated from increased lipolysis of fat and subsequent conversion of fatty acids to ketoacids.

Type 2 DM, which accounts for 90%–95% of the disease burden, is caused by a combination of tissue insulin resistance and inadequate compensatory insulin secretory response. In contrast to type 1 diabetics, these patients typically do not require exogenous insulin administration to survive, at least initially. The risk of developing type 2 DM increases with age, obesity, and inactivity. At earlier stages, it is asymptomatic and frequently goes undiagnosed for years as hyperglycemia develops gradually. However, these patients are already at risk for developing chronic microvascular and macrovascular complications associated with DM. Table 26-1 outlines the major differences between type 1 and type 2 DM.

Other rare causes of DM include genetic defects of the pancreatic β cells or genetic abnormalities in insulin action. Diffuse injury to the pancreas from pancreatitis, trauma, infection, cancer, or pancreatectomy can cause diabetes, if extensive. Acromegaly, Cushing syndrome, and pheochromocytoma can cause DM. Gestational DM, which affects 7% of all pregnancies, is glucose intolerance that is first recognized during pregnancy. Insulin resistance usually resolves postpartum, but these patients are at increased risk for developing type 2 DM later in life.

**BOX 26-1 Diagnostic Criteria for Diabetes Mellitus**

$HbA_{1c}$ ≥6.5%
Fasting plasma glucose ≥126 mg/dL
Two-hour plasma glucose ≥200 mg/dL during oral glucose tolerance test
Symptomatic hyperglycemia and random plasma glucose ≥200 mg/dL

TABLE 26-1 **Characteristics of Type 1 and Type 2 Diabetes Mellitus**

| | Type 1 | Type 2 |
|---|---|---|
| Frequency | 5%–10% | 90%–95% |
| Pathophysiology | Autoimmune β cell destruction | Increasing age, obesity, inactivity |
| Defect | Insulin deficiency | Insulin resistance |
| Treatment | Exogenous insulin required | Oral medications early in disease |
| Complications | Propensity toward DKA | Propensity toward HHS |

*DKA,* Diabetic ketoacidosis; *HHS,* hyperglycemic hyperosmolar state.

## 2. What are the end-organ effects of diabetes mellitus, and how do they affect the perioperative course?

DM affects nearly every organ system. Preoperative evaluation should focus on systems that are most relevant in the perioperative period.

### *Autonomic Dysfunction*

Damage to the nervous system from long-standing hyperglycemia can lead to autonomic dysfunction. Patients with autonomic dysfunction are at greater risk for intraoperative hypothermia from impaired peripheral vasoconstriction. Similarly, these patients are susceptible to orthostatic hypotension, hemodynamic lability, and an increased risk of cardiovascular events. They are prone to hypotension on induction of anesthesia, so doses should be adjusted accordingly. Advanced autonomic dysfunction may involve denervation of vagal control and cardiac accelerator control of the heart rate. Changes in heart rate normally seen with atropine or β-adrenergic blockers can be blunted in patients with autonomic dysfunction.

### *Gastroparesis*

Chronic hyperglycemia damages the gastrointestinal ganglion cells, delaying gastric emptying and increasing the risk of gastric aspiration during anesthesia. Diabetic patients suspected or known to have gastroparesis should be treated with full stomach precautions, so rapid-sequence induction should be employed. Premedication with gastric neutralizing agents and metoclopramide may also be considered.

### *Fluid And Electrolyte Disturbances*

Hyperglycemia can lead to volume depletion through osmotic diuresis and in extreme cases can cause hyperosmolar hyponatremia. Diabetic nephropathy is associated with hyperkalemia, and with metabolic acidosis from bicarbonate loss and retention of organic acids. Patients with chronic kidney disease can also present with anemia from reduced erythropoietin production and platelet dysfunction secondary to uremia.

### *Cardiovascular Risk*

Coronary artery disease is more prevalent in diabetics and is often silent owing to neuropathy. DM is an independent risk factor for postoperative cardiac morbidity and mortality and is included in the Revised Cardiac Risk Index. Preoperative cardiac risk assessment is especially important in patients with DM.

## 3. Discuss the oral medications and insulin preparations available to treat diabetes mellitus and how they should be managed perioperatively.

Oral agents used in the treatment of DM are outlined in Table 26-2. Insulin preparations for subcutaneous use are presented in Table 26-3.

Metformin, an oral hypoglycemic agent that is typically the first-line treatment for newly diagnosed type 2 DM, warrants special mention because of the rare but potentially life-threatening side effect of lactic acidosis associated with this drug. The perioperative period may manifest with conditions leading to increased risk for lactic acidosis, including impaired renal or liver function, hemodynamic instability, and decreased tissue perfusion. Metformin should be held the morning of surgery, and use of metformin should be resumed only when renal function and circulatory status are stabilized postoperatively. Metformin is also discontinued before and for 24–48 hours after the administration of iodinated contrast material for radiologic examination.

When administered as a solo agent, metformin does not cause hypoglycemia. Other oral diabetic agents are associated with hypoglycemia, particularly the sulfonylureas. These medications should be held the morning of surgery and throughout the perioperative period, as long as the patient is fasting.

Type 1 and type 2 diabetics who are not adequately managed with oral agents typically receive basal-bolus insulin maintenance regimens. Basal insulin is meant to replace the patient's baseline insulin that would be produced during fasting. The total daily dose of insulin is usually divided into a 50% basal component and a 50% prandial component, either continuously via an insulin pump or by subcutaneous injection of a long-acting insulin once (insulin glargine) or twice (insulin detemir) daily plus short-acting boluses with food. Basal insulin can be continued in the perioperative period because it

TABLE 26-2 **Oral Therapy for Diabetes Mellitus**

| Medication | Mechanism of Action | Adverse Reactions |
|---|---|---|
| Biguanides (metformin) | Decrease hepatic gluconeogenesis<br>Decrease intestinal absorption of glucose<br>Improve insulin sensitivity | Gastrointestinal side effects<br>Lactic acidosis |
| Sulfonylureas (acetohexamide, chlorpropamide, gliclazide, glimepiride, glipizide, glyburide, tolbutamide) | Stimulate insulin release from pancreatic β cells<br>Decrease hepatic gluconeogenesis<br>Improve insulin sensitivity | Hypoglycemia<br>Weight gain |
| Meglitinides (repaglinide, nateglinide) | Stimulate insulin release from pancreatic β cells | Hypoglycemia<br>Weight gain |
| Thiazolidinediones (rosiglitazone, pioglitazone) | Increase insulin sensitivity | Weight gain<br>Fluid retention<br>Potential increased risk of cardiovascular events (rosiglitazone)<br>Potential increased risk of bladder cancer (pioglitazone) |
| DPP-4 inhibitors (sitagliptin, saxagliptin) | Inhibit breakdown of incretin hormones<br>Increase insulin release from pancreatic β cells<br>Decrease glucagon secretion from pancreatic α cells, decrease hepatic gluconeogenesis | Hypoglycemia<br>Fluid retention |
| α-Glucosidase inhibitors (acarbose, miglitol) | Delayed intestinal glucose absorption | Hypoglycemia<br>Gastrointestinal upset |

*DDP-4,* Dipeptidyl peptidase-4.

covers the fasting state. However, when type 2 diabetics use long-acting insulins as their sole insulin, this is not meant to be basal dosing, and the dose should be reduced perioperatively to avoid hypoglycemia. Intermediate-acting agents, such as NPH (neutral protamine Hagedorn) and insulin lispro protamine, display peaks in activity (6 hours and 4–12 hours, respectively) that can cause hypoglycemia during fasting. These agents require dosing adjustments in the perioperative period. Patients are typically instructed to take half of their usual dose on the morning of surgery. Insulin pumps can be continued intraoperatively, usually for procedures lasting <2 hours, if secured away from the surgical field.

TABLE 26-3 **Insulin Preparations**

| Type | Onset (hours) | Peak (hours) | Duration of Action (hours) |
|---|---|---|---|
| Insulin aspart, lispro, glusiline | 5–15 minutes | 45–75 minutes | 2–4 |
| Regular | 30 minutes | 2–4 | 5–8 |
| NPH (neutral protamine Hagedorn) | 2 | 6 | 15 |
| Insulin lispro protamine | 2 | 4–12 | 18–24 |
| Insulin detemir | 2 | 3–9 | 6–24 |
| Insulin glargine | 2 | No peak | 18–26 |

In-hospital glycemic management is best achieved with the use of insulin rather than oral diabetic agents. In the perioperative period, frequent changes in fasting status, unpredictable intestinal absorption of medications, and rapidly changing clinical conditions make the use of oral agents potentially less effective and unpredictable, and there is a risk for hypoglycemia. Correction of hyperglycemia in the perioperative period can be accomplished with subcutaneous doses of ultra-rapid-acting insulin or regular insulin for ambulatory patients or patients in the postanesthesia care unit who will be admitted to a regular nursing floor. Rough estimates for dosing are 1–4 units of insulin per 50 mg/dL decrease in glucose desired. Outside of the immediate perioperative period, it is important to include a basal insulin component meant to suppress gluconeogenesis between meals. This is particularly essential for type 1 diabetics, who without basal insulin can rapidly develop DKA.

For critically ill patients, glycemic control is best achieved with intravenous insulin infusions. These patients can have unpredictable subcutaneous absorption of insulin because of edema, hypotension, and peripheral vasoconstriction. The same is true for patients undergoing procedures where large fluid shifts or hemodynamic lability are expected because skin perfusion can vary greatly under these conditions.

### 4. What impact does hyperglycemia have on perioperative morbidity and mortality?

Hyperglycemia is common in the perioperative period both in diabetics and in nondiabetics. The neuroendocrine stress response to surgery causes release of counterregulatory hormones glucagon, epinephrine, and cortisol, which inhibit insulin secretion, increase insulin resistance, mobilize glycogen, and increase gluconeogenesis. The severity of insulin resistance and resulting hyperglycemia are directly related to the degree of surgical trauma. Hyperglycemia is especially common after cardiac surgery and major abdominal surgery. It is also more common for procedures lasting a long duration and in open procedures more so than laparoscopic procedures. Inhaled anesthetics contribute to perioperative hyperglycemia by depressing insulin secretion in response to increasing blood glucose levels. Perioperative steroid administration further exacerbates the propensity toward hyperglycemia.

Hyperglycemia in the perioperative period is associated with increased risk of infection secondary to impaired leukocyte function—specifically, impaired chemotaxis, phagocytosis, and intracellular bacterial killing. It is also associated with impaired collagen synthesis and decreased nitric oxide production, reducing local perfusion and delaying wound healing. Vascular reactivity can be altered with increased levels of angiotensin II and enhanced systemic vascular resistance. Elevated glucose levels are also associated with renal injury, pulmonary complications, myocardial infarction, cerebrovascular insult, longer hospital and intensive care unit (ICU) stays, and increased mortality. These adverse outcomes are found to be more prevalent in patients without a previous diagnosis of DM who develop hyperglycemia perioperatively than in patients with a known history of DM.

### 5. What is "tight glucose control," and what are its advantages and disadvantages?

Adverse outcomes associated with perioperative hyperglycemia are well documented. The next practical question is whether interventions to decrease blood glucose levels in surgical patients improve outcomes. Several studies evaluated the benefits of insulin therapy targeting near-euglycemia (i.e., serum glucose 80–110 mg/dL) versus conventional management (i.e., serum glucose <180–200 mg/dL). Early reports in critically ill patients advocated intensive glycemic control to reduce mortality, bacteremia, acute kidney injury, blood transfusions, critical illness neuropathy, duration of mechanical ventilation, and ICU stays. More recent trials and meta-analyses failed to find reduced mortality or significant improvement in other outcomes with "tight glucose control" compared with more liberal glucose management. Severe hypoglycemia is six times more common in tightly controlled groups than conventionally managed patients. Subsequent trials were halted early because of safety concerns for hypoglycemia in treatment groups. Criticisms of the initial studies include high ratios of nurses and physicians to patients, which make study conditions unlikely to be generalizable to other ICU settings, and parenteral nutrition for nearly all patients included in the study, which is known to cause hyperglycemia and insulin resistance. After initial positive studies advocated tight glycemic control, several professional societies recommended strict glycemic control guidelines, but those original guidelines have subsequently been called into question.

More recent trials have also questioned the benefits of "tight glucose control" (as determined by glycosylated hemoglobin [$HbA_{1c}$] levels) in outpatients with type 2 DM, showing a higher risk of cardiovascular complications and mortality rate in tightly controlled groups. Hypoglycemia correlated with mortality in these studies.

Particularly concerning is that signs of hypoglycemia may be masked in the perioperative period. Such signs include blurred vision, confusion, diaphoresis, palpitations, and weakness. Interrupted nutritional support during a hospital stay without adjustment of insulin dosing can also lead to hypoglycemia. Insulin is metabolized by the liver and kidney. Organ dysfunction can prolong the drug's duration of action, resulting in hypoglycemia. If improperly dosed, insulin is a very dangerous medication. Overdoses can lead to profound, life-threatening hypoglycemia.

Conflicting evidence surrounding glucose control has led to a new paradigm in thinking about target glucose levels—that glycemic variability may be as important as hyperglycemia when it comes to the detrimental effects of DM. Increased oxidative stress is seen with wide swings in blood glucose. Oxidative stress from glycemic variability is even more substantial than oxidative stress associated with sustained hyperglycemia, which leads to free radical production. Free radicals are implicated in causing vascular damage. Glucose fluctuations may also trigger increases in cytokine expression and apoptosis. Greater glucose variability has been associated with increased mortality in surgical patients.

Studies aimed at delineating the precise goals for optimum inpatient glucose management are ongoing, and guidelines will likely continue to change. At this point, the association between hyperglycemia and increased morbidity and mortality is strong, but the value of "tight glucose control" has not been proven. The ideal blood glucose target and true efficacy of perioperative glycemic control remain to be clarified. Based on the balance of evidence to date, it is recommended by most professional societies, including the American Association of Clinical Endocrinologists and American Diabetes Association, to target a blood glucose level of 140–180 mg/dL for most inpatients, while carefully monitoring for and treating hypoglycemia should it arise.

### 6. Describe and contrast diabetic ketoacidosis and hyperglycemic hyperosmolar states.

DKA usually occurs in type 1 diabetics but can occur in type 2 diabetics. It is the result of decreased insulin levels that reduce glucose utilization and increase lipolysis leading to the formation of fatty acids that are oxidized in the liver to ketone bodies. Manifesting symptoms include dehydration, deep and rapid breathing (Kussmaul respiration), fruity smelling breath, nausea and vomiting, and

abdominal pain. At significantly higher glucose levels, confusion or even coma may be present. Laboratory abnormalities include hyperglycemia, ketones in blood and urine, increased anion gap, acidosis, and elevated lactate levels if perfusion is compromised. Serum sodium ($Na^+$) concentrations may be spuriously low because of hyperglycemia and hypertriglyceridemia. For every 100 mg/dL of glucose >200 mg/dL, the sodium measured decreases by 1.6 mEq/L. The following equation is used to determine the corrected serum sodium level:

$$Na^+_{Corrected} = Na^+_{measured} + \frac{1.6\,(glucose_{measured} - 200)}{100}$$

For example, if the glucose measured is 700 mg/dL and the serum $Na^+$ is 128 mEq/L, the corrected $Na^+$ level is 136 mEq/L. Serum osmolality varies depending on glucose levels.

HHS usually occurs in type 2 diabetics and is the result of decreased glucose utilization owing to inadequate insulin levels. However, insulin levels are sufficient to prevent lipolysis. Manifesting symptoms include dehydration and altered mental status. Laboratory findings consist of hyperglycemia and hyperosmolality secondary to severe dehydration (Table 26-4).

The most common causes of DKA and HHS are inadequate insulin therapy and infection. Other causes include myocardial infarction, cerebrovascular accident, pulmonary embolism, pancreatitis, and alcohol abuse. Certain medications may precipitate DKA or HHS as well.

## 7. Outline the management of diabetic ketoacidosis and hyperglycemic hyperosmolar states.

The overlying principles of treatment are similar for DKA and HHS (Box 26-2) and include searching for an underlying cause, insulin administration, and correction of fluid and electrolyte abnormalities. Initial evaluation always begins with airway, breathing, and circulation and assessment of mental status. Appropriate ventilatory and hemodynamic support should be initiated without delay. Laboratory evaluation includes the following:

- Glucose (measured every hour until stable)
- Electrolytes (measured every 2–4 hours until stable)
- Calculation of anion gap (normal 3–11 mEq/L)
  - [sodium ($Na^+$) + potassium ($K^+$)] − [chloride ($Cl^-$) + bicarbonate ($HCO_3^-$)]
- Arterial or venous blood gas (measured every 2–4 hours)
- Blood urea nitrogen and creatinine
- Complete blood count with differential
- Plasma osmolality
- Urinalysis
- Urine ketones

Fluid loss in DKA can range from 3–6 L and in HHS may exceed 8 L secondary to osmotic diuresis. Fluid administration is aimed at replacing these losses to restore circulating blood volume without inducing cerebral edema (and possible herniation) secondary to rapid reduction in plasma osmolality. Normal saline should be infused as quickly as possible in patients who present in shock or at a rate of 10–15 mL/kg/hour in the absence of shock during the first few hours. Subsequent replacement of fluid losses occurs over 48 hours. Frequent

**TABLE 26-4 Findings in Diabetic Ketoacidosis and the Hyperglycemic Hyperosmolar State**

| | Diabetic Ketoacidosis | Hyperglycemic Hyperosmolar State |
|---|---|---|
| Mental status | Depends on severity | Confused, coma |
| pH | <7.3 | >7.3 |
| Ketones | | |
| Urine | + | 0, minimally + |
| Serum | + | 0, minimally + |
| Bicarbonate | ≤18 mEq/L | >20 mEq/L |
| Osmolality | Variable | >315 mOsm/L |
| Anion gap | >10 | Variable |

Adapted from Kitabchi AE, Nyenwe EA: Hyperglycemic crises in diabetes mellitus: diabetic ketoacidosis and hyperglycemic hyperosmolar state. Endocrinol Metab Clin N Am 35:725, 2006.

**BOX 26-2 Management of Diabetic Ketoacidosis and Hyperglycemic Hyperosmolar State**

**Assessment**

- Assess ABC and mental status—treat accordingly
- Obtain glucose, electrolytes, BUN, creatinine, arterial or venous blood gas, CBC, plasma osmolality, urinalysis, and urine ketones
- Calculate anion gap

**Fluid Management**

- If signs of shock
  - Rapid normal saline infusion until signs of shock resolve
- In absence of shock
  - Normal saline infusion at 10–15 mL/kg/hour for first several hours
- Once intravascular volume replete
  - If corrected serum sodium is normal or elevated—half-normal saline at 4–14 mL/kg/hour
  - If corrected serum sodium is low—continue normal saline
- Add dextrose when glucose is 200 mg/dL
- Add potassium when
  - Serum potassium is <5.3 mEq/L
  - Urine output is confirmed
- Administer sodium bicarbonate over 1–2 hours only if
  - pH <7.0
  - Life-threatening hyperkalemia

**Insulin Therapy**

- Start insulin infusion at 0.1 units/kg/hour
- Titrate so that glucose levels decrease 50–100 mg/dL/hour

*ABC*, Airway, breathing, and circulation; *BUN*, blood urea nitrogen; *CBC*, complete blood count.

monitoring of electrolytes is important to ensure that corrected sodium levels are increasing but not too rapidly. A target increase of 4–6 mEq/L in 24 hours is appropriate. An increase of >9 mEq/L in 24 hours can lead to osmotic demyelination syndrome (formerly called central pontine myelinolysis). Similarly, glucose levels should decrease by no more than 50–100 mg/dL/hour. Neurologic status should also be monitored frequently so that cerebral edema (e.g., headache, altered mental status) can be detected early.

After initial fluid resuscitation, serum electrolyte levels determine the type of fluid administered. If the corrected serum sodium is normal or elevated, half-normal saline can be administered at 4–14 mL/kg/hour. If the corrected serum sodium is low, normal saline can be continued. When the serum glucose reaches 200 mg/dL in DKA or 300 mg/dL in HHS, dextrose is added to fluids to prevent hypoglycemia and reduce the risk of cerebral edema. Similarly, potassium (20–30 mEq/L) should be added to fluids when the serum potassium concentration becomes <5.3 mEq/L and urine output is confirmed. Patients typically have substantial total body potassium deficits because of urinary losses, although serum concentrations can be elevated from intracellular to extracellular potassium shifts. The potassium shift can result from insulin deficiency, serum hyperosmolality, acidosis, or a combination of these. When potassium is added to fluids, the choice of saline should be altered to prevent delivering hypertonic fluids that would not correct hyperosmolality.

The use of sodium bicarbonate can be considered in patients with DKA and severe acidemia (arterial pH <7.0) or in the presence of life-threatening hyperkalemia. If administered, it should not be given as a bolus but rather infused over 1–2 hours. Outside of these two scenarios, administration of sodium bicarbonate should be avoided because it delays the rate of recovery from ketosis by increasing hepatic ketogenesis.

Insulin therapy by continuous infusion is typically initiated at 0.1 units/kg/hour. If serum glucose levels do not decrease by at least 50 mg/dL in the first hour, the infusion rate should be doubled every hour until a steady decline (i.e., 50–100 mg/dL/hour) in serum glucose is achieved. Resolution is marked by closure of the anion gap in DKA (i.e., <11 mEq/L) or normal mentation and plasma osmolality <315 mOsm/L in HHS. At this time, insulin infusions can be tapered and transitioned to subcutaneous insulin regimens.

## 8. When should elective surgery be delayed because of hyperglycemia?

The prevalence of DM is increasing, and patients frequently arrive for elective surgery with elevated fasting glucose levels as a result of holding oral medications, refraining from insulin, or overall poor outpatient long-term glucose control. It remains to be shown whether controlling glucose or decreasing $HbA_{1c}$ to a given level preoperatively improves perioperative outcomes. Before proceeding with elective surgery, it is prudent to evaluate patients with markedly elevated glucose (>300 mg/dL) for evidence of ketoacidosis with either blood chemistry or urine dipstick. If significant acid-base or electrolyte disturbances exist, surgery should be postponed until the patient's metabolic derangements have normalized. There are no recommendations regarding an absolute glucose cutoff level above which elective surgery should be postponed if there are no other metabolic derangements. However, some institutions have policies in place to guide practitioners. In the absence of an institutional policy, practitioners should base their decision on the urgency of the procedure, the risks of the procedure, and the ability to achieve better glucose control if surgery is postponed.

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CASE 27

# Thyroid Disease

Allan P. Reed, MD

## QUESTIONS



A 30-year-old woman presented for thyroidectomy. She had a history of anxiety, palpitations, heat intolerance, and weight loss. Her blood pressure was 150/90 mm Hg, and her pulse rate was 100 beats per minute. Her medications at home included methimazole and metoprolol. On physical examination, there was a fullness of her neck.

### 1. How are thyroid hormones produced?

Thyroid hormones affect metabolic function by facilitating biochemical reactions that increase heat production and oxygen consumption. They also contribute to upregulation of β-adrenergic receptors and in that way enhance catecholamine effects. Their synthesis originates in the hypothalamus, which produces thyrotropin-releasing hormone that stimulates the anterior pituitary to secrete thyroid-stimulating hormone (TSH). TSH allows iodine absorption into the thyroid, where triiodothyronine ($T_3$) and thyroxine ($T_4$) are produced. $T_4$ is altered by other tissues to make $T_3$. $T_3$ is substantially more potent than $T_4$. Both $T_3$ and $T_4$ are highly protein bound. Only the unbound portion is physiologically active. TSH levels are good screening tests for thyroid function. TSH is low in thyrotoxicosis and high in hypothyroidism.

### 2. Describe the classic presentation of thyrotoxicosis.

Thyrotoxicosis is a state of increased metabolic rate. Classically, patients present with nervousness, weight loss, and heat intolerance. The history also includes insomnia, fatigue, tremors, copious perspiration, and muscle weakness. Typical cardiovascular signs include sinus tachycardia and hypertension. High-output cardiac failure and ischemia may also be seen. Ophthalmic problems are associated with Graves disease–related hyperthyroidism (Box 27-1).

### 3. How does thyroid storm differ from thyrotoxicosis?

The transition between thyrotoxicosis and thyroid storm is usually blurred. Thyroid storm is a state of decompensation from thyrotoxicosis. It can be precipitated by physiologic or pharmacologic stresses. Examples include surgery, trauma, large amounts of iodine, cessation of antithyroid medications, diabetic ketoacidosis, myocardial infarction, and cerebrovascular accident. It can occur intraoperatively or up to 18 hours postoperatively. Signs and symptoms include fever (>38.5° C), severe tachycardia, atrial fibrillation, congestive heart failure, hypertension, agitation, altered mentation, nausea, vomiting, diarrhea, and liver failure. Fluid losses from perspiration, nausea, vomiting, and diarrhea predispose to hypovolemic hypotension. Heart failure can also produce hypotension. Without treatment, mortality rates can reach 90%. The accompanying fever could result in hypovolemia, tachycardia, congestive heart failure, shock, and coma. The differential diagnosis of thyroid storm includes malignant hyperthermia, neuroleptic malignant syndrome, sepsis, hemorrhage, pheochromocytoma, and transfusion reaction.

### 4. Describe the treatment of thyroid storm.

Treatment of thyroid storm revolves around three principles: (1) Block thyroid hormone production and secretion. (2) Stop the conversion of $T_4$ to $T_3$. (3) Antagonize the β-adrenergic effects of thyroid hormones. Propylthiouracil (PTU) and methimazole are the classic antithyroid drugs for hyperthyroidism. They inhibit thyroid hormone synthesis but require several weeks to reduce thyroid hormone levels toward normal. PTU offers the added benefit of reducing conversion of $T_4$ to $T_3$. After thyroid hormone production is reduced with antithyroid medications for several hours, thyroid hormone secretion can be addressed. High-dose iodine in the form of Lugol solution, saturated solution of potassium iodide, or iopanoic acid reduces

**BOX 27-1 Problems Associated with Thyroid Disease**

- Hyperthyroidism
  - Nervousness/anxiety
  - Weight loss
  - Tremor
  - Atrial fibrillation
  - Congestive heart failure
  - Myocardial ischemia
  - Thrombocytopenia
- Medullary cancer
  - Multiple endocrine neoplasms—pheochromocytoma

thyroid hormone release from the gland. Unless thyroid hormone synthesis has already been blocked, high-dose iodine therapy enhances hormone production and exacerbates thyroid storm. For patients with iodine allergies, lithium carbonate can be substituted for high-dose iodine preparations. Conversion of $T_4$ to $T_3$ is reduced with glucocorticoids. PTU and iopanoic acid also share this property.

β-Adrenergic blockade is the primary method of controlling catecholamine-like symptoms. When immediate cardiovascular control is required, esmolol is preferred. If β blockade is contraindicated, calcium-channel blockers, such as diltiazem, might be helpful. Table 27-1 outlines the treatment of thyroid storm.

TABLE 27-1 **Therapy for Thyroid Storm**

| | |
|---|---|
| **Block thyroid hormone production** | |
| PTU | 200-400 mg PO every 6-8 hours |
| Methimazole | 20-25 mg PO every 6 hours |
| **Block thyroid hormone release** | |
| Lugol solution | 4-8 drops PO every 6-8 hours |
| SSKI | 5 drops PO every 6 hours |
| Iopanoic acid | 1 g PO every 8 hours for 1 day, then 500 mg PO every 12 hours |
| Lithium carbonate | 300 mg PO every 8 hours |
| **Block $T_4$ to $T_3$ conversion** | |
| Hydrocortisone | 100 mg IV every 8 hours |
| **Block adrenergic-like effects** | |
| Propranolol | 1-2 mg IV every 10-15 min *or* 20-120 mg PO every 4-6 hours |
| Esmolol | 50-100 μg/kg/min |
| Diltiazem | 5-10 mg/hour IV *or* 60-120 mg PO every 6-8 hours |
| **Supportive therapy** | |
| Fluids | |
| Cooling | |
| Meperidine to inhibit shivering | 12.5 mg IV every 10 min × 2 |
| Acetaminophen | 650 mg PO every 4-6 hours |

*IV,* Intravenously; *PO,* by mouth (per os); *PTU,* propylthiouracil; *SSKI,* saturated solution of potassium iodide; $T_3$, triiodothyronine; $T_4$, thyroxine.

Supportive care in an intensive care setting is important. Vigorous fluid resuscitation, cooling, and acetaminophen are required to treat fever. Patients with heart failure may need inotropic support and vasopressors.

## 5. Describe aspects of the preoperative evaluation for thyroid surgery.

Preoperative evaluation includes examining the airway and listening to the voice for dysphonia from vocal cord involvement. Although goiters frequently displace the trachea, the larynx is usually midline. Significant tracheal compression and tracheomalacia are very unusual. Preoperative chest x-rays assist in diagnosing tracheal deviation. Alternatively, computed tomography (CT) scans provide a better understanding of thyroid and airway anatomy. It is a good idea to review diagnostic studies before induction of anesthesia.

Retrosternal goiters occur frequently but are rarely consequential. However, large retrosternal goiters could produce superior vena cava syndrome with thrombosis, facial swelling, and jugular venous distention. Retrosternal goiters can also produce arterial compression resulting in cerebral hypoperfusion, phrenic nerve palsy, recurrent laryngeal nerve palsy, pleural effusion, chylothorax, and pericardial effusion. CT scans are used to delineate mediastinal masses.

Arrest of normal embryologic development could result in a lingual thyroid. If enlarged, lingual thyroid could complicate laryngoscopy.

Optimally, patients should be euthyroid before elective surgery. β blockers, iodine, and antithyroid medications should be continued through surgery. Patients with thyrotoxicosis require all three classes of medications before elective surgery; however, it may take 2 to 6 weeks to attain a euthyroid state. Patients who are actively hyperthyroid are more likely to develop thyroid storm intraoperatively. For emergency surgery, β blockers can be administered for the purpose of decreasing heart rates to 100 beats per minute or less. Care should be taken in patients with congestive heart failure when administering β blockade. Esmolol offers the advantage of short duration of action, so it may be a good idea for patients at risk for myocardial depression. Iodine and antithyroid medications should be administered as well.

Premedication is used to decrease sympathetic discharge related to anxiety. When anxiolysis is desired in patients with airway compromise, benzodiazepines are beneficial because they do not depress respiratory drive. Fever, diaphoresis, hypertension, and diarrhea predispose to hypovolemia, which should be treated with fluids and direct-acting vasopressors.

Medullary carcinoma of the thyroid is associated with coexisting pheochromocytoma. Evaluation for pheochromocytoma before surgery consists of CT scan and 24-hour urine collection for epinephrine.

## 6. What are the complications of thyroid surgery?

The most important complications of thyroid surgery result in respiratory distress and include recurrent laryngeal nerve palsy, hypocalcemia, tracheal compression,

phrenic nerve injury, and pneumothorax. Recurrent laryngeal nerve injury can occur from stretching or transecting the nerve. Bilateral injury can lead to respiratory distress. Controlled ventilation by anesthesia facemask is usually sufficient to prevent hypoxia in the short-term. Reintubation or tracheostomy (or both) is required. Unilateral recurrent laryngeal nerve injury results in hoarseness, ineffective cough, and aspiration but not respiratory distress.

Hypoparathyroidism can result from thyroidectomy when one or more parathyroids are removed. Parathyroid hormone helps maintain blood calcium levels. The absence of parathyroid hormone results in hypocalcemia, which produces muscle irritability. Chvostek (facial spasm) and Trousseau (carpal spasm) signs are classic bedside tests for hypocalcemia. Ionized calcium levels obtained immediately are probably the best way to make the diagnosis. Hypocalcemia can result in laryngeal muscle tetany, producing upper airway obstruction. The immediate treatment is airway management followed by calcium replacement. Hypocalcemia usually occurs 36 hours after surgery.

Tracheal compression can result from arterial bleeding. Blood lost under arterial pressure may dissect through fascial planes and pool posterior to the trachea. The posterior tracheal wall is membranous, not cartilaginous. Pressurized blood behind the trachea can push the membrane into the tracheal lumen, producing narrowing. Immediate treatment requires opening the surgical wound and evacuating the blood. If tracheal patency is not restored, intubation is in order.

Phrenic nerve injury and pneumothorax both produce restrictive lung disease. Phrenic nerve palsy reduces diaphragmatic excursion, and pneumothorax reduces lung volume.

Other complications of thyroid surgery relate to the extremes of thyroid function. Early on, thyroid storm is a possibility, and later on hypothyroidism can manifest (Box 27-2).

## 7. What are the intraoperative anesthetic considerations for thyroid surgery?

Preoperative airway evaluation determines potential methods for securing the airway. In most cases, airway management is achieved in the usual manner. However, anticipated impossible mask ventilation or severe airway stenosis could indicate alternative airway management techniques. Examples include awake or asleep flexible fiberoptic intubation. Tracheal compression by a retrosternal goiter may make passage of the tracheal tube difficult. Armored tracheal tubes or smaller than usual standard tracheal tubes may be necessary to pass through tortuous tracheas. In the United Kingdom, supraglottic devices have been used, but there is a risk of displacement and laryngospasm during gland manipulation.

For most cases, standard induction and intubation works well. Exaggerated hypotension may be seen on induction because of hypovolemia secondary to fever, diaphoresis, hypertension, and diarrhea. Treatment includes fluid administration and direct-acting vasopressors. Acute thyroid crisis during induction of anesthesia can manifest with increased heart rate, elevated blood pressure, and increasing end-tidal carbon dioxide. This presentation mimics malignant hyperthermia. Malignant hyperthermia is associated with muscle rigidity and elevated creatine phosphokinase, whereas acute thyroid crisis is not.

No one anesthetic technique or agent has proved to be better than others. The goals of anesthetic management are to avoid hypertension and tachycardia. Minimum alveolar concentration does not increase in patients with hyperthyroidism. Muscle relaxants are the best choice to prevent movement during tracheal manipulation. However, they are contraindicated when recurrent laryngeal nerve monitoring is employed. In these cases, opioids, by depression of laryngeal reflexes, help prevent intraoperative patient movement and provide the added benefit of inhibiting coughing on emergence. Coughing on emergence may predispose to bleeding from increased venous pressure. Graves disease is associated with myasthenia gravis and other myopathies. Muscle relaxants should be given judiciously in these patients.

Medications that stimulate the sympathetic nervous system should be avoided. Examples include ketamine, pancuronium, epinephrine, and ephedrine. Anticholinergics, such as atropine, may increase the heart rate to a greater rate than under normal circumstances in these patients. Glycopyrrolate may be used with caution.

Careful eye protection for patients with proptosis is necessary to avoid complications from desiccation or mechanical trauma. Carotid sinus manipulation may lead to bradycardia, which should be treated with local anesthetic infiltration or anticholinergics or both.

Tracheomalacia is diagnosed by digital palpitation of a soft, thin tracheal segment after the thyroid gland is removed. After extubation, airway obstruction from tracheal collapse may occur. If this happens, a tracheal tube or tracheostomy tube should be inserted beyond the collapsed segment.

At the end of the procedure, residual neuromuscular blockade is antagonized. In the past, it was routine to observe vocal cord motion during extubation. To facilitate this, deep extubation is followed by placement of a supraglottic device through which a fiberoptic scope is inserted to observe vocal cord movement. However, this practice is no longer routinely performed.

**BOX 27-2 Recognized Complications of Thyroid Surgery**

**Complications with the Potential for Respiratory Distress**

- Recurrent laryngeal nerve palsy
- Hypocalcemia
- Tracheal compression
- Phrenic nerve injury
- Pneumothorax

**Complications That Do not Result in Respiratory Distress**

- Hypothyroidism
- Thyroid storm

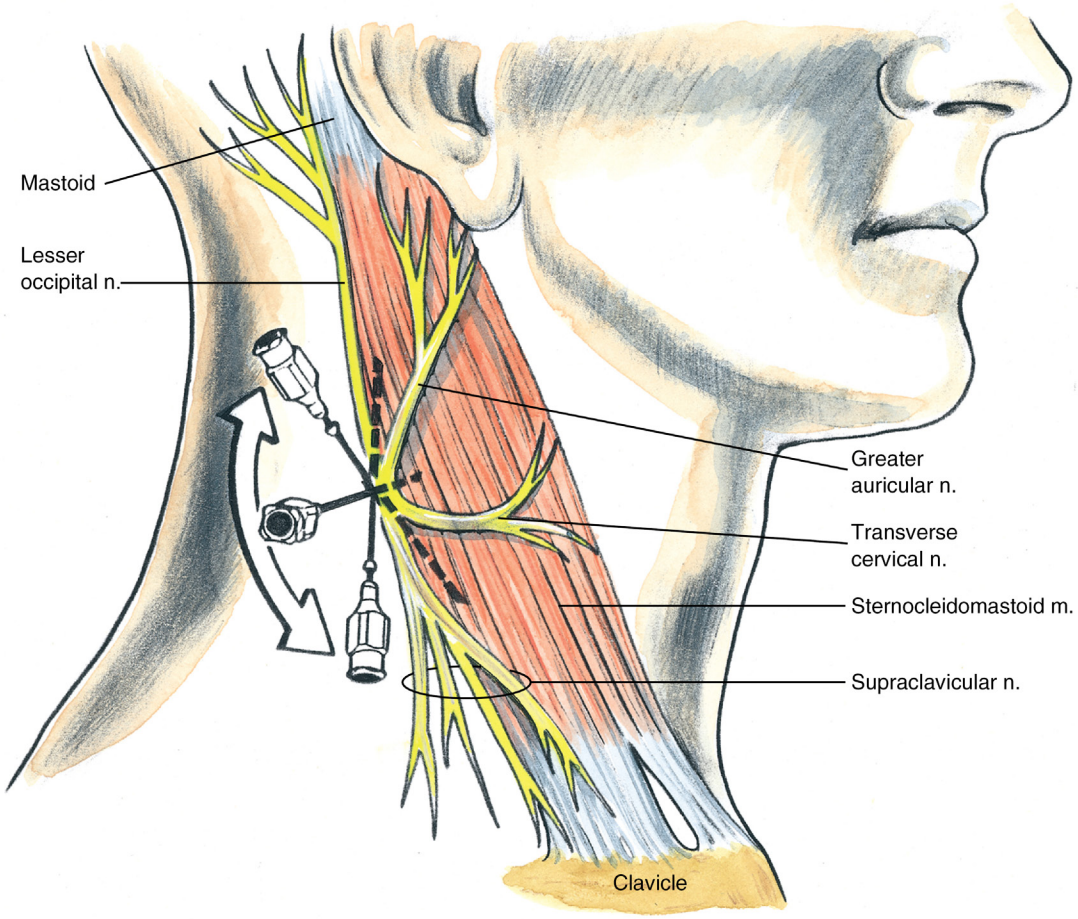


**FIGURE 27-1** ■ **Superficial cervical plexus block.** (From Brown DL: Atlas of Regional Anesthesia, 4th ed. Saunders, Philadelphia, 2010. p. 181.)

After extubation and in the postanesthesia care unit, assessment for respiratory distress or obstruction should be ongoing. Respiratory abnormalities may occur because of neck hematomas, recurrent laryngeal nerve injury, hypocalcemia, phrenic nerve injury, and pneumothorax.

## 8. How is regional anesthesia performed for thyroid surgery?

Local anesthesia for thyroidectomy is not a new concept; it dates back to 1907. Regional anesthesia for thyroid surgery is frequently performed under cervical plexus block. The superficial cervical plexus receives contributions from cervical nerve roots 1 through 4 ($C_{1-4}$). It supplies sensory innervation to the lateral scalp (lesser occipital nerve), pinna (greater auricular nerve), neck (transverse cervical nerve), and upper chest (supraclavicular nerve) (Figure 27-1). The superficial cervical plexus courses subcutaneously at the midlateral border of the sternocleidomastoid muscle. The superficial cervical plexus block is a field block. Bupivacaine or another long-lasting local anesthetic without epinephrine is injected deep to and along the posterior border of the sternocleidomastoid muscle. Approximately 5 to 10 mL of local anesthetic is sufficient.

The deep cervical plexus block is intended to provide neck muscle relaxation. To perform a deep cervical plexus block, local anesthesia is injected just above the anterior surface of the $C_4$ transverse process. Approximately 10 mL of local anesthetic is injected with the hope that it will spread along the paravertebral space. Deep cervical plexus block is almost always complicated by partial or full phrenic nerve block. For this reason, bilateral deep cervical plexus block is not recommended. Even unilateral block should be used cautiously for patients with poor pulmonary function. Other complications of deep cervical plexus block are intravascular injection (vertebral artery), cervical epidural or subdural injection, cervical sympathectomy with Horner syndrome, and recurrent laryngeal nerve involvement producing hoarseness. Horner syndrome includes ptosis, myosis, and anhidrosis.

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CASE 28

# Parathyroidectomy

**Allan P. Reed, MD**

## QUESTIONS

1. Describe the physiology of calcium regulation.
2. What are the clinical features of hypercalcemia?
3. How is hypercalcemia treated?
4. How could hypercalcemia complicate anesthetic care?
5. Discuss a typical general anesthetic for parathyroid surgery.
6. How is parathyroid surgery performed under regional anesthesia?
7. What are the recognized complications of parathyroid surgery?
8. How is hypocalcemia treated?

A 50-year-old woman presents for parathyroidectomy. She has a history of hypertension, cholelithiasis, and nephrolithiasis. She denies seizures, syncope, palpitations, and diaphoresis. She underwent general anesthesia for repair of a fractured femur without complications. Her calcium concentration is 13 mg/dL.

### 1. Describe the physiology of calcium regulation.

Extracellular calcium concentrations are regulated by vitamin D and parathyroid hormone (PTH). Vitamin D increases calcium absorption from the gastrointestinal tract and augments the effects of PTH. PTH increases calcium release from bone, increases calcium absorption from intestines, enhances vitamin D production, and decreases renal clearance of calcium. Under normal circumstances, PTH levels are inversely related to ionized calcium concentrations. Calcitonin tends to decrease calcium levels. It is produced in the thyroid.

Calcium exists in two forms, bound and unbound. The bound portion is mostly attached to albumin. A small percentage is complexed with anions such as citrate and phosphate. The remainder is unbound. Unbound calcium is referred to as ionized or free calcium. Ionized calcium is the physiologically important form. Alkalosis decreases ionized calcium levels and predisposes to clinically significant hypocalcemia.

### 2. What are the clinical features of hypercalcemia?

Hypercalcemia occurs most commonly in association with hyperparathyroidism from single benign parathyroid adenomas. Other causes include malignant tumors, immobility, thyroid toxicity, Paget disease, renal failure, acquired immunodeficiency syndrome (AIDS), and adrenal insufficiency. Parathyroid hyperplasia can be related to pituitary adenomas and multiple endocrine neoplasia (MEN).

Hypercalcemia affects the cardiovascular, renal, gastrointestinal, hematologic, and central nervous systems. Calcium levels >13 mg/dL predispose to renal stones and other end-organ effects. Calcium concentrations >14 mg/dL are associated with uremia, coma, and cardiac arrest. Table 28-1 summarizes the clinical presentation of hypercalcemia.

### 3. How is hypercalcemia treated?

The first step in treating hypercalcemia is to stop administration of calcium. Generally, this means eliminating calcium oral intake but could include intravenous administration. Simultaneous fluid administration with normal saline at 150 mL/hour and diuresis with furosemide are key points. Thiazide diuretics are contraindicated because they can increase calcium levels. This type of fluid management risks congestive heart failure, hypovolemic hypotension, hypokalemia, and hypomagnesemia. Dialysis may be needed for patients with preexisting heart failure or renal failure. Bisphosphonates such as pamidronate are reserved for life-threatening hypercalcemia. Salmon calcitonin, gallium nitrate, and glucocorticoids have also been used.

### 4. How could hypercalcemia complicate anesthetic care?

Preoperative treatment for life-threatening hypercalcemia involves intricate fluid management. Large volumes of infused fluids predispose to hypervolemia and heart failure. Diuretic therapy risks hypokalemia. Hypercalcemia complicates neuromuscular blockade in an unpredictable fashion. Consequently, muscle relaxants are best administered in multiple small doses, with neuromuscular blockade monitoring. Osteoporosis predisposes to bone fractures during positioning. Arrhythmias and conduction abnormalities may be present. Metabolic and respiratory acidosis increase ionized calcium levels.

TABLE 28-1 **Clinical Presentation of Hypercalcemia**

| System | Presentation |
|---|---|
| Cardiovascular | Hypertension<br>Cardiac conduction abnormalities<br>Arrhythmias<br>Catecholamine secretion |
| Musculoskeletal | Weakness/atrophy<br>Fatigability<br>Osteoporosis<br>Bone fractures |
| Central nervous | Seizures<br>Disorientation/psychosis<br>Memory loss<br>Sedation/lethargy/coma<br>Anxiety/depression |
| Renal | Polyuria<br>Nephrolithiasis<br>Renal failure |
| Hematologic | Thrombosis<br>Anemia |
| Gastrointestinal | Nausea/vomiting<br>Pancreatitis<br>Stomach ulcer<br>Abdominal pain<br>Anorexia/constipation |

Approximately 10% of patients with parathyroid hyperplasia have MEN. MEN type 2 is associated with pheochromocytoma. Consequently, a small percentage of seemingly benign cases of hyperparathyroidism have coexisting pheochromocytoma.

## 5. Discuss a typical general anesthetic for parathyroid surgery.

General anesthesia for parathyroid surgery is straightforward. Almost any combination of agents and adjuvants is acceptable. Recurrent laryngeal nerve monitoring during parathyroid surgery may not be as common as during thyroid surgery. Nevertheless, many surgeons perform nerve monitoring during parathyroid surgery. In such cases, intraoperative paralysis is contraindicated. Muscle relaxation for laryngoscopy and intubation can be achieved with succinylcholine. In places where sugammadex is available, nondepolarizing neuromuscular blockers can be administered for laryngoscopy and antagonized before surgery begins. To avoid patient movement in the absence of muscle relaxants, deep general anesthesia is required; this is frequently achieved with potent inhalation agents, intravenous anesthetics, or combinations of both. Opioid-based anesthetics depress laryngeal reflexes and minimize intraoperative coughing during surgical manipulations. Opioid depression of laryngeal reflexes also provides for smooth emergence from anesthesia, with minimal bucking. Coughing tends to increase venous pressure, predisposing to bleeding in the neck. Neck bleeding increases the risks of hematoma and airway obstruction.

To determine whether the offending parathyroid gland has been removed, PTH levels are frequently analyzed intraoperatively. Baseline PTH levels are drawn before laryngoscopy to avoid the possibility that laryngoscopy will increase PTH levels. PTH has a half-life of approximately 5 minutes, so rapid decreases in PTH levels occur after excising the correct gland. A decrease in PTH concentration by half is a good predictor of successful surgery. If PTH levels decrease and then trend upward during the first 20 minutes after adenoma excision, searching for another hypertrophied gland may be indicated. Blood draws are most easily performed from arterial catheters. Large-bore venous catheters are frequently adequate but could be difficult to access under surgical drapes.

## 6. How is parathyroid surgery performed under regional anesthesia?

Parathyroid surgery is amenable to local and regional anesthesia, both of which are demanding on surgeons and patients. Patient selection is critical. Patients generally do best under local or regional anesthesia when they are motivated for the technique. Patients who start out with high anxiety tend to react vigorously to nonpain sensations. Pressure and pulling sensations result in patient movement. Increasing levels of sedation to overcome the problem risk airway compromise. Exploration of multiple glands significantly increases surgical time and can consume hours. Well-localized single lesions can be excised in <45 minutes. For properly selected patients with well-localized lesions, either local or regional anesthesia is a good choice.

Cervical plexus block provides good analgesia for parathyroid surgery. The cervical plexus receives contributions from the upper four cervical nerves. The superficial cervical plexus provides sensory innervation to the anterolateral neck and lateral scalp. The plexus and its terminal nerves wrap around the posterior border of the sternocleidomastoid muscle. Superficial cervical plexus blocks are easily performed by infiltrating local anesthesia along the middle third of the posterior border of the sternocleidomastoid muscle (Figure 28-1). Long-acting local anesthetics, such as bupivacaine 0.5%, are frequently used; 5–10 mL of volume is sufficient. Recorded complications of this block include intravascular injection, unilateral phrenic nerve paralysis, hematoma formation, and deep cervical plexus block. These complications seem to be rare.

In the author's opinion, deep cervical plexus blocks are of little benefit to parathyroid surgery and pose substantial potential risks. Among the recognized complications are vertebral artery injection leading to seizures and blindness, epidural or subdural block, phrenic nerve block, and recurrent laryngeal nerve block.

## 7. What are the recognized complications of parathyroid surgery?

The recognized complications of parathyroid surgery are similar to complications of thyroid surgery. The most important problems relate to airway patency and include recurrent laryngeal nerve damage, hemorrhage, and hypocalcemia. Unilateral recurrent laryngeal nerve injuries cause hoarseness and potentially aspiration. Bilateral

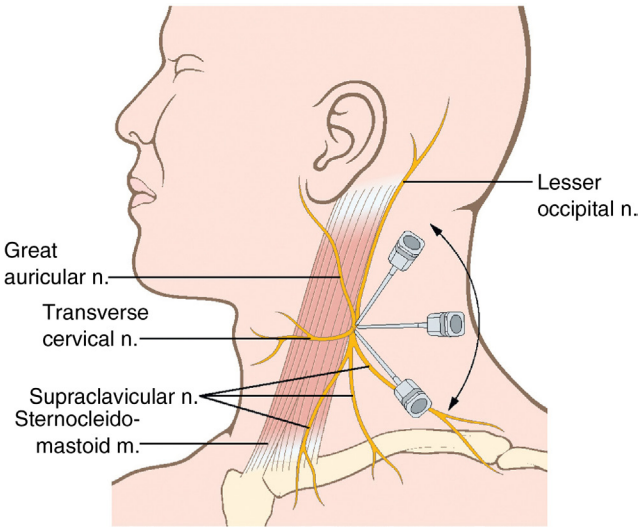


**FIGURE 28-1** ■ Site of needle insertion for superficial cervical plexus block. (From Collins AB, Gray AT: Peripheral nerve blocks. In Miller RD, Pardo M [eds.]: Basics of Anesthesia. Saunders, Philadelphia, 2011. Adapted from Brown DL, Factor DA [eds.]: Regional Anesthesia and Analgesia. Philadelphia, Saunders, 1996.)

**BOX 28-1 Recognized Complications of Parathyroid Surgery**

**Airway Patency**
- Recurrent laryngeal nerve damage
  - Unilateral—hoarseness, aspiration
  - Bilateral—stridor, airway obstruction
- Hemorrhage
  - Tracheal compression
  - Laryngeal edema
- Hypocalcemic tetany
  - Laryngospasm

**Neuromuscular Irritability**
- Muscle cramps
- Chvostek's sign
- Trousseau's sign

**Paresthesias**
- Circumoral
- Hand
- Foot

**Central Nervous System**
- Psychosis
- Seizures

recurrent laryngeal nerve damage can produce respiratory obstruction. Patients with partial respiratory obstruction present with stridor. Total airway obstruction produces apnea. Arterial bleeding can drive blood through fascial planes; collect posterior to the membranous trachea; and force the membrane into the airway, decreasing the trachea's luminal size. Hypocalcemia can produce muscular tetany. This phenomenon is widely recognized in the face and hands. When laryngeal muscles develop tetany, vocal cords close, and the airway becomes obstructed. Following parathyroidectomy, hypocalcemia can occur on the day of surgery or weeks later. Definitive diagnosis of hypocalcemia is made by analyzing blood for ionized calcium concentrations.

Non–life-threatening problems are also associated with acute hypocalcemia. Neuromuscular irritability leads to muscle cramping. Facial nerve irritability is demonstrated by Chvostek's sign. A positive Chvostek's sign is facial muscle spasm after tapping the facial nerve in the region of the parotid gland. Carpal irritability is demonstrated with Trousseau's sign. A positive Trousseau's sign is carpal spasm with tourniquet ischemia for 3 minutes. Circumoral, hand, or foot paresthesias can result. Severe hypocalcemia can also produce coagulopathy, hypotension, psychosis, or seizures (Box 28-1).

### 8. How is hypocalcemia treated?

Symptomatic or severe hypocalcemia requires treatment with intravenous calcium. Ten mL of calcium chloride provides 273 mg of calcium. Ten mL of calcium gluconate provides 93 mg of calcium. Intravenous administration of 10 mL of calcium chloride or 20 mL of calcium gluconate over 20 minutes is recommended. Parenteral calcium replacement should be monitored with electrocardiograms and blood levels of calcium, potassium, phosphorus, magnesium, and creatinine. Calcium irritates veins, so central administration generally provides greater patient comfort. Calcium is incompatible with bicarbonate. Combining the two produces a precipitate of calcium.

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CASE 29

# Perioperative Corticosteroid Administration

Adel M. Bassily-Marcus, MD • Andrew B. Leibowitz, MD

## QUESTIONS

1. Where are steroids naturally produced, and what type of steroids are they?
2. What are the physiologic effects of glucocorticosteroids?
3. What steroids are available for administration, and what are their equivalent doses?
4. How much cortisol is normally produced, and what is Addison disease?
5. What are Cushing syndrome and Cushing disease?
6. Does this patient require "stress" dose steroids?
7. What is a stress dose of steroids; do you need to add mineralocorticoids?
8. How long after discontinuation of steroids should a patient be considered adrenally suppressed and treated accordingly?
9. What clinical scenarios frequently require steroid administration?
10. How is adrenal reserve evaluated?
11. If this patient develops septic shock from a bile leak in the postanesthesia care unit, should steroids be withheld or administered?
12. What is the duration of steroid treatment for critical illness related to corticosteroid insufficiency?
13. If etomidate was used in this patient, is steroid replacement warranted?

A 68-year-old man presented for laparoscopic cholecystectomy. He had been taking prednisone 10 mg per day for treatment of polymyalgia rheumatica. He had no other relevant medical history.

### 1. Where are steroids naturally produced, and what type of steroids are they?

The adrenal cortex produces three different classes of steroids derived from the same basic cholesterol molecule: glucocorticosteroids (cortisol), mineralocorticoids (aldosterone), and androgens (testosterone). The adrenal medulla produces catecholamines via a different metabolic pathway, under different neurohumoral control, and derived from the amino acid tyrosine.

### 2. What are the physiologic effects of glucocorticosteroids?

Glucocorticosteroids are produced by the adrenal glands in response to stimulation by adrenocorticotropic hormone (ACTH). ACTH is secreted by the pituitary in response to corticotropin-releasing hormone, which is produced in the hypothalamus. Glucocorticosteroids primarily affect intermediary metabolism. They diffuse through cell membranes and bind to specific glucocorticosteroid receptors, creating a complex that migrates to the nucleus and alters gene transcription. Resulting physiologic effects include an increase in blood glucose, mobilization of fatty acids, catabolism, and antiinflammation.

### 3. What steroids are available for administration, and what are their equivalent doses?

Dexamethasone (e.g., Decadron), methylprednisolone (e.g., Solu-Medrol), prednisone, and hydrocortisone (e.g., Solu-Cortef [intravenous form], Cortef [oral form]) are the four main steroids available for enteral or parenteral administration (not inhaled or topically applied). Their relative dose equivalents are:

- Dexamethasone 0.75
- Methylprednisolone 4
- Prednisone 5
- Hydrocortisone 20

For example, a patient taking oral prednisone, 5 mg per day, who needs to be changed to an intravenous steroid of identical potency would receive 20 mg of hydrocortisone intravenously.

### 4. How much cortisol is normally produced, and what is Addison disease?

Under normal conditions, approximately 30 mg of cortisol is produced daily. During periods of extreme stress (e.g., thoracic aortic surgery or septic shock), 300 mg may be produced over the course of 24 hours.

Addison disease results from chronic lack of endogenous cortisol (and usually aldosterone) production. Clinical manifestations include fatigue, weakness, anorexia, increased skin pigmentation, hypotension, hypoglycemia, hyponatremia, and hyperkalemia (Table 29-1). Most cases are idiopathic.

**TABLE 29-1 Cushing Syndrome and Addison Disease**

| | Cushing Syndrome | Addison Disease |
|---|---|---|
| Etiology | Excessive cortisol | Lack of endogenous cortisol |
| Cause | BAH<br>Excessive pituitary ACTH<br>Ectopic ACTH secretion<br>Iatrogenic<br>Exogenous cortisol | Iatrogenic |
| Features | Hypertension<br>Hyperglycemia<br>Truncal obesity<br>Hirsutism<br>Weakness<br>Abdominal striae<br>Edema | Hypotension<br>Hypoglycemia<br>Fatigue<br>Weakness<br>Anorexia<br>Increased skin pigmentation<br>Hyponatremia<br>Hyperkalemia |

*ACTH,* Adrenocorticotropic hormone; *BAH,* bilateral adrenal hyperplasia.

Addisonian "crisis" is an acute adrenocortical insufficiency resulting in the same findings but with a more severe presentation in which shock, coma, and death can occur. Acute adrenocortical insufficiency may occur in the case of an absolute or relative lack of glucocorticosteroids. Chronic exogenous steroid administration impairs the ability of the adrenal gland to respond with increased production of glucocorticosteroids during periods of stress. In such instances, additional exogenous steroid administration is necessary to prevent the abovementioned sequelae.

## 5. What are Cushing syndrome and Cushing disease?

Cushing syndrome is caused by excessive cortisol levels. The most common etiology is iatrogenic secondary to excessive steroid administration. The most common noniatrogenic cause is bilateral adrenal hyperplasia secondary to excessive pituitary or ectopic ACTH secretion. The term "Cushing disease" is reserved for patients with pituitary tumors causing excessive ACTH secretion. The most notable features of Cushing syndrome are truncal obesity, hirsutism, weakness, hypertension, abdominal striae, edema, and hyperglycemia (see Table 29-1).

## 6. Does this patient require stress dose steroids?

Laparoscopic cholecystectomy without surgical complications, such as large blood loss, would usually not result in any significant increase in endogenous cortisol production. The administration of full-dose "stress" steroids is not indicated for this patient. However, most sources recommend a modest increase in steroid administration. For example, the patient can safely be instructed to take prednisone, 10 or 15 mg orally, on the day of surgery and perhaps the day after or the equivalent dose of another steroid.

## 7. What is a stress dose of steroids; do you need to add mineralocorticoid?

A stress dose is the hydrocortisone equivalent of 200 to 300 mg per day in three to four divided doses. Common dosing is hydrocortisone, 100 mg every 8 hours or 50 mg every 6 hours or less commonly a continuous infusion (bolus of 100 mg followed by continuous infusion at 10 mg per hour). Most experts suggest that 200 mg maximum is more than adequate for all patients and procedures and may prevent the rare patient from experiencing a complication from the larger dose of 300 mg per day. The mineralocorticoid activity of hydrocortisone in these doses is sufficient; there is no need to administer a mineralocorticoid (e.g., fludrocortisone) in addition.

## 8. How long after discontinuation of steroids should a patient be considered adrenally suppressed and treated accordingly?

The duration and dose of steroid therapy determine the duration and degree of suppression that result. Short courses of high-dose prednisone therapy, such as may be administered to treat poison ivy (e.g., prednisone 50 mg per day for 5 days), have been shown to cause abnormal response to ACTH stimulation testing for up to 5 days. Recovery after prolonged exposure to oral steroids is highly variable but may take 1 year. Exposure to lower doses of steroids from inhalers and enemas results in an unknown degree of adrenal suppression. In the absence of ACTH testing, the authors adhere to the following principles:

- Only major surgical procedures require doses of hydrocortisone in the 200 mg per day range for 2 or more days.
- Intermediate-dose (hydrocortisone 100 to 150 mg per day) steroids for 1 to 2 days carry very little risk.
- Antinausea prophylactic doses of dexamethasone (e.g., 8 mg intravenously) are equivalent to 200 mg of hydrocortisone and alone more than suffice to prevent adrenal insufficiency resulting from all commonly performed surgeries (e.g., hernia repair, cholecystectomy, lumpectomy, hysterectomy) and some major surgeries (e.g., bowel resection, peripheral vascular surgery, joint replacements).

## 9. What clinical scenarios frequently require steroid administration?

Steroids may be administered for various therapeutic effects as follows:

- Prevent or treat postoperative nausea and vomiting
- Reduce swelling (e.g., traumatic intubation or laryngeal surgery)
- Prevent transplant rejection
- Treat asthma
- Treat colitis
- Treat arthritis
- Treat septic shock

- Treat acute respiratory distress syndrome
- Manage vasogenic cerebral edema (e.g., brain tumors, spinal cord compression, acute pneumococcal meningitis)

## 10. How is adrenal reserve evaluated?

The most commonly performed outpatient test for adrenal reserve is a 24-hour urinary free cortisol collection. For hospitalized patients, the ACTH stimulation test is most commonly performed to determine the presence of adequate adrenal function. This screening test entails the measurement of a baseline plasma cortisol, followed by a measurement at 30 minutes and 60 minutes after intravenous administration of 250 μg of cosyntropin, an ACTH analogue. During periods of stress, the baseline plasma cortisol level should exceed 20 mg/dL, and all patients should have an increase in plasma cortisol level of at least 9 mg/dL above baseline with stimulation unless they have adrenal insufficiency.

## 11. If this patient develops septic shock from a bile leak in the postanesthesia care unit, should steroids be withheld or administered?

Although administration of steroids for patients who are known to be adrenally suppressed is straightforward, steroid administration in patients with septic shock has long been debated. Steroid administration sometimes can improve vascular responsiveness to catecholamine administration. Steroids are still administered in patients with vasopressor-resistant septic shock, although clinical trials have generally revealed greater harm than benefit.

In a study by Annane et al. (2002), patients with septic shock who received stress dose steroids and were proved to be adrenally insufficient based on cosyntropin (ACTH) stimulation test had lower mortality rates compared with patients who received placebo (53% vs. 63% at 28 days and 58% vs. 70% at the end of the intensive care unit stay) (Box 29-1). A subsequent multicenter, randomized, double-blind, and placebo-controlled trial (CORTICUS) is now the "gold standard." This trial assessed whether "low" doses of corticosteroids improve survival from septic shock. In this investigation, patients in septic shock underwent a cosyntropin stimulation test. Patients were randomly assigned to receive either hydrocortisone, 50 mg by intravenous bolus every 6 hours, or a placebo. In the hydrocortisone group, septic shock was reversed more quickly than in the placebo group but with more episodes of superinfection, including new sepsis and septic shock. The study showed no difference in 28-day mortality for responders and nonresponders to the test whether they received corticosteroids or placebo.

Based primarily on this investigation, the Society of Critical Care Medicine recommends hydrocortisone administration only in the treatment of vasopressor-resistant shock, defined as the need for increasingly higher doses of vasopressors or the need for a second vasopressor after adequate fluid resuscitation. Although final conclusive evidence is lacking, there is no utility at the present time in performing ACTH stimulation tests before administration of hydrocortisone in patients requiring vasopressors in the management of presumed septic shock.

In the patient in the present case, who was almost certainly adrenally suppressed because of long-term steroid administration, stress dose steroid administration would generally be considered reasonable.

**BOX 29-1 Suggested Steroid Treatment in Septic Shock**

**Perform ACTH Stimulation Test**

In patients requiring vasopressor therapy start:
Hydrocortisone 50 mg intravenously every 6 hours
Fludrocortisone 50 mg orally once daily (if enteral access and absorption present)

**Stimulation Test Results**

Baseline cortisol level < 20 mg/dL, or
Rise from baseline level < 9 mg/dL
Continue therapy for 7 days
Baseline cortisol level > 20 mg/dL, or
Rise from baseline level > 9 mg/dL
Discontinue therapy

## 12. What is the duration of steroid treatment for critical illness related to corticosteroid insufficiency?

The required duration of hydrocortisone replacement therapy is unknown. In clinical trials, it has usually been 5 to 10 days and in practice usually depends on the clinical response to therapy. If symptoms of hypotension or shock recur after discontinuation of steroids, the regimen should be resumed at the prior dose and tapered slowly, if no other cause is found.

## 13. If etomidate was used in this patient, is steroid replacement warranted?

Etomidate administration has been independently associated with poorer outcomes in critically ill patients. One explanation is its preferential use in sicker patients, especially patients with severe sepsis who frequently already have adrenal insufficiency. There is also some disagreement concerning the need to administer steroids to patients receiving etomidate. One large retrospective study in patients with severe sepsis by Payen et al. (2012) found no association between etomidate and changes in vasopressor requirement, intensive care unit length of stay, ventilator days, or hospital mortality. In exploring the effect of etomidate on outcome in patients with severe sepsis, two randomized studies showed no outcome difference compared with ketamine or midazolam. Finally, in another randomized study, empiric steroid supplementation after etomidate administration did not change outcome compared with placebo.

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CASE 30

# Pheochromocytoma

David B. Wax, MD

QUESTIONS

1. What is a pheochromocytoma?
2. What are the signs and symptoms and diagnostic criteria?
3. How is pheochromocytoma managed preoperatively?
4. What are intraoperative surgical and anesthetic considerations?
5. What are postoperative concerns and outcomes?

A 45-year-old, previously healthy woman was having increasingly frequent "panic attacks" accompanied by palpitations, sweating, trembling, and headache. She was evaluated by her internist and was found to be moderately hypertensive. This suggestive history prompted evaluation for possible pheochromocytoma. Plasma metanephrine levels were elevated, and subsequent imaging showed an adrenal mass. She was started on doxazosin and referred to a surgeon. Her blood pressure improved, but other symptoms persisted. Atenolol was added to her medication regimen, and she was scheduled for laparoscopic adrenalectomy.

## 1. What is a pheochromocytoma?

A pheochromocytoma is a tumor of neuroendocrine tissue arising in the adrenal medulla from chromaffin cells that synthesize catecholamines. Neoplastic proliferation of these cells can lead to release of one or more substances (norepinephrine, epinephrine, or dopamine) in varying amounts and can cause catecholamine toxicity. Most pheochromocytomas are solitary, benign, and sporadic, but they are occasionally multifocal, malignant, or part of a syndrome (e.g., multiple endocrine neoplasias, von Hippel–Lindau syndrome, neurofibromatosis, tuberous sclerosis, Sturge-Weber syndrome, ataxia-telangiectasia). They can also occur in pediatric and obstetric settings. Similar tumors can arise in extraadrenal locations from paraganglial cells of the autonomic nervous system (e.g., in the organ of Zuckerkandl or carotid body) and in the heart or pericardium. These paragangliomas are less likely to be functional compared with adrenal tumors. Incidence of pheochromocytoma in the United States is approximately 1000 cases per year.

## 2. What are the signs and symptoms and diagnostic criteria?

Signs and symptoms of pheochromocytoma are related to catecholamine excess and vary, depending on which catecholamine predominates. Norepinephrine secretion is most common and is usually sustained, with effects related to α-adrenergic stimulation. Epinephrine release is less common and more often paroxysmal, causing episodic effects related to β-adrenoreceptor stimulation. Dopamine release is least common and has less specific signs and symptoms. Table 30-1 lists typical signs and symptoms as well as uncommon but more severe end-organ manifestations of catecholamine toxicity.

Catecholamine release (and symptoms) from the tumor may be provoked by postural changes, exercise, anxiety, trauma, or pain. Foods and medications (e.g., antidepressants, cold/flu medications, weight-loss medications, cocaine, tobacco, alcohol) may also exacerbate symptoms by their effects on catecholamine metabolism. Pheochromocytoma may first manifest during anesthesia and surgery for another related tumor or unrelated condition or during pregnancy and may be confused with other conditions such as thyrotoxicosis, malignant hyperthermia, or preeclampsia.

Diagnosis of pheochromocytoma is made by laboratory testing in patients with suggestive signs and symptoms. Elevated levels of metanephrine and normetanephrine measured in plasma (for patients with sustained signs and symptoms) or 24-hour urine collection (for patients with paroxysmal signs and symptoms) confirm the diagnosis. Absolute catecholamine concentrations may not always correlate with the severity of signs and symptoms because of temporal variation, difference in the predominant catecholamine, and adrenoreceptor desensitization that may occur with chronic exposure. Computed tomography, magnetic resonance imaging, metaiodobenzylguanidine scintiscan, or 18F-fluorodopa positron emission tomography scanning can be used for tumor localization and surgical planning. Before surgical intervention, echocardiography may be performed to detect cardiomyopathy and monitor improvement after preoperative medical therapy.

TABLE 30-1 **Signs and Symptoms of Pheochromocytoma**

| Norepinephrine-Related | Epinephrine-Related | Other Manifestations |
|---|---|---|
| Hypertension | Palpitations | Dysrhythmia |
| Headache | Tachycardia | Cardiomyopathy |
| Sweating | Panic/anxiety | Myocardial infarction |
| Pallor | Tremors | Encephalopathy |
| Bradycardia | Hyperglycemia | Stroke |
| | | Renal insufficiency |
| | | Tumor mass effect |

### 3. How is pheochromocytoma managed preoperatively?

The initial goal of preoperative medical therapy is to block the toxic effects of catecholamines to prevent and reverse end-organ damage. Table 30-2 presents agents commonly used for this purpose. Therapy usually begins by reversing α-adrenoreceptor-induced vasoconstriction. Phenoxybenzamine, a noncompetitive, nonselective, α-adrenoreceptor antagonist, is the traditional first-line agent. Dosage is increased until blood pressure improves or intolerable side effects (e.g., postural hypotension, tachycardia, nasal congestion) develop. Selective, competitive, $\alpha_1$-adrenoreceptor antagonists (e.g., prazosin, doxazosin, terazosin) have also been used successfully. These agents may cause less tachycardia than phenoxybenzamine, and their shorter elimination times may be advantageous in avoiding postoperative hypotension. Both classes of α-blocking agents may cause postural hypotension, which may be alleviated by salt and fluid supplementation.

Calcium-channel blockers have also been used as a second agent in patients who have refractory hypertension with a single agent, are intolerant of the aforementioned agents, have only paroxysmal hypertension, or have coronary vasospasm. Metyrosine, an inhibitor of catecholamine synthesis, may also be used preoperatively. Long-acting medications may be discontinued 24 to 48 hours before surgery to help prevent postoperative hypotension when the source of excess catecholamines is removed.

When blood pressure is normalized, consideration may be given to β Blockade. However, this treatment is necessary only for patients with predominantly epinephrine-secreting tumors or patients who have developed tachycardia from vasodilator therapy. β Blockers (especially nonselective ones) are not given until α blockade is achieved because $\beta_2$ blockade can block skeletal muscle vasodilation, which could exacerbate hypertension when combined with $\alpha_1$ agonism by norepinephrine from the tumor. β Blockade could also potentially cause decompensation of catecholamine-induced cardiomyopathy. When indicated, $\beta_1$-selective agents, such as atenolol or metoprolol, are typically used. Mixed β and $\alpha_1$ antagonists, such as labetalol or carvedilol, may also be used, but they are not considered

TABLE 30-2 **Pharmacologic Agents for Pheochromocytoma Management**

| Mechanism of Action | Drug | Dosage | Duration |
|---|---|---|---|
| Selective $\alpha_1$-adrenergic antagonists | Prazosin | 1-5 mg p.o. q.d.-t.i.d. | 6 hours |
| | Terazosin | 1-20 mg p.o. q.d.-b.i.d. | 12 hours |
| | Doxazosin | 1-16 mg p.o. q.d. | 24 hours |
| Nonselective α-adrenergic antagonist | Phenoxybenzamine | 10-40 mg p.o. b.i.d.-t.i.d. | 36 hours |
| Tyrosine hydroxylase inhibitor | Metyrosine | 250-750 mg p.o. q.i.d. | 6 hours |
| Nitric oxide–mediated vasodilators | Nitroprusside | 0.5-1.5 μg/kg → 0.3-10 μg/kg/min IV | 5 minutes |
| | Nitroglycerin | 0.5-1.5 μg/kg → 0.3-10 μg/kg/min IV | |
| Nonselective α-adrenergic antagonist | Phentolamine | 5 mg IV | 30 minutes |
| Selective $\beta_1$-antagonists | Esmolol | 0.5-1 mg/kg → 0.05-0.3 mg/kg/min IV | 20 minutes |
| | Metoprolol | 2-20 mg IV , 25-100 mg p.o. q.d.-b.i.d. | 8 hours |
| | Atenolol | 5-10 mg IV, 50-200 mg p.o. q.d. | 12 hours |
| Sodium channel blockade | Lidocaine | 0.7-1.4 mg/kg IV → 0.01-0.05 mg/kg/min IV | 15 minutes |

*b.i.d.,* Twice a day; *IV,* intravenously; *p.o.,* per os (orally); *q.d.,* once every day; *q.i.d.,* four times a day; *t.i.d.,* three times a day.

adequate as single-agent therapy because of the weak α effects and potential for causing worsening of hypertension owing to $\beta_2$ blockade.

### 4. What are intraoperative surgical and anesthetic considerations?

Surgical resection is the definitive treatment for pheochromocytoma. Surgery may be performed with open laparotomy technique or laparoscopic (with or without robotic assistance) technique. Surgical technique and patient positioning depend on tumor size, number, and location. For familial or bilateral adrenal tumors, partial adrenalectomy may be attempted to avoid permanent adrenal insufficiency. Regardless of technique, occlusion of the adrenal or other draining vein is desirable early in the procedure to decrease catecholamine release into the circulation during surgical manipulation of the tumor.

The intraoperative period may be complicated by hemodynamic instability and blood loss. Large-bore peripheral intravenous access and intraarterial blood pressure monitoring are advisable, and preoperative volume loading may be warranted. Central venous cannulation may be considered for vasoactive infusions or volume resuscitation but may not improve outcome compared with peripheral-only access. Pulmonary artery catheterization is probably unnecessary other than in exceptional cases of cardiovascular compromise. Similarly, intraoperative monitoring with transesophageal echocardiography is probably not warranted in all cases but may be helpful in some circumstances. It is unknown whether using other cardiac output monitoring technologies for goal-directed therapy improves outcomes in this setting. Thoracic epidural catheterization for postoperative pain management may improve analgesia after laparotomy. However, the sympathetic blockade would not be expected to completely control intraoperative hypertension caused by circulating catecholamines released from the tumor and may increase postoperative hypotension.

Various stimuli have been implicated in provoking catecholamine surges during the procedure, including anesthesia induction, depolarizing neuromuscular blockade, tracheal intubation, patient positioning, skin incision, and pneumoperitoneum. Succinylcholine-induced muscle fasciculation in the abdomen can cause tumor compression and catecholamine release. Medications associated with histamine release or undesirable autonomic effects (e.g., ketamine, halothane, atracurium, tubocurarine, pancuronium, morphine, meperidine, ephedrine, metoclopramide, chlorpromazine, prochlorperazine, droperidol) should be avoided, if possible. Aside from those agents, most modern intravenous induction agents, opioids, neuromuscular blockers, and inhaled agents can be used safely; no agents are clearly superior to the others.

Surgical manipulation and other events can trigger catecholamine release, resulting in acute hypertension and dysrhythmias. Medications must be immediately available to treat such episodes. Short-acting agents may be preferable given the generally short-lived nature of the catecholamine surges. Various agents (see Table 30-2) can be used depending on availability and practitioner preference. For supraventricular and ventricular dysrhythmias, β blockers and lidocaine are usually effective. For hypotension, fluid administration and direct-acting adrenergic agonists (e.g., phenylephrine, norepinephrine) can be used.

### 5. What are postoperative concerns and outcomes?

Postoperative hypotension is common and, in addition to the usual causes, may be due to persistent adrenergic blockade from preoperative or intraoperative medications that are still acting in the absence of opposing circulating catecholamines. Other causes of hypotension include downregulation of contralateral adrenal output or adrenal insufficiency after bilateral adrenalectomy. Alternatively, hypertension may persist because of residual tumor, stored catecholamines, or chronic downregulation of adrenergic receptors. Hypoglycemia may result from rebound hyperinsulinism.

Major morbidity and mortality associated with pheochromocytoma resection have decreased from 20% historically to less than 5% more recently. These improvements in outcomes have been attributed to various factors, including newer pharmacologic agents, better tumor localization techniques, refined surgical techniques, closer attention to hemodynamics, and practitioner experience.

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CASE 31

# Carcinoid Syndrome

**Maria D. Castillo, MD**

## QUESTIONS

1. What are carcinoid tumors?
2. Where do carcinoid tumors occur?
3. Describe the pathophysiology of carcinoid syndrome.
4. What is carcinoid crisis?
5. What are anesthetic concerns for patients with carcinoid syndrome?
6. How does somatostatin work?
7. Outline the perioperative management of patients with carcinoid tumors.

A 42-year-old woman presented with abdominal pain, diarrhea, episodic facial flushing, and occasional wheezing. On physical examination, a midsystolic heart murmur was heard loudest along the left lower sternal border. A mass was discovered in the ileocolic region during colonoscopy, and increased levels of 5-hydroxyindoleacetic acid (5-HIAA) were found by 24-hour urine assay. The patient was admitted for ileocolic resection with a presumptive diagnosis of carcinoid syndrome.

## 1. What are carcinoid tumors?

Carcinoid tumors are slow-growing neoplasms of neuroendocrine tissue originating from enterochromaffin or Kulchitsky cells, with a reported incidence of 1 to 2 cases per 100,000 individuals. The term "carcinoid" originally was used to describe a small bowel tumor that was slow-growing but capable of metastatic spread. Carcinoid tumors can secrete an array of bioactive substances, including serotonin, histamine, prostaglandins, vasoactive intestinal peptide, adrenocorticotropic hormone, motilin, kallikreins, bradykinins, and tachykinins (e.g., substance P, neuropeptide K, neurokinin A). Carcinoid tumors arising from the ileum or jejunum appear as dense nests of cells with uniform size and nuclear appearance. Bronchogenic carcinoids may have a typical carcinoid appearance or may resemble oat cell carcinoma of the lung.

Diagnosis of carcinoid tumors can be made by urine and plasma assays of serotonin and its metabolite 5-HIAA; however, 20% of patients with carcinoid syndrome may have normal urinary 5-HIAA levels. Imaging techniques such as computed tomography scan, magnetic resonance imaging, endoscopy, endoscopic ultrasound, abdominal ultrasound, selective mesenteric angiography, and barium small bowel radiography can help identify the primary tumor and, if possible, any metastases. Bronchoscopy can be useful for locating a tumor in the bronchial tree. Localization studies such as radiolabeled somatostatin analogue scintigraphy, bone scintigraphy, and positron emission tomography can be used to identify primary and metastatic tumors. In the absence of carcinoid syndrome, carcinoid tumor may be diagnosed incidentally on chest or abdominal x-ray. Carcinoid syndrome may also be diagnosed in patients undergoing unrelated surgery who present with carcinoid crisis in the perioperative period.

## 2. Where do carcinoid tumors occur?

Most carcinoid tumors occur in the gastrointestinal tract, most commonly in the appendix, ileum, and rectum. They may also occur in the bronchial tree, genitourinary tract, thyroid, breast, pancreas, thymus, and liver. Because they are slow-growing tumors, carcinoid tumors are usually asymptomatic or produce vague, nonspecific symptoms such as abdominal pain. Over time, these tumors may cause intestinal obstruction or hemoptysis.

Metastatic disease occurs most commonly in the liver, but carcinoid can spread to bone, mesenteric lymph nodes, myocardium, breasts, orbits of the eyes, adrenal glands, ovaries, spleen, pancreas, and lungs. Mesenteric metastases can cause intermittent bowel obstruction and abdominal pain.

Traditional classification of carcinoid tumors is based on the embryonic site of origin because it affects the clinical presentation, the vasoactive substances that are secreted, and overall survival. Foregut carcinoid tumors are located in the thymus, esophagus, stomach, duodenum, pancreas, gallbladder, bronchus, lung, and trachea. Foregut carcinoid tumors may secrete adrenocorticotropic hormone and produce Cushing syndrome. Histamine release is more often associated with foregut carcinoid tumors, particularly tumors arising in the stomach. This histamine release may be due to the presence of histidine decarboxylase in normal gastric mucosa. Midgut carcinoid tumors are found in the jejunum, ileum, Meckel diverticulum, appendix, and colon. These tumors are more often associated with serotonin release and classic carcinoid syndrome. Hindgut carcinoid tumors are located in the rectum and are more likely to manifest with gastrointestinal bleeding. An alternative

classification system assigns the term "carcinoid tumor" only to midgut carcinoid tumors. Tumors arising from any other site are referred to as neuroendocrine tumors of the site of origin.

### 3. Describe the pathophysiology of carcinoid syndrome.

Although about 25% of carcinoid tumors actively secrete bioactive substances, less than 10% of patients develop classic carcinoid syndrome. Because the liver is very efficient at metabolizing these bioactive substances, the syndrome occurs with primary tumors that are located in areas that do not drain into the portal system or with hepatic, bone, gonadal, or pulmonary metastases that bypass hepatic metabolism. Although tumor size may not correlate with the clinical course of the patient, large liver tumors may secrete so much of these bioactive substances that the liver's ability to inactivate them may be overwhelmed. Carcinoid syndrome may result when the active forms of neuropeptides and amine substances are released into the systemic circulation.

Signs and symptoms of classic carcinoid syndrome include hypotension, hypertension, wheezing, diarrhea, and episodic cutaneous flushing of the head, neck, trunk, and upper extremities. Other possible manifestations include abdominal pain, nausea, vomiting, telangiectasia, right-sided valvular disease, arrhythmias, pericardial effusion, and pellagra (dermatitis, diarrhea, and dementia) (Box 31-1). Dizziness and wheezing may occur with these episodes, which can be triggered by stress, exercise, or ingestion of alcohol, coffee, or serotonin-rich foods such as bananas, avocados, plums, tomatoes, pineapples, kiwis, eggplant, plantains, or walnuts.

Serotonin can cause vasoconstriction or vasodilation, which may manifest as hypertension or hypotension. Elevated serotonin levels can cause inotropic and chronotropic responses in cardiac function; increased gut motility, vomiting, bronchospasm, hyperglycemia, and secretion of water, sodium, chloride, and potassium by the small intestine. Because serotonin is synthesized from tryptophan via hydroxylation and decarboxylation, producing large amounts of serotonin may deplete the body's tryptophan stores. Tryptophan is an essential amino acid necessary for the synthesis of proteins and nicotinic acid. Hypoproteinemia, hypoalbuminemia, decreased protein synthesis, decreased nicotinic acid production, and the symptoms of pellagra may result.

Histamine release may cause bronchospasm and possibly produce flushing, although this remains unclear. Kallikreins are protease enzymes that generate kinins from kininogens on release into the bloodstream. Bradykinin release may cause profound vasomotor relaxation resulting in severe hypotension. Bradykinins can also cause bronchospasm, particularly in asthmatics and in the presence of cardiac disease, and flushing, likely via increased nitric oxide synthesis. Tachykinins, including neuropeptide K, neurokinin A, vasoactive intestinal peptide, and substance P, may cause flushing and longer term cardiac manifestations. Although the etiology is unclear, elevated levels of serotonin and tachykinins are likely involved in the development of right-sided valvulitis and fibroblast proliferation. Tricuspid regurgitation is a common finding, but tricuspid stenosis, pulmonary insufficiency, and pulmonary stenosis may also develop. These valvular lesions may lead to right-sided heart failure, with edema, hepatomegaly, and fatigue on exertion. Left-sided valvular lesions, including aortic and mitral insufficiency, although less common, may occur. Fibrous tissue growth can interfere with electrical pathways, causing arrhythmias. Pericardial effusions, carcinoid plaques, and myocardial metastases are additional possible complications. Bronchial tumors may be associated with left-sided lesions, pulmonary hypertension, and bronchospasm.

**BOX 31-1 Signs and Symptoms of Carcinoid Syndrome**

- Episodic cutaneous flushing
- Hypertension
- Hypotension
- Diarrhea
- Abdominal pain
- Bronchospasm
- Nausea and vomiting
- Delayed emergence from anesthesia
- Hepatomegaly
- Hyperglycemia
- Hypoalbuminemia and hypoproteinemia
- Gastrointestinal bleeding
- Pellagra
- Right heart failure
- Valvular disorders (tricuspid insufficiency, pulmonary stenosis)

### 4. What is carcinoid crisis?

Carcinoid crisis is a life-threatening form of carcinoid syndrome characterized by severe flushing with dramatic changes in blood pressure, cardiac arrhythmias, bronchoconstriction, mental status changes, and circulatory collapse. It results from the sudden release of excessive amounts of tumor mediator substances (Box 31-2). Carcinoid crisis can occur spontaneously, during induction of anesthesia, during tracheal intubation, with physical manipulation of the tumor, with chemical stimulation, with tumor necrosis from chemotherapy, and with hepatic artery ligation or embolization.

### 5. What are anesthetic concerns for patients with carcinoid syndrome?

The major perioperative goal is to prevent release of bioactive mediators; this can be achieved by avoiding triggering factors to prevent precipitating carcinoid crisis. A thorough history should be taken and a physical examination should be performed to determine the presence and severity of signs and symptoms of carcinoid syndrome, including flushing, diarrhea, wheezing, and heart murmur, and any triggers such as particular foods, caffeine, or alcohol. Laboratory tests including blood count, chemistry and liver function panels, blood glucose concentration, and electrocardiogram (ECG) should

**BOX 31-2 Carcinoid Crisis**

**Triggering Factors**

- Anxiety
- Pain
- Hypoxia
- Hypercarbia
- Hypothermia
- Tumor compression or manipulation
- Catecholamine-releasing agents
- Histamine-releasing agents

**Treatment**

- Stop surgical manipulation of tumor
- Intravenous fluid bolus
- Octreotide
- $H_1$- and $H_2$-receptor blocking agents
- Aprotinin
- Phenylephrine
- Vasopressin

be performed. Urinary 5-HIAA assay results should be reviewed.

Of patients with carcinoid tumors, 30% to 50% have carcinoid heart disease, which usually manifests as right-sided valvular disease or heart failure. Even mild symptoms may warrant a cardiac work-up with transthoracic echocardiography to provide vital information. Tricuspid insufficiency, pulmonary stenosis, and pulmonary hypertension are most commonly associated with carcinoid tumors. More rarely, left-sided valvular lesions such as aortic and mitral insufficiency may occur. Valvular lesions may be related to serotonin-induced and tachykinin-induced fibrous tissue growth within the endocardium. This fibrous tissue growth can also cause interruption of electrical pathways, causing arrhythmias. Pericardial effusions, carcinoid plaques, and myocardial metastases can also be present in these patients. Carcinoid heart disease and high levels of urinary 5-HIAA have been associated with an increase in postoperative complications.

Patients who have been experiencing vomiting or diarrhea may exhibit severe dehydration and electrolyte derangements. Depletion of tryptophan for the synthesis of serotonin may result in hypoproteinemia, hypoalbuminemia, and niacin deficiency, which can lead to the symptoms of pellagra. Excess serotonin can cause hyperglycemia, which may be exacerbated by the administration of corticosteroids.

Patients may present with wheezing or bronchospasm that is not responsive to $\beta_2$-adrenergic agonists, theophylline, or epinephrine. These drugs may worsen symptoms by further stimulating mediator release. The treatment of choice for bronchospasm in these patients is octreotide; corticosteroids, ipratropium bromide, and antihistamines can be useful adjuvants.

### 6. How does somatostatin work?

Somatostatin is a cyclic peptide that inhibits gastrointestinal motility, gastric acid production, pancreatic enzyme secretion, and bile and colonic fluid secretion. It inhibits glucagon, insulin, secretin, and vasoactive intestinal peptide secretion. Somatostatin receptors are G protein–coupled receptors; at least five subtypes have been identified, which are referred to as sst1 through sst5. Most carcinoid tumors have a high concentration of sst2 receptors. Octreotide, a somatostatin analogue, binds with the highest affinity to sst2 and sst5. Octreotide is very effective in treating carcinoid crisis, controlling symptoms, and possibly slowing tumor progression. In contrast to somatostatin, which must be administered by continuous intravenous infusion and is associated with postinfusion rebound hypersecretion, octreotide can be administered by subcutaneous or intravenous injections or by continuous intravenous infusion.

### 7. Outline the perioperative management of patients with carcinoid tumors.

Hemodynamic instability, intravascular volume depletion, hyperglycemia, bronchospasm, and electrolyte imbalances should be corrected preoperatively, if possible. Octreotide, 50 to 100 μg subcutaneously, can be given preoperatively as a prophylactic measure. An alternative approach would be to run an intravenous infusion of octreotide at 50 to 100 μg per hour to prevent mediator release. Octreotide bolus doses of 25 to 200 μg intravenously may be given as needed to treat symptoms.

Neuraxial anesthesia can offer good pain control and blunt the stress response; however, spinal anesthesia could exacerbate hypotension and cause subsequent reflex sympathetic nervous stimulation. Epidural catheter placement for anesthesia or postoperative analgesia may be a better option than spinal anesthesia because dosing can be achieved in a more controlled manner. Sufficient anxiolysis and subcutaneous infiltration of ample local anesthetic before needle placement are particularly important for these patients. Local anesthetic given through the epidural catheter should be carefully titrated to avoid hypotension and resultant mediator release.

Because anxiety can trigger carcinoid crisis, anxiolysis and sedation with benzodiazepines and antihistamines are recommended. After large-bore intravenous access is secured and standard monitors are placed, an arterial catheter should be inserted before induction of anesthesia to closely monitor blood pressure changes, which can be dramatic. Depending on the presence and extent of cardiac involvement and expected fluid shifts and blood loss, central venous access, pulmonary artery catheterization, or transesophageal echocardiography may be necessary. Transesophageal echocardiography may prove useful for patients with significant valvular disease and to monitor cardiac output and volume status.

Induction of anesthesia should proceed cautiously, avoiding medications that cause histamine release, such as thiopental, morphine, meperidine, or atracurium, and any medications that stimulate the nervous system, such as ketamine (Table 31-1). Slow titration of fentanyl, etomidate, and propofol can decrease the risk of hypotension. The neuromuscular blocking agents vecuronium, rocuronium, and cisatracurium all have been used successfully in these patients. There have been some concerns regarding the theoretical effects of succinylcholine-induced fasciculations on abdominal tumors causing release of mediators;

TABLE 31-1 **Anesthetic Drugs and Carcinoid Syndrome**

| Safe | Use with Caution | May Trigger Carcinoid Crisis |
|---|---|---|
| Benzodiazepines | Neuraxial anesthesia | Morphine |
| Antihistamines | Succinylcholine | Meperidine |
| Fentanyl | | Ketamine |
| Remifentanil | | Atracurium |
| Propofol | | |
| Etomidate | | |
| Vecuronium | | |
| Rocuronium | | |
| Cisatracurium | | |
| Volatile agents | | |

however, succinylcholine also has been used successfully in reported cases. Anesthesia can be maintained using infusions of propofol or remifentanil or inhalation anesthetics such as isoflurane, sevoflurane, or desflurane, or a combination of infusions and inhalation agents. Hypotension from inhalation anesthetic–induced peripheral vasodilation and myocardial depression can precipitate carcinoid crisis. Because serotonin can result in delayed emergence from anesthesia, shorter acting volatile agents with lower blood-gas solubility may be more desirable for these cases. Nitrous oxide also has been used safely in patients with carcinoid syndrome.

Airway pressures should be monitored to detect the onset of bronchospasm. Arterial blood gas measurements can be used to help avoid hypercarbia and hypoxia and manage hyperglycemia and electrolyte imbalances. Temperature should be monitored, and warming devices such as forced air warming blankets and fluid warmers should be used to avoid hypothermia, another trigger of mediator release.

Intraoperative hypotension should be treated with intravascular volume expansion and octreotide. If surgical manipulation of tumor is coincident with hypotension, the manipulation should stop until blood pressure increases to acceptable levels. Octreotide, 50 to 200 μg, can be given intravenously to treat severe hypotension and bronchospasm, with doses repeated as necessary. Although octreotide can be a lifesaving treatment, large doses may have been linked in at least one case to significant effects on the cardiac conduction system, including bradycardia, Mobitz type II atrioventricular block, and complete heart block. Other medications that may be useful in the management of hemodynamic instability include rapid-onset, short-acting drugs such as esmolol, phenylephrine, and phentolamine. $H_1$-Receptor and $H_2$-receptor blockers may be useful adjuvant therapies. Aprotinin, a kallikrein inhibitor, has been effective in the treatment of hypotension refractory to octreotide.

Other vasopressors that have been used safely include phenylephrine and vasopressin. Medications that cause catecholamine release, such as ephedrine, should be avoided. Epinephrine, norepinephrine, and dopamine can make hypotension worse by further stimulating the release of vasoactive mediators. However, in cases of carcinoid-related cardiac valvular surgery, vasopressors have been used successfully with octreotide. In the event that one of these vasoactive drugs becomes necessary, a small dose can be administered and the response evaluated before further dosing.

Intraoperative hypertension can be treated with deepened anesthesia, opioids such as fentanyl or remifentanil, β blockers such as esmolol, and octreotide. Nitroglycerin and sodium nitroprusside must be used with caution because resultant hypotension may trigger mediator release.

Patients with carcinoid tumor may present for hepatic artery embolization rather than tumor resection. Although the liver receives 75% of its blood supply from the portal vein, most of the blood flow to the hepatic carcinoid tumor arrives via the hepatic artery, making embolization an effective means of tumor destruction while preserving hepatic function. With tumor destruction comes the possibility of massive tumor mediator release with resultant carcinoid crisis. Postoperatively, these patients may also experience abdominal pain, nausea, vomiting, fever, and possible liver dysfunction.

Because vasoactive mediators may remain in the circulation for a period of time after tumor resection and because of the possibility of some remaining undetected metastases, careful postoperative hemodynamic monitoring in an intensive care setting is prudent. Patients may experience prolonged recovery from anesthesia because of elevated serotonin levels. Fluids and serum electrolytes should be closely monitored. Octreotide administration should be continued in the postoperative period. Adequate analgesia should be maintained, either with intravenous fentanyl or local anesthetic administered through the epidural catheter. Vigilance should be maintained to avoid further triggers such as hypothermia, hypoxia, and hypercarbia. Ondansetron, a serotonin antagonist, is the antiemetic of choice because it may help attenuate symptoms caused by serotonin excess.

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SECTION 6

# ABDOMEN

CASE 32

# Full Stomach

**Laurence M. Hausman, MD**

## QUESTIONS

1. What are the mechanisms a conscious person has to prevent regurgitation and pulmonary aspiration?
2. Discuss the risk factors for regurgitation and pulmonary aspiration during general anesthesia.
3. When can aspiration occur during the perioperative period?
4. Explain the problems associated with pulmonary aspiration.
5. If aspiration occurs, what are the usual course, treatment, and prognosis?
6. How should the nasogastric tube be managed?
7. What pharmacologic interventions can decrease the risk of aspiration?
8. Why is cricoid pressure applied during rapid-sequence induction, and what are some of the problems associated with applying cricoid pressure?
9. Describe the effects of commonly used anesthetic agents on lower esophageal sphincter tone.
10. Outline an acceptable anesthetic plan for this patient.

A 37-year-old woman with small bowel obstruction but otherwise in good general health presented to the operating room for exploratory laparotomy, lysis of adhesions, and possible bowel resection. Her past surgical history was significant for cholecystectomy 3 years ago, under general anesthesia, and cesarean delivery 1 year ago with spinal anesthesia. Both procedures were without complication. She weighed 65 kg. In the preoperative holding area, her vital signs were heart rate, 97 beats per minute, blood pressure, 130/65 mm Hg, and respiratory rate, 12 breaths per minute. She was found to have acute abdominal tenderness, and she had a nasogastric tube in place. The tube was draining approximately 25mL per hour of bilious fluid. Her hematocrit was 39%.

### 1. What are the mechanisms a conscious person has to prevent regurgitation and pulmonary aspiration?

The lower esophageal sphincter (LES) is the primary barrier to gastroesophageal reflux. The LES is 2 to 5 cm long and moves upward with inspiration and downward with exhalation. On swallowing, the esophagus undergoes peristaltic contractions to allow the passage of food, and the LES relaxes. This sphincter traverses the diaphragm and has a resting pressure greater than gastric pressure. The difference in these pressures (LES pressure minus gastric pressure) is known as "barrier pressure." In normal subjects, an increase in abdominal pressure triggers an increase in lower esophageal pressure, maintaining barrier pressure. Gastroesophageal reflux disease (GERD) occurs when the barrier pressure decreases. Reflux occurs when either the LES pressure decreases or the gastric pressure increases.

The angle where the esophagus meets the stomach also protects against GERD. If the angle is oblique, high gastric pressures are required to cause reflux. However, if the angle is small (as often occurs in patients with morbid obesity or a gravid uterus), reflux may occur at low gastric pressures.

Another protective mechanism is the diaphragmatic crura that tighten at the lower esophagus to prevent reflux. The upper esophageal sphincter (striated muscle that is not under conscious control) is a third mechanism to protect against regurgitation. Virtually all commonly used general anesthetics including muscle relaxants cause relaxation of this sphincter.

Finally, there are intrinsic airway reflexes that protect the airway against aspiration in the event of regurgitation. These include the cough reflex (a period of brief inspiration followed by a forceful expiration), the expiration reflex (expiration without inspiration), laryngospasm and apnea (closure of both the false cords and the true cords), and spasmodic panting (rapid shallow breathing) (Box 32-1).

### 2. Discuss the risk factors for regurgitation and pulmonary aspiration during general anesthesia.

General anesthesia is associated with loss of protective upper airway reflexes. A patient under general anesthesia who has regurgitation is at risk to aspirate the regurgitant. Any condition associated with an increase in intragastric volume, an increase in intragastric pressure, or a decrease in LES tone may result in regurgitation and pulmonary aspiration (Box 32-2).

**BOX 32-1 Mechanisms to Prevent Regurgitation and Pulmonary Aspiration**

- Lower esophageal sphincter
- Gastroesophageal angle
- Diaphragmatic crura
- Upper esophageal sphincter
- Airway reflexes
  - Cough
  - Expiration reflex
  - Laryngospasm and apnea
  - Spasmodic panting

**BOX 32-2 Conditions Associated with Regurgitation and Pulmonary Aspiration for which Rapid-Sequence Induction Should Be Considered**

- Obesity
- Abdominal surgery
- Depressed level of consciousness
- History of gastritis or ulcer
- Bowel obstruction
- Pain or stress
- Emergency surgery
- American Society of Anesthesiologists Physical Status IV-V
- Esophageal disorders or previous esophageal surgery
- Recent meal
- Diabetes mellitus, if associated with gastroparesis
- Ileus
- Trauma
- Concurrent opioid administration
- Symptomatic hiatal hernia

*ASA*, American Society of Anesthesiologists.

### 3. When can aspiration occur during the perioperative period?

Aspiration can occur at any time during the perioperative period. Specifically, it can occur at the following times:

- Before induction
- During induction before laryngoscopy
- During mask ventilation
- During laryngoscopy
- During extubation
- Immediately after tracheal extubation
- In the postanesthesia care unit

However, most of the time, aspiration occurs at induction during laryngoscopy.

### 4. Explain the problems associated with pulmonary aspiration.

Aspiration during general anesthesia is very rare with estimates of occurrence ranging from 1 in 4000 to 1 in 9000. However, when aspiration does occur, it is a serious problem. Aspiration of large gastric particles can completely obstruct the airway anywhere along the tracheobronchial tree making ventilation difficult or impossible. A chemical pneumonitis, known as Mendelson syndrome (first described by Mendelson in 1946), resulting from aspiration of gastric contents can occur. This syndrome is associated with a gastric aspirate having a pH less than 2.5 and a volume greater than 0.4 mL/kg, which is approximately equal to 25 mL in an adult. Lower pH or higher volume of the aspirate is associated with worse outcomes.

### 5. If aspiration occurs, what are the usual course, treatment, and prognosis?

If aspiration occurs, treatment is symptomatic. The oral pharynx should be suctioned at the time of the aspiration. If the patient is supine, the head should be turned sideways to facilitate suctioning. The patient should also be placed in the Trendelenburg position to allow pooling of the regurgitant in the oropharynx, lessening the volume of pulmonary aspiration. Irrigation of the airway is *not* advised because it may spread the aspirate, creating more profound pulmonary destruction. Bronchoscopy may be needed to remove large particulate matter. Supplemental oxygen should be administered. Mechanical ventilation is often necessary. $\beta_2$-Adrenergic agonist inhalers may be helpful for treating bronchospasm. The routine use of steroids has *not* been shown to be beneficial, and antibiotics should be started only after a positive culture.

Signs of clinically significant aspiration usually occur within 2 hours of the event. Signs include bronchospasm, a decrease in room air oxygen saturation of greater than 10% from baseline, an alveolar-arterial gradient of greater than 300 mm Hg on 100% oxygen, and a chest x-ray revealing atelectasis or an infiltrate (most commonly a right lower lobe infiltrate). Intrapulmonary damage can progress to interstitial and alveolar edema, with hyaline membrane formation and destruction of lung tissue. Acute respiratory distress syndrome often occurs in patients requiring more than 24 hours of mechanical ventilation. The prognosis in patients with pulmonary aspiration is usually favorable, provided that the patient was in good health preoperatively. A poor outcome is associated with significant comorbid conditions.

### 6. How should the nasogastric tube be managed?

The management of nasogastric tubes (NGTs) is controversial. If a NGT is present, it is virtually universally recommended that the tube be suctioned before induction. However, one school of thought calls for removal because the presence of a NGT decreases both LES and upper esophageal sphincter tone (by causing mechanical interference) as well as interfering with esophageal compression that theoretically occurs with the application of cricoid pressure (used during a rapid-sequence induction). These claims have not been proven. A second school of thought recommends leaving a NGT in place; this allows for continuous drainage of gastric fluid and air, reducing the increase in gastric pressure associated with induction, which occurs because of abdominal contents pushing

against the diaphragm. Furthermore, the presence of a NGT has not been proven to limit the usefulness of cricoid pressure. A third school of thought suggests withdrawing the NGT to the midesophageal level (approximately 30 cm from the nares) to allow for an increase in LES tone and a decrease in overall esophageal pressure during induction, decreasing not only the risk of regurgitation but also the risk of esophageal rupture.

### 7. What pharmacologic interventions can decrease the risk of aspiration?

*Metoclopramide*, a derivative of procainamide, facilitates gastric emptying by causing gastric peristalsis and relaxation at the pylorus. The effect of decreasing stomach volume takes approximately 20 to 30 minutes. Metoclopramide also increases LES tone within 1 to 3 minutes of intravenous administration. Metoclopramide should be avoided in cases of bowel obstruction. Because it is a dopaminergic antagonist, it should be avoided in patients with Parkinson disease or depression. It can also cause extrapyramidal side effects. The positive effects of this drug are often inhibited by opioids that cause a delay in gastric emptying.

*Cimetidine* and *ranitidine* are competitive $H_2$ blockers. They decrease basal gastric acid secretion that occurs in response to gastrin and food. Their onset of action is approximately 20 to 30 minutes when given intravenously.

*Sodium citrate* is a nonparticulate antacid that increases gastric pH immediately on oral consumption. A nonparticulate formulation is important because aspiration of particulate alkalis may also produce a chemical pneumonitis.

*Proton pump inhibitors* (e.g., omeprazole, rabeprazole, lansoprazole) block hydrogen and potassium adenosine triphosphatase enzyme systems at the secretory surface of parietal cells in the stomach. These drugs decrease the volume and increase the pH of gastric secretions.

*Glycopyrrolate* and *atropine*, both anticholinergics, increase gastric pH by inhibiting vagally mediated gastric acid production. Although glycopyrrolate also decreases LES tone, atropine does not.

### 8. Why is cricoid pressure applied during rapid-sequence induction, and what are some of the problems associated with applying cricoid pressure?

The cricoid cartilage is the only complete cartilaginous circular ring in the trachea. In 1961, Sellick reported that posterior or rostral pressure applied to the cricoid cartilage would occlude the upper esophagus against the cervical vertebrae and prevent regurgitation of gastric contents into the oropharynx, precluding aspiration of gastric contents. Theoretically, if gastroesophageal reflux should occur while cricoid pressure is applied, regurgitation into the pharynx should not occur. However, cricoid pressure is poorly tolerated in an awake patient and can cause the patient to retch. Retching can increase intraesophageal pressure and predispose to esophageal rupture.

Maximum intragastric pressure is 25 mm Hg in starved supine patients. Gastric distention with 750 mL of volume can increase the intragastric pressure to 35 mm Hg. A force of 30 N (Newton) on the cricoid can prevent regurgitation associated with 40 mm Hg of intragastric pressure. Older studies recommended 40 N of force. However, this much force is poorly tolerated, often distorts laryngeal anatomy making intubation difficult, and predisposes to esophageal rupture. One solution is to provide 20 N of force to a conscious patient. This relatively small amount of force gives some protection against regurgitation; however, if intraesophageal pressure increases too much, regurgitation *will* occur but esophageal rupture *will not*. When the patient loses consciousness, 30 N of force should be applied to the cricoid cartilage until the trachea is successfully intubated. Cricoid pressure can increase the difficulty of mask ventilation, if it is undertaken. Mask ventilation may be required in cases of difficult intubation.

Newer studies cast doubt on the effectiveness of cricoid pressure to prevent regurgitation and aspiration. Cricoid pressure may make visualization of the vocal cords during laryngoscopy more difficult by displacing the larynx laterally, and it may completely occlude the airway. Cricoid pressure has also been shown to decrease LES tone and may promote gastric reflux. However, literature both in favor and against the use of cricoid pressure during rapid-sequence induction is sparse. The standard of care as of this writing requires the use of cricoid pressure during induction of anesthesia for patients at increased risk for aspiration.

### 9. Describe the effects of commonly used anesthetic agents on lower esophageal sphincter tone.

Drugs that *increase* LES pressure and *increase* barrier pressure include the following:

- α-Adrenergic agonists
- Antacids
- Antiemetics
- Cholinergics
- Edrophonium
- Histamines
- Metoclopramide
- Metoprolol
- Neostigmine
- Pancuronium
- Succinylcholine

Drugs that *decrease* LES tone and *decrease* barrier pressure include the following:

- β-Adrenergic agonists
- Dopamine
- Glycopyrrolate
- Inhalation agents
- Nitroglycerin
- Opioids
- Sodium nitroprusside
- Thiopental

Drugs that have *no* effect on LES tone include the following:

- Cimetidine
- Propranolol
- Ranitidine
- Vecuronium

Propofol lowers both esophageal and gastric pressure and has no effect on barrier pressure.

### 10. Outline an acceptable anesthetic plan for this patient.

Induction methods in patients with a full stomach vary depending on several factors. One important factor is an airway evaluation. The airway evaluation should always include a thorough history of the patient's prior airway management problems. For patients with an acceptable airway evaluation, rapid-sequence induction with cricoid pressure is indicated. Adequate time for preoxygenation and denitrogenation is very important. The endpoint for preoxygenation is an end-tidal oxygen value greater than 90%. This concentration of oxygen is associated with denitrogenation of the functional residual capacity. Induction agents should be selected from agents with rapid predictable onset times. Commonly used agents are propofol, etomidate, and ketamine (sometimes a combination of two or more is employed). Muscle relaxants should also have rapid onset times. Classically, the neuromuscular blocking agent used for rapid-sequence inductions has been succinylcholine. However, if succinylcholine is contraindicated for any reason (e.g., hyperkalemia, burn, crush injury), rocuronium can be administered. Rocuronium is the only other neuromuscular blocking agent approved for rapid-sequence induction. When administering rocuronium for rapid-sequence induction, the dose is doubled. The disadvantage of using a nondepolarizing neuromuscular blocking agent is that prolonged mask ventilation may be necessary if intubation is unsuccessful. If both mask ventilation and intubation are unsuccessful, a medical emergency may exist, which could require a surgical airway.

Even in the face of a normal airway examination, intubation may be difficult. Often the only adjustments that need to be made are repositioning the patient's head into better sniffing position and changing the laryngoscope blade. If intubation is still unsuccessful, help from anesthesia colleagues should be sought. At this point, it would be prudent to ventilate the patient gently through cricoid pressure, keeping peak airway pressures less than 20 cm $H_2O$; this would limit ventilation of the stomach. Ventilation should be continued until the patient awakens. If mask ventilation is difficult, ventilation through a supraglottic airway, such as a laryngeal mask airway, is indicated. Gastric suctioning and tracheal intubation are possible through many types of supraglottic airways. Both mask ventilation and supraglottic airway placement can be impeded by cricoid pressure.

However, if the patient's airway looks as though it may be difficult to manage by conventional means or if the patient has a history of difficult airway management, rapid-sequence induction is contraindicated. In this case, the most prudent approach would be awake spontaneously breathing intubation, which is most oftenaccomplished with flexible fiberoptic equipment. Awake intubation poses unique challenges in patients with a full stomach. Awake instrumentation of the airway requires profound airway anesthesia eliminating protective coughing and gag reflexes. However, awake, unsedated patients know if they are going to vomit and can turn their heads to the side. Under such circumstances, it is preferable to perform awake intubation rapidly and smoothly. Otherwise, bleeding, swelling, copious secretions, and vomiting can compromise the process.

Inhalation induction by mask is contraindicated and should be performed only under exceptional circumstances for patients who are at increased risk for aspiration.

After the trachea has been intubated with a cuffed tracheal tube, the anesthetic can be maintained in numerous ways including general anesthesia consisting of air, oxygen, an inhalation agent, opioid, and muscle relaxant or total intravenous anesthesia. Even with a cuffed tracheal tube in place, microaspiration may still occur around the cuff. However, a cuffed tracheal tube provides more protection than an uncuffed tube.

Extubation of the trachea is another period during which aspiration may occur. Before extubation, the patient should be awake, alert, responsive, breathing spontaneously, and able to protect the airway.

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CASE 33

# Major Hepatic Resection

**Samuel DeMaria, Jr., MD • Andrew M. Perez, MD**

## QUESTIONS

1. Describe liver cirrhosis and its systemic effects.
2. How do you evaluate a patient with severe liver disease, and how does the liver disease affect the choice of anesthetic agents?
3. What are the intraoperative considerations for major hepatic resection in a noncirrhotic patient?
4. Is there a difference between right and left liver lobectomies?
5. Why is avoidance of transfusion a reasonable request?
6. How would you manage the fluids for this case and avoid transfusion?
7. What are the concerns when using the Pringle maneuver, and what are the concerns when using total caval isolation?
8. How is postoperative pain best managed in patients after hepatic resection?

A 62-year-old man with hypertension, hepatitis C, and hepatocellular carcinoma presented for right liver partial lobectomy. The patient did not appear to have cirrhosis, and laboratory studies were within normal limits. He underwent an inguinal hernia repair under general anesthesia 13 years ago without difficulty. General anesthesia was induced with propofol and fentanyl. Muscle relaxation was achieved with vecuronium. General anesthesia was maintained with isoflurane and fentanyl. An intraarterial catheter and two large-bore peripheral intravenous catheters were placed.

During the case, the surgeon asks you to limit fluid administration and avoid transfusion, if possible. Before resection of the tumor, the surgeon announces the "Pringle is on," and the patient becomes hypotensive and tachycardic.

### 1. Describe liver cirrhosis and its systemic effects.

Cirrhosis of the liver affects approximately 3 million Americans and is the 12th leading cause of death in the United States. Chronic hepatitis refers to liver disease in which inflammation and necrosis are present for at least 6 months and is most commonly due to hepatitis C virus infection or alcohol abuse. The disease can be divided into two major categories: cholestatic disease and hepatocellular disease. Cholestatic diseases (e.g., primary biliary cirrhosis, primary sclerosing cholangitis) are uncommon causes of chronic hepatitis, whereas hepatocellular causes (e.g., infectious, autoimmune, steatohepatitis, or alcoholic) predominate and more often lead to hepatic resection or transplantation.

Cirrhosis of the liver is a major challenge to the anesthesiologist because it leads to problems in nearly every organ system. Most patients with long-standing liver disease are functionally unwell and have poor nutritional status and exercise tolerance on presentation. Table 33-1 outlines common problems related to chronic liver disease that must be considered by the anesthesiologist.

### 2. How do you evaluate a patient with severe liver disease, and how does the liver disease affect the choice of anesthetic agents?

In addition to the usual directed history and physical examination of surgical patients, patients with cirrhosis of the liver require a thorough assessment regarding the severity of disease and recognition of the risk it entails. The urgency of surgery dictates the time allowed to optimize coexisting medical problems. In acute hepatitis, elective surgery is generally contraindicated, and emergency surgery carries a very high degree of risk. Common signs and symptoms of liver disease should be sought to assess overall well-being. Jaundice, ascites, petechiae, and ecchymoses are easy to assess quickly on first encountering the patient. Figure 33-1 presents a rational approach to a patient with suspected liver disease.

A well-accepted method by which the severity of liver disease can be assessed is the Child-Pugh score (Table 33-2). Although the Child-Pugh score has been used for more than 30 years as a prognostic indicator for cirrhosis, it has several limitations, including two subjective variables of the five variables used, lack of a renal function correlate to survival, and overemphasis on measures of synthetic function (i.e., albumin and prothrombin time). Child-Pugh scores are considered a good, although not perfect, predictor of severity and subsequent mortality in these patients. The Model for End-Stage Liver Disease (MELD) score is a more useful model for population comparison and for use in transplant selection because it does not rely on subjective data. Instead, MELD scores involve nonempirically derived objective variables: bilirubin, creatinine, international normalized ratio, and cause of cirrhosis.

TABLE 33-1 **Complications of End-Stage Liver Disease**

| Organ System | Complication | Details |
|---|---|---|
| Central nervous system | Hepatic encephalopathy | Variable manifestations—confusion, personality changes, sleep disorder, coma<br>Can be precipitated by anesthesia or surgery if hepatic perfusion is impaired (e.g., hypotension, hypoxemia) |
| Cardiovascular system | Hyperdynamic state | Patients have profoundly reduced systemic vascular resistance with resultant high cardiac output, low to normal blood pressure, mildly elevated heart rate (probable nitric oxide effects) |
| | Cardiomyopathy | Signs and symptoms of congestive heart failure |
| | Altered blood flow | Increased splanchnic blood flow with resultant central hypovolemia<br>Arteriovenous collateralization with increased mixed venous oxygen saturation |
| | Portal hypertension | Increased portal venous pressure leads to increased portosystemic collateral development and plays a role in ascites and encephalopathy<br>Resultant esophageal varices are at a high risk for bleeding if traumatized |
| Pulmonary system | Hypoxemia | True pulmonary shunting can occur from increased atelectasis (from fluid retention as ascites or pleural effusions), impaired hypoxic pulmonary vasoconstriction<br>Hepatopulmonary syndrome with intrapulmonary vascular dilation and shunting |
| | Pulmonary hypertension | Portopulmonary hypertension is pulmonary and portal hypertension existing simultaneously as a result of long-standing liver disease |
| Renal system | Hepatorenal syndrome | Develops as a result of prerenal failure from advanced cirrhosis often precipitated by sudden decreases in cardiac output (e.g., various anesthetic agents)<br>Generally, disease is responsive to albumin and vasopressin analogues |
| | Edema and ascites | Major factors in development of ascites are portal hypertension and sodium and water retention<br>Patients are often on salt-restricted diets and diuretic therapy<br>Electrolyte abnormalities are common<br>Albumin therapy is the mainstay of treatment. Infection of ascitic fluid (spontaneous bacterial peritonitis) may lead to sepsis and renal failure |
| Hematologic system | Coagulopathy/ hypercoagulability | Variable impairment in clotting and fibrinolysis despite results of "synthetic" liver function test (i.e., PT, INR)<br>Patients may be coagulopathic or prothrombotic with expectant complications of either state occurring in an unpredictable fashion |
| | Thrombocytopenia | Portal hypertension induces splenomegaly and platelet sequestration (main cause of thrombocytopenia), but bone marrow suppression and immune-mediated destruction of platelets also play a role |
| Endocrine system | Abnormal glucose use | Multifactorial insulin resistance can lead to hyperglycemia<br>Loss of glycogen stores can lead to hypoglycemia |
| Gastrointestinal system | Esophageal varices | Long-term portal hypertension can lead to varices that if ruptured (during NG tube placement, TEE placement) can prove fatal |

*INR,* International normalized ratio; *NG,* nasogastric; *PT,* prothrombin time; *TEE,* transesophageal echocardiography.

However, the MELD score is less useful in stratifying risk in cirrhotic patients for nontransplant procedures.

Generally, severe liver disease portends a poor outcome because of increased morbidity and mortality from hepatic problems. Concurrent coexisting diseases increase the risks. Class B or C patients are generally not candidates for extensive hepatic resection. Because few effective mechanical replacements exist for the failing liver (in contrast to the kidneys or heart), anesthesiologists must be able to assess severity adequately and care for patients with an appropriate level of intensity. Morbidity and mortality are also directly associated with the magnitude of the surgical procedure. Cirrhotic patients undergoing laparoscopic procedures tend to have better outcomes than patients undergoing laparotomy.

Although liver disease may affect the management of a patient's anesthetic, minor operations generally have little effect on liver function. Perioperative liver damage is more likely dependent on the surgery than the anesthetic choice.

Common issues with cirrhotic patients include the following:

- Decreased doses or avoidance of premedicants (e.g., benzodiazepines) in the setting of even mild encephalopathy

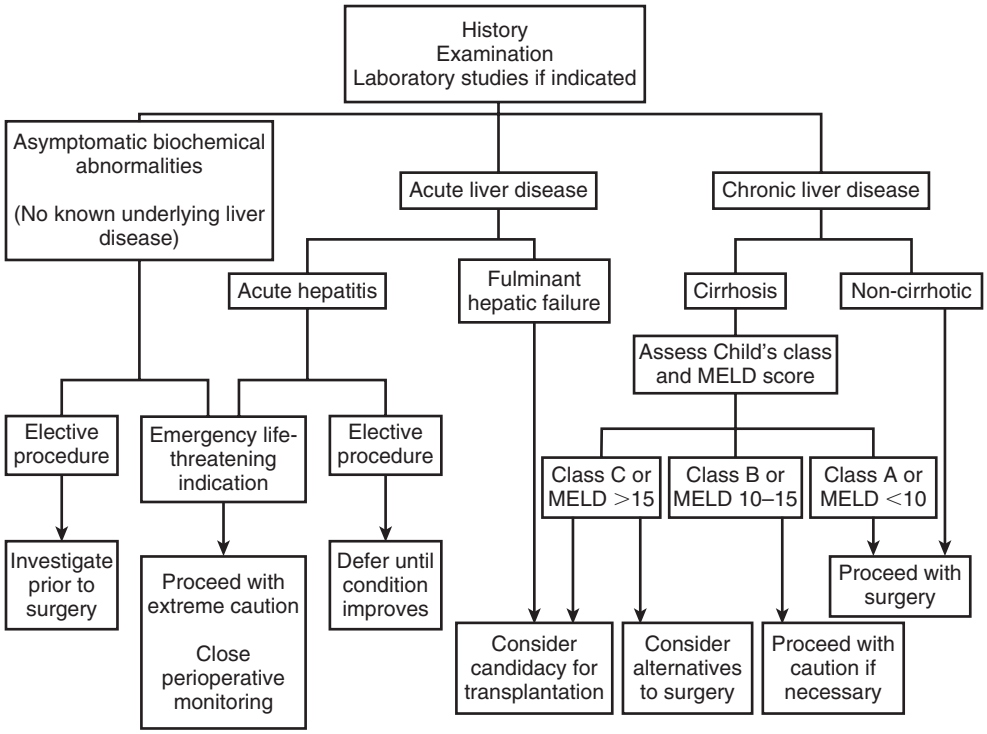


**FIGURE 33-1** ■ Preoperative assessment of a patient with liver disease. (Adapted from: Patel T. Surgery in the patient with liver disease. Mayo Clin Proc 1999;74:593.)

TABLE 33-2 **Child-Pugh Score for Liver Disease Severity**

| Criteria | Points | | |
|---|---|---|---|
| | 1 | 2 | 3 |
| Encephalopathy | None | Mild to moderate | Severe |
| Ascites | None | Mild to moderate | Severe |
| Bilirubin (mg/dL) | <2 | 2–3 | >3 |
| Albumin (g/dL) | >3.5 | 2.8–3.5 | <2.8 |
| Prothrombin time | | | |
| Seconds prolonged | <4 | 4–6 | >6 |
| International normalized ratio | <1.7 | 1.7–2.3 | >2.3 |

Class A (least severe): 5–6 points.
Class B: 7–9 points.
Class C (most severe): 10–15 points.

- Presence of a full stomach owing to ascites and decreased gastric motility
- Endotracheal intubation to secure the airway (facemasks and laryngeal mask airways should be avoided)

Abnormalities of protein binding, protein concentration, volume status, volume of distribution, and metabolism from hepatocyte derangement all have a significant impact on drug metabolism and pharmacokinetics (Table 33-3). The severity of liver disease directly influences all of these variables and sensitivity to many anesthetic agents in the setting of encephalopathy. Severe liver disease predictably alters the metabolism of drugs with large extraction ratios (e.g., lidocaine) where clearance is dependent on hepatic blood flow. Conversely, low-extraction drugs (e.g., midazolam) are influenced by protein binding allowing increased unbound drug to exert effects. Drug pharmacokinetics in liver disease are complex. All medications given to patients with diseased livers should be titrated to effect. Depending on the agent, alterations in protein anabolism by the liver as well as fluid shifts make dosing of common anesthetic agents a challenge. In contrast to the increased responsiveness to anesthetic agents, patients with significant portal hypertension may have decreased responsiveness to catecholamines and either require increased doses or require nonadrenergic vasoactive drugs (e.g., vasopressin) for hemodynamic support (see Table 33-3).

TABLE 33-3 **Effects of Chronic Liver Disease on Administration of Common Anesthetic Agents**

| Agents | Suggested Alterations in Drug Administration | Description |
|---|---|---|
| **Inhaled anesthetics** | | |
| Nitrous oxide | No change | Encephalopathic patients may need less anesthetic overall, and overdose is easy. Volatile anesthetics at high doses can induce hypotension and exacerbate disease state through hypoperfusion. Sevoflurane, desflurane, and isoflurane preserve hepatic blood flow and function well. |
| Volatile anesthetics | No change | |
| **Induction agents** | | |
| Propofol | No change/decrease dose | Intravenous anesthetics have a modest impact on hepatic blood flow and postoperative liver function *when arterial blood pressure is maintained*. Lower dose of propofol is sometimes necessary if patient is hypovolemic or encephalopathic. |
| Etomidate | No change | |
| Ketamine | No change | |
| **Opioids** | | |
| Fentanyl | No change | Fentanyl is metabolized by the liver, but rapid redistribution prevents significant alteration in elimination secondary to liver disease. Remifentanil is metabolized by blood and tissue esterases, and its elimination is unaltered. All other opioids are significantly affected by liver disease, leading to accumulation and prolonged or profound effects. |
| Remifentanil | No change | |
| Morphine, meperidine, hydromorphone, sufentanil, alfentanil | Decrease dose/avoid altogether | |
| **Neuromuscular blockers** | | |
| Succinylcholine | No change | Decreased cholinesterase levels may prolong effect of succinylcholine. This is rarely the case. |
| Nondepolarizing agents | No change: atracurium, cisatracurium<br>Decreased dose: vecuronium, rocuronium, mivacurium | Increased dosage for induction (increased volume of distribution); decreased incremental or infusion doses for maintenance (decreased hepatic clearance). |
| **Adjunctive agents** | | |
| Benzodiazepines | Decreased dose | Decreased protein binding and increased free fractions of midazolam and diazepam cause prolonged duration of action and enhanced sedative effects. |
| Dexmedetomidine | Decreased dose | Primarily metabolized in the liver with minimal renal clearance. |

### 3. What are the intraoperative considerations for major hepatic resection in a noncirrhotic patient?

For primary liver cancers or hepatic metastases, hepatic resection is the "gold standard" and treatment of choice. In the 1970s, mortality was nearly 20% and was most commonly caused by hemorrhage or postoperative liver failure. Many large series of patients undergoing hepatectomy report more recent mortality rates of less than 5%. Although the intricacies of chronic liver disease complicate anesthetic management for any surgical procedure, most patients presenting for major hepatic resection are not cirrhotic. Approximately 90% of operative lesions are malignant, and 80% of these are metastatic (usually colorectal cancer). The most common primary liver lesion is hepatocellular carcinoma (about 80% of lesions). The second most common is cholangiocarcinoma. Benign lesions include hemangiomas, focal nodular hyperplasia, and hepatic adenomas. Although laparoscopic approaches are becoming more widespread and safer, large central lesions and bulky right lobe lesions with vascular involvement are best addressed through an open approach. Purported advantages of laparoscopic liver resection include decreased postoperative pain, less postoperative ileus, and quicker recovery time. However, most of these cases are performed open and are often large. Bleeding is the major concern of anesthesiologists.

Preoperative preparation for hepatic resection involves risk assessment and a complete review of the patient record. Imaging studies, ultrasound findings, and a discussion with surgical staff are important to determine the presence of esophageal varices, hepatic lesion size and location, and expected difficulties during the case (e.g., vascular involvement of the tumor). Severe thrombocytopenia, large varices, significant anemia, and coagulopathy should be corrected preoperatively.

General anesthesia is required for all patients undergoing hepatic resection. Two well-running, large-bore intravenous catheters (≥16-gauge) are mandatory because the risk of sudden and brisk blood loss is the main concern in these cases. Central venous cannulation may be desirable for patients with poor peripheral access, although mandatory central line placement for access or central venous pressure (CVP) monitoring is unnecessary and introduces a nidus for infection. Arterial catheterization allows for closer hemodynamic monitoring and frequent arterial blood sampling. An arterial catheter is placed for all liver resections except in patients with small, left lobar lesions where blood loss is rarely

expected to be greater than 1 L. An arterial line does not need to be placed before induction unless the patient's other comorbidities (e.g., cardiac disease, severe liver disease) warrant it.

Although the interactions between liver disease and anesthetic agents are important to consider, noncirrhotic patients can often undergo a "straightforward" anesthetic. Placement of spinal morphine or an epidural catheter is often used for postoperative analgesia (see Q8). Anesthesia can be induced in the fashion most suited to the particular patient (e.g., rapid sequence for patients with large-volume ascites). General anesthesia is usually maintained with inhalation agents rather than intravenous agents because the slight decrease in hepatic blood flow seen with these agents is thought to limit bleeding. Rocuronium or vecuronium is often administered for muscle relaxation. In the presence of significant liver disease, cisatracurium is beneficial. Fentanyl, without spinal morphine, is given in higher doses because subcostal and upper abdominal incisions for open hepatectomy can be very painful (Figure 33-2). Doses of 8 to 15 μg/kg SD for the case generally suffice.

The use of patient warming devices, such as forced-air warming blankets, is essential to avoid hypothermia, which can exacerbate coagulopathy. An orogastric tube is usually placed, unless large or active varices are present. Positive end expiratory pressure is avoided to limit back pressure in the venous system, reducing congestion and bleeding.

The patient's arms are abducted, and care must be taken to pad bony prominences for the purpose of reducing nerve injury. Fluid management and blood product administration are discussed subsequently. Generally, normovolemia to slight hypovolemia is targeted, but the often requested "dry" (e.g., hypovolemic) patient is rarely necessary to limit bleeding. Throughout the case, "mugging" (i.e., compression) of the vena cava may occur as the liver is mobilized and retracted, acutely decreasing venous return and consequently leading to hypotension (often profound). Vasoactive substances (e.g., phenylephrine, vasopressin) should be available at all times to treat significant hypotensive episodes.

Emergence from anesthesia generally involves the resumption of spontaneous ventilation after fascial closure so that titration of analgesics to a respiratory rate less than 20 breaths per minute can be accomplished. Antagonism of neuromuscular blockade should be performed regardless of when the last dose was administered to limit the likelihood of postoperative respiratory events. Postoperatively, patients should be observed in the postanesthesia care unit until transferred to a step-down unit where invasive monitoring can be continued. Patients should be monitored for respiratory depression (from residual narcotics or splinting from painful incisions), rebleeding, and acute liver failure.

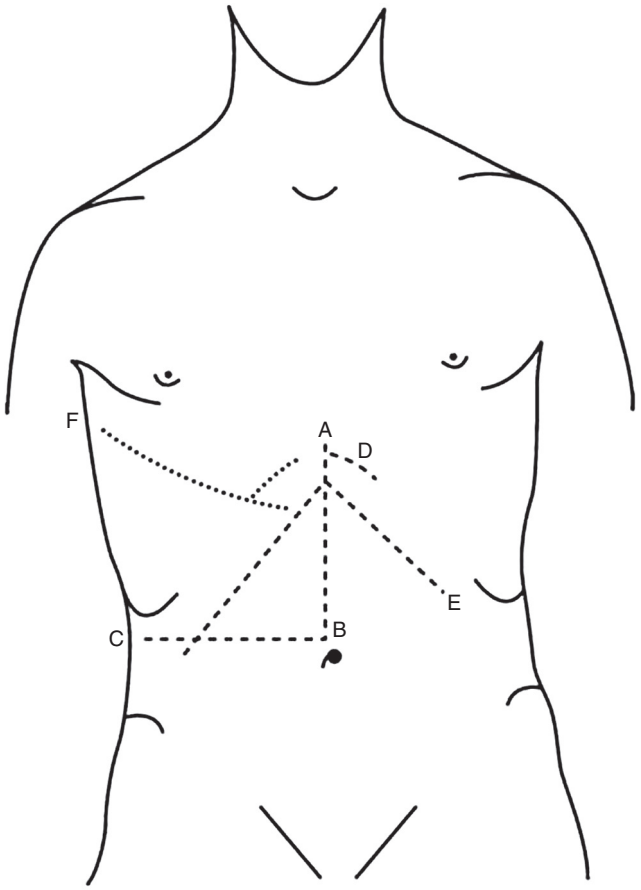


**FIGURE 33-2** ■ Incisions for liver resection *(A-F)*. Initial upper midline exploration *(B-D)*. Hockey-stick incision, ideal for exposure of the whole liver *(A-C)*. Classic chevron incision *(C-E)* with (Mercedes) extension *(A-D)*. Right subcostal incision *(C, D)*. Thoracoabdominal extension *(F)*. (Adapted from: Blumgart LH, et al., editors. Surgery of the liver, biliary tract, and pancreas, 4th ed. Philadelphia: Saunders; 2007.)

## 4. Is there a difference between right and left liver lobectomies?

The liver is highly vascular, receiving approximately one third of the resting cardiac output. The portal vein supplies approximately 80% and the hepatic artery supplies approximately 20% of the total hepatic blood flow. Most venous drainage is by three hepatic veins that join the vena cava. The liver is divided into four lobes; the right and left lobes are divided by the falciform ligament anteriorly, with two other lobes posteriorly (the caudate and quadrate lobes). Resection of 75% of the liver mass can be performed without leading to liver failure, and liver cells replicate rapidly (i.e., within 24 hours), resulting in complete compensation in a few weeks.

Appreciation of the segmental anatomy has been a key advance in the perioperative management of hepatic resection. Couinaud demonstrated eight anatomic segments (Figure 33-3). Knowledge of these segments enables safe resection of involved tissue and preservation of viable tissue by ensuring adequate blood supply to the remaining segments during resection.

If the right lobe is to be resected, multiple small venous branches from the inferior vena cava to the liver must be individually dissected, controlled, and divided. Large accessory hepatic veins are common and may require further division or control with clamps and ligatures. The left lobe does not lie on the vena cava, and an extensive caval dissection is unnecessary. However, downward traction on the liver and cephalad traction on the diaphragm help left lobe exposure, and "mugging" of the vena cava can occur with brief yet profound periods

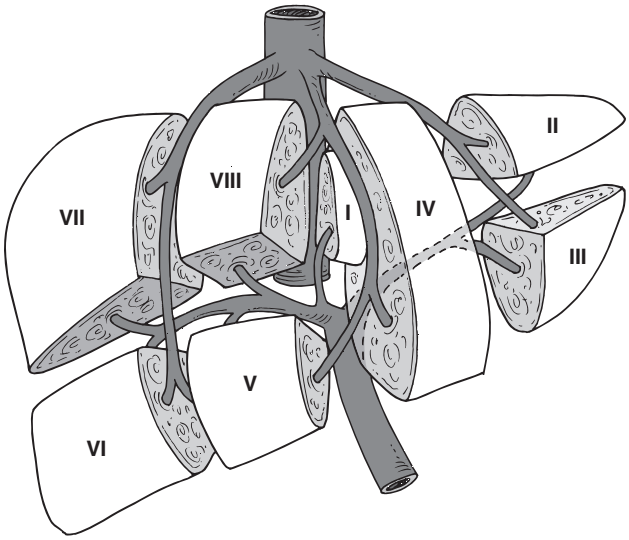


**FIGURE 33-3** ■ Couinaud's eight liver segments (posterior view). (Adapted from: Iwalsuki S, Sheahan DG, Starzl TE. The changing face of hepatic resection. Curr Probl Surg 1989;25:281.)

of hypotension. Given the anatomic and surgical considerations of right hepatic surgery, larger blood losses are anticipated, and invasive arterial monitoring and two well-functioning, large-bore intravenous catheters are mandatory. The number of resected segments is as important as the lobe being resected. With only one segment resected, morbidity and mortality are relatively low. If three or more segments are resected, mortality consistently doubles.

### 5. Why is avoidance of transfusion a reasonable request?

Liver resection for malignant lesions or living donor transplantation carries the risk of substantial blood loss. Prudent administration of fluids or blood products or both is crucial. A major untoward effect of blood transfusion in patients with tumors is immunosuppression and subsequent tumor recurrence. In addition, blood transfusion correlates with mortality in these patients. In this respect, the premise that blood transfusion may adversely affect patient outcomes is clear. All efforts should be made to limit the amount of blood lost during hepatic surgery so as to obviate the need for blood products and reduce the risk of tumor recurrence.

### 6. How would you manage the fluids for this case and avoid transfusion?

Overall fluid management during major hepatic resection is controversial despite risks of hemorrhage and the need to avoid blood transfusion. At some centers, fluid is used liberally in the early portions of dissection with the goal of increasing intravascular volume as a buffer against sudden blood loss. Most other centers favor maintenance of a low CVP to minimize blood loss from valveless hepatic veins or the vena cava because they predominantly contribute to the bleeding during resection. A modest degree of Trendelenburg position potentially maintains or increases cardiac preload and cardiac output and potentially lessens hepatic venous pressure; however, this generally increases CVP, in direct contrast to the typical recommendation for these cases.

The basic concept of measuring CVP intraoperatively is hypothetical and imperfect science, yet low CVP techniques have been touted as standard practice for major hepatic resection. These studies demonstrated decreased blood loss during hepatectomies except for left lobotomy without increased risk of complications. The most rigorous study supporting low CVP is limited by larger than expected blood loss values and questionable relevance to modern practice. Contradictory evidence exists that CVP monitoring did not appear to reduce blood loss in elective liver resections. In this study, patients without CVP monitoring or CVP manipulation did not have more blood loss than patients who did have CVP monitoring. A low CVP must be balanced with the potential risk of organ hypoperfusion and the low but potentially serious risk of air embolus (<1%).

Intraoperative changes of transthoracic pressure are caused by mechanical ventilation and pressure of surgical retractors on the thorax and right atrium. These transthoracic pressures are likely to alter CVP interpretation, as are ascites and the zero-reference point of the CVP itself. Liver resection has become safer and is associated with low intraoperative bleeding because of improved surgical skill and techniques. In addition, the link between reduced blood loss per se and improved outcome remains speculative, provided that no blood products are given. Finally, the methods often used to achieve a low CVP (e.g., pharmacologic interventions, phlebotomy) are not without risks in elderly patients with coexisting diseases and preexisting organ dysfunction or limited reserve. These risks include, but are not limited to, renal dysfunction and air embolism. The evidence favoring lower CVPs during major hepatic surgery is still controversial.

With an arterial catheter in place, anesthesiologists can estimate the patient's volume status through various methods (e.g., pulse pressure variation, systolic pressure variation). A reasonable approach to fluid management of these patients is as follows:

- Target normovolemia, not hypovolemia, during the resection.
- Limit fluids to less than 1 L of crystalloid before resection.
- Administer judicious doses of phenylephrine to maintain a mean arterial pressure greater than 70 mm Hg.
- Initiate full fluid resuscitation after resection is complete.
- There is no evidence to support the superiority of either colloids or crystalloids.

### 7. What are the concerns when using the Pringle maneuver, and what are the concerns when using total caval isolation?

Once the liver is mobilized, vascular isolation via inflow and outflow control is necessary to limit bleeding. In the extrahepatic approach, the hepatic artery and portal vein branches are dissected at the porta hepatis and controlled outside of the liver—the so-called Pringle maneuver. This

maneuver effectively limits blood flowing into the liver with the result that bleeding is principally a result of hepatic venous pressure, which itself is significantly reduced by maintaining low CVP and mean arterial pressure. The advantage of this approach is early vascular control before transection. The disadvantages are a tedious dissection and the potential for injury to contralateral structures. The time limit imposed by potential liver ischemia and reperfusion injury, leading to liver insufficiency or hepatic failure postoperatively, means that a period of less than 45 minutes during surgery is optimal. Although the liver has been shown to tolerate 1 hour of warm ischemia, some technical variations of the Pringle maneuver include intermittent vascular occlusion with cycles of approximately 15 minutes on and 5 minutes off. At either point in the Pringle maneuver (clamp on or clamp off), hypotensive episodes may occur. Hypotension during application of the clamp is due to decreased venous return that can be successfully treated with boluses of phenylephrine or fluid or both. Hypotension during release of the clamp is due to reperfusion injury and release of ischemic mediators leading to vasodilation and cardiac depression (so-called stunning) from inflammatory mediator release. Judicious use of vasopressors or inotropic agents (e.g., ephedrine) or both generally alleviates the derangements. Lactic acidemia may also ensue following the Pringle maneuver and can be corrected by judicious fluid use. It may persist despite adequate resuscitation and should be followed in the immediate postoperative period as an early marker of liver failure.

Total vascular isolation involves clamping of the upper and lower vena cava in addition to the porta hepatis. Although total vascular isolation was used in the past, it is rarely necessary other than for the largest and most complex lesions. Although the advantage of total caval isolation is markedly reduced blood loss at the liver itself, the major disadvantages of lack of collateral flow to nondiseased areas and loss of venous return usually obviate its use. Large blood losses during liver resection are now rare, with median values of 200 to 500 mL. There is a strong emphasis on reduction of intraoperative blood loss through a combination of anesthetic techniques as described earlier and established surgical techniques. For this reason, caval isolation is rarely employed. If it is planned, large-bore intravenous access beyond the "usual" for hepatic resections in the form of a central line (8.5F or 9F) is advisable for rapid fluid resuscitation. Additional hemostasis may be provided by the application of adjunctive hemostatic agents to the cut surface of the liver. These are purely adjunctive measures and do not eliminate the need for good vascular control of bleeding.

### 8. How is postoperative pain best managed in patients after hepatic resection?

Management of postoperative pain in patients after liver resection presents many challenges. As mentioned previously, a large incision means severe postoperative pain is possible, and the location of the incision means that "splinting" may be common, leading to poor respiratory recovery. The "best" analgesic regimen after these procedures is still debated.

There are two schools of thought with regard to how one should approach neuraxial analgesia: epidural or single-shot spinal opioid. The concern for potential changes in clotting profiles after surgery is the primary reason epidural catheter placement is avoided by some clinicians. Single-shot spinal opioid placement (usually morphine) is avoided by some clinicians because of the changes in postoperative drug metabolism that may lead to toxicity. Postoperative epidural analgesia has repeatedly been shown to be safe, although approximately 10% of patients have prolonged coagulation times. Analgesia from intrathecal morphine has been shown to be equivalent to epidural analgesia, but pruritus and nausea occurred more frequently. One analgesic regimen consists of 250 μg of intrathecal morphine administered at the start of the case, limiting intravenous fentanyl to 3 to 8 μg/kg over the course of the resection, and intravenous patient-controlled analgesia pump in the recovery period. After the acute recovery period, all patients should be nursed in a monitored setting (e.g., step-down unit) where respiratory depression can be detected expeditiously.

If epidural placement is desired, the American Society of Regional Anesthesia and Pain Medicine (ASRA) guidelines should be followed for epidural catheter removal, to avoid the risk of epidural hematoma. If intravenous agents are to be the sole analgesic strategy, the intraoperative administration of long-acting opioids such as methadone, morphine, or hydromorphone is advisable. Tracheal extubation can be performed in most patients at the end of surgery, but respiratory depression must be watched for closely.

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CASE 34

# Open Abdominal Aortic Repair

**Ronald A. Kahn, MD**

## QUESTIONS

1. Explain the natural history of aortic aneurysms.
2. How is a patient with an aortic aneurysm evaluated preoperatively?
3. Which medications are administered preoperatively?
4. Which anesthetic agents are used for aortic aneurysm surgery?
5. How are patients undergoing aortic aneurysm surgery monitored?
6. Explain the consequences of aortic cross-clamping.
7. Describe some options for postoperative analgesia.

A 71-year-old man with a 6-cm infrarenal aortic aneurysm presented for conventional aortic repair. His past medical history was significant for hypertension, stable angina, hypercholesterolemia, and smoking.

### 1. Explain the natural history of aortic aneurysms.

The natural history of all aneurysms is to expand in size. The tendency to rupture primarily depends on wall stress. With increases in aneurysm diameters, the wall stress increases as described by LaPlace law, increasing the risk of rupture:

$$\text{Wall stress} = \frac{\text{pressure} \times \text{radius}}{2 \times \text{wall thickness}}$$

The average growth rate of aortic aneurysms is 0.4 cm per year. In a follow-up study of high-risk patients, the overall rupture rate was 3%, with a surgical mortality (elective surgery for aneurysms >6 cm or symptomatic aneurysms) of 4.9%. Approximately 34% of deaths were due to causes unrelated to the aneurysm. The 5-year survival rate for untreated abdominal aortic aneurysms greater than 6 cm was less than 10%, and the 5-year survival rate for untreated abdominal aortic aneurysms less than 6 cm was 50%. Elevated diastolic blood pressure, aneurysm anteroposterior diameter greater than 5 cm, and obstructive pulmonary disease were independent predictors of rupture. Predicted 5-year rupture rates ranged from 2% when these risk factors were absent to 100% when all three risk factors were present.

### 2. How is a patient with an aortic aneurysm evaluated preoperatively?

Nearly all patients presenting for aortic surgery have coexisting medical conditions that can significantly affect anesthetic management. Problems include diseases of the cardiovascular, pulmonary, renal, and central nervous systems. The goal of preoperative evaluation is to detect coexisting diseases, assess the risk of adverse outcomes, optimize the patient's medical status, and devise an anesthetic technique that minimizes complications. It is not always possible to perform a complete preoperative evaluation when surgery is required on an urgent basis, so preoperative optimization of the patient is not always feasible.

It is imperative to evaluate myocardial reserves before aortic surgery. Risk factors for myocardial ischemia include history of previous myocardial infarction, angina, congestive heart failure, male gender, smoking, hypercholesterolemia, diabetes mellitus, and limited exercise tolerance. Patients at low risk for myocardial ischemia may proceed to surgery without further evaluation; this represents a very small subset of patients with aortic aneurysms. Patients with a negative stress test within 2 years of surgery or who have had coronary artery bypass graft surgery without postoperative symptoms probably do not require further work-up for myocardial ischemia. Although stress testing is probably most appropriate for patients with moderate risk, coronary angiography is recommended for patients at high risk for myocardial ischemia.

There are two components to stress testing: "stressing" the myocardium and detection of myocardial ischemia or infarction. "Stressing" is performed by either mechanical (e.g., exercise via treadmill or hand-crank) or pharmacologic means. Pharmacologic stress may involve drugs such as dobutamine that increase myocardial oxygen demand or drugs such as dipyridamole that cause "myocardial steal." Myocardial ischemia is detected by electrocardiogram (ECG), nuclear studies, or echocardiography. Ischemic myocardium is characterized by changes in ST segment elevations that occur with exercise. On nuclear studies, the absence of nuclear tracer uptake during stress and uptake of nuclear tracers with rest is known as a reversible defect. Fixed defects (i.e., absence of uptake during stress and rest) is consistent with old infarction. Ischemic myocardium

**BOX 34-1 Preoperative Evaluation of the Cardiovascular System**

**Risk Factors**

- History of previous myocardial infarction
- Angina
- Congestive heart failure
- Male gender
- Smoking
- Hypercholesterolemia
- Diabetes mellitus
- Limited exercise tolerance

**Further Work-up Not Required**

- Negative stress test within 2 years
- Coronary artery bypass graft surgery without postoperative symptoms

**Further Work-up Required**

- Stress test for moderate-risk patients
- Coronary angiography for high-risk patients

is characterized on echocardiography as significant change in wall motion during "stressing." Myocardial segments that remain akinetic both during rest and during exercise may be assumed to be infarcted. In each of these studies, it is important to determine whether there is myocardium at risk (i.e., myocardium that may become ischemic with stress) as opposed to myocardium that is infarcted. If patients have significant areas of myocardium at risk, further optimization (either pharmacologic or interventional) is warranted before surgery (Box 34-1).

Patients with significant coronary artery disease (CAD) may be candidates for myocardial revascularization such as percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery. Examples of PCI are balloon angioplasty, bare metal stent (BMS) placement, and drug-eluting stent (DES) placement. The efficacy of DESs is greater than that of BMSs, which is greater than balloon angioplasty. All three PCI procedures are associated with restenosis, and patients who have undergone PCI are placed on dual antiplatelet therapy (e.g., aspirin and clopidogrel). Dual antiplatelet therapy continues for 2 to 4 weeks after balloon angioplasty, for 6 weeks after BMS placement, and for at least 1 year after DES placement. Because of the inflammatory and hypercoagulability response seen with surgical interventions, premature discontinuation of dual antiplatelet therapy is associated with a greater incidence of adverse myocardial events and in-stent stenosis. Present recommendations are that elective surgery that requires discontinuation of antiplatelet drugs should be postponed 2 to 4 weeks after balloon angioplasty, 6 weeks to 3 months after placement of BMSs, and greater than 1 year after placement of DESs. Similarly, if patients presenting for aortic aneurysm repair have significant CAD requiring PCI, the type of intervention and the type of stent placed (if any) must be weighed against the urgency of surgery (Box 34-2).

**BOX 34-2 Preoperative Myocardial Revascularization for Patients with Myocardium at Risk**

Percutaneous coronary intervention

- Balloon angioplasty—elective surgery that requires discontinuation of antiplatelet drugs should be postponed 2 to 4 weeks
- BMS—elective surgery that requires discontinuation of antiplatelet drugs should be postponed 6 weeks to 3 months
- DES—elective surgery that requires discontinuation of antiplatelet drugs should be postponed more than 1 year

Coronary artery bypass graft surgery

*BMS*, Bare metal stent; *DES*, drug eluting stent.

### 3. Which medications are administered preoperatively?

All antihypertensive and antianginal medications should be continued up to the time of surgery. Preoperative sedation should be based on the patient's clinical condition and concurrent medical diseases. Anxiolysis is recommended to reduce preoperative hypertension and tachycardia, which may increase the risk of aneurysm leakage or rupture as well as induce myocardial ischemia in patients with concurrent CAD. Patients with aortic aneurysm are at particular risk for hemodynamic instability secondary to hemorrhage, myocardial ischemia, or congestive heart failure. Organ malperfusion is also a major problem. Patients presenting for emergency aortic aneurysm surgery require intense monitoring to control blood pressure and to resuscitate appropriately.

In patients with aortic disease, the paramount goal is the maintenance of hemodynamic stability, while providing adequate amnesia, analgesia, and immobility. Because the aorta remains at risk for rupture or extension of dissection, blood pressure must be strictly controlled. β-Adrenergic blockers and vasodilators are the mainstays for minimizing the driving force and the ejection velocity of blood, while maintaining adequate perfusion pressure. On the other end of the spectrum are patients who present in hypovolemic shock secondary to leaking or rupture of the aorta. In this situation, maintaining volume status, securing the airway, and immediate surgical control are the main goals.

This surgical population also includes many patients with occlusive CAD, in whom hemodynamic aberrations may induce myocardial ischemia by adversely affecting myocardial oxygen supply and demand balance. The use of perioperative β-adrenergic blockade is controversial. β-adrenergic blockade in patients with significant risk factors for CAD decreases the incidence of adverse cardiac outcomes. The acute discontinuation of long-term β-adrenergic blockade before surgery has been associated with an increased incidence of myocardial events. However, a large randomized controlled study, POISE (PeriOperative ISchemia Evaluation), has cast doubts on the unrestricted use of β-adrenergic blockade during the perioperative period. Although patients receiving β-adrenergic blockade had a lower incidence of primary myocardial events, they had a greater incidence of

hypotension with an associated increased rate of stroke and greater mortality. If patients have significant risk of CAD, β-adrenergic blockade should be carefully titrated to heart rate and blood pressure.

### 4. Which anesthetic agents are used for aortic aneurysm surgery?

All patients presenting for emergency aortic surgery are treated as if they have a full stomach, whereas elective cases must be considered individually. Avoiding hemodynamic aberrations during induction and tracheal intubation are desirable. Various anesthetic agents can accomplish these goals, and the choice is a personal decision that depends on the clinical situation. High-dose opioid techniques are still commonly employed for patients in whom postoperative ventilatory support is anticipated; however, normothermic, hemodynamically stable patients may be considered for early extubation. Although no evidence-based practices favor one anesthetic technique over another, it is probably most important to use a technique that achieves the desired hemodynamic goal. Vasoactive medications, such as nitroprusside, nitroglycerin, and esmolol, should be prepared preoperatively, including diluted amounts for bolus administration.

### 5. How are patients undergoing aortic aneurysm surgery monitored?

Standard American Society of Anesthesiologists (ASA) monitors are placed for all patients presenting for surgery of the aorta. ECG with the ability to monitor limb and precordial leads (II and $V_5$ at the minimum) is desirable to detect myocardial ischemia and arrhythmias. Foley catheterization is also prudent to assess volume status and to provide early indication of renal malperfusion. Because of the increased incidence of myocardial ischemia, coagulopathy, and wound infection, patients should remain normothermic perioperatively.

Anesthesia for aortic surgery is frequently complicated by marked sudden blood pressure lability. Shifts in intravascular volume, the effects of anesthetic agents, and surgical manipulations are the major causes. Sudden losses of significant amounts of blood may induce severe hypovolemia at almost any time. Changes in preload may be due to sudden and profound hemorrhage from intercostal artery back-bleeding, aortic disruptions, extensive anastomotic suture leaks, and evaporative and third space losses. Large-bore intravenous access is extremely important in aortic surgery. Aortic rupture can occur at any time, and the ability to infuse intravenous fluids and blood or blood products rapidly is necessary. One or two large-bore peripheral intravenous lines are recommended in addition to central venous access. A rapid infusion system with a fluid warmer should be immediately available. Blood salvaging techniques for autotransfusion are recommended. The easiest blood salvaging technique to employ is a centrifugal device that scavenges and washes erythrocytes. The disadvantages of this method are delays in filling the centrifuge bowl; time consumed processing the blood; and lost plasma volume, proteins, coagulation factors, and platelets.

A safe and reliable method of measuring acute changes in blood pressure is required during aortic surgery. Intraarterial monitoring accomplishes this goal by providing continuous, beat-to-beat indication of arterial pressure and waveform. An indwelling arterial catheter enables frequent sampling of arterial blood for laboratory analyses.

Cannulation of a central vein is routinely performed for aortic surgery to measure filling pressures in the heart (using a central venous catheter or a pulmonary artery catheter), provide a central route for drug administration, and enable rapid infusion of fluids. Central venous access can be accomplished with a large-bore cannula ("introducer") in the right internal jugular vein or left subclavian vein. Cannulation of the left internal jugular vein may be associated with a greater incidence of innominate vein perforation; because of the acute changes in directions, catheterization of the pulmonary artery is more difficult from the left internal jugular or right subclavian vein.

Central venous pressure (CVP) does not give a direct indication of left heart filling pressure, but it may be used as an estimate of left-sided filling pressures in patients with good left ventricular function. CVP has been shown to correlate with left-sided filling pressures during a change in volume status in patients with CAD and ejection fractions greater than 40%. Other studies have not shown a consistent relationship between CVP and pulmonary capillary wedge pressure.

Pulmonary artery catheterization should be strongly considered in patients with decreased ventricular function, pulmonary hypertension, severe valvular disease, or advanced systemic organ dysfunction. Monitoring of right-sided pressures as the sole indication of volume status is probably not sufficient because of the inability of the right heart pressures to reflect left heart preload. Pulmonary artery catheters may also be used to determine afterload, cardiac output by thermodilution, and oxygen delivery by measuring pulmonary artery oxygen saturation. Although pulmonary artery catheters are probably warranted in high-risk patients, no study has demonstrated better outcome with the use of this modality.

Transesophageal echocardiography (TEE) is a very useful monitoring tool during aortic surgery. Ventricular dysfunction and regional wall motion abnormalities may be diagnosed. TEE produces images of the heart and great vessels, affording information such as regional wall motion abnormalities, indirect measurements of stroke volume and ejection fraction, valvular abnormalities, and aortic and pericardial pathology. Ventricular function and intravascular volume status are probably the best indications for using TEE during these procedures. Competency in TEE is certified by the National Board of Echocardiography.

### 6. Explain the consequences of aortic cross-clamping.

The most consistent hemodynamic response to acute aortic occlusion is an abrupt increase in afterload with a resultant increase in proximal aortic pressure. During

supraceliac aortic occlusion, there is an increase in preload secondary to volume redistribution from veins distal to the site of aortic occlusion. These increases in afterload, preload, and possibly contractility are associated with enhanced myocardial oxygen demand and possibly myocardial ischemia. Because of the expected increases in preload from aortic occlusion, preload should be maintained low before occlusion. Venodilators such as nitroglycerin, may be titrated to decrease preload further, and arterial dilators may be used to control increases in afterload. During aortic occlusion, attention should be directed toward maintenance of preload, which may be complicated by continued blood loss.

Intraoperative hypotension may result from multiple causes. Hypovolemia, myocardial depression, and decreases in afterload should be considered. One common etiology of hypotension is reperfusion. Unclamping hypotension may be caused by central hypovolemia secondary to blood pooling in reperfused tissues, hypoxia-mediated vasodilation, and accumulation of vasoactive or myocardial-depressant metabolites such as lactate. Treatment should be directed toward rapid correction of hypovolemia, acidosis, and hypocalcemia and the judicious administration of vasoactive drugs. If there is difficulty obtaining hemodynamic stability, the aorta can be temporarily reoccluded while resuscitation continues.

Renal insufficiency may occur as a result of abdominal aortic reconstruction. It is possible that pharmacologic agents may provide renal protection during repair. Although mannitol may result in greater diuresis on postoperative day 1 and less subclinical glomerular and renal tubular damage, it probably has no effect on postoperative blood urea level, serum creatinine concentration, or creatinine clearance. There is little evidence of the effectiveness of furosemide as a renal protective agent.

Theoretically, the perioperative use of low doses of dopamine may confer renal protection in high-risk individuals. Low-dose dopamine (1 to 3 μg/kg/min) dilates renal afferent arterioles and increases renal blood flow, independent of its cardiac effects. Dopamine infusion during aortic clamping results in a significant increase in urine sodium output, potassium output, creatinine clearance, and urine volume. The use of perioperative dopamine during aortic surgery is associated with increases in effective renal plasma flow and glomerular filtration rate and fractional excretion of sodium during the postoperative period. However, studies have not demonstrated a renal protective effect of low-dose dopamine use. It is likely that renal dose dopamine administration during the perioperative period confers no advantage over the maintenance of euvolemia in most patients with vascular disease during infrarenal abdominal aortic aneurysm repair.

Fibrinolysis occurs with aortic cross-clamping. Visceral ischemia (which does not occur with infrarenal aortic clamping) may initiate fibrinolysis. Antifibrinolytic agents should be strongly considered if supraceliac occlusion is anticipated. Aminocaproic acid, tranexamic acid, and aprotinin all are effective in decreasing fibrinolytic activity; however, aprotinin is no longer clinically available.

### 7. Describe some options for postoperative analgesia.

Intravenous opioid administration has the advantage of rapid uptake and attainment of therapeutic levels. However, this mode of administration is also associated with rapid declines in drug concentration during which patients may experience pain. Although using larger doses may increase the duration of analgesia, higher doses may be associated with a greater number of adverse side effects. To minimize these side effects, small, frequent doses of opioids may be administered via a patient-controlled pump (i.e., patient-controlled analgesia). This technique allows greater comfort control during the hospital course and may prevent overmedication. Although this technique is safe, respiratory depression may occur, so routine postoperative nursing care should include careful monitoring of respiratory status.

An attractive alternative to the use of intravenous opioids is epidural administration of analgesics. Local anesthetics, opioids, and other agents such as $\alpha_2$ agonists have been described as effective in significantly decreasing the intensity of postoperative pain. Although this method can provide profound pain relief, it may be associated with significant side effects. Local anesthetics cause sympathetic blockade (with resultant decreases in preload and afterload that may produce hypotension and tachycardia), motor blockade, and local anesthetic toxicity. Opioids may cause pruritus, nausea, vomiting, urinary retention, or respiratory depression. These side effects can usually be treated with conventional therapy (e.g., antihistamines, antiemetics) or specific opioid antagonists. Epidural opioids have the advantage of specificity of action, without major hemodynamic changes and motor blockade that are associated with local anesthetics.

Preoperative epidural catheter insertion for postoperative analgesia is probably safe when perioperative anticoagulation is anticipated. Epidural anesthesia may increase coronary blood flow, but there is contradictory evidence on the effect of epidural anesthesia on myocardial ischemia during noncardiac surgery. There have been multiple reports of attenuation in the stress response with perioperative and postoperative epidural anesthesia and analgesia during vascular surgery. Supplemental epidural anesthesia may significantly attenuate catecholamine release during aortic occlusion and reperfusion. This reduction in the stress response by epidural anesthesia or analgesia could decrease postoperative hypercoagulability.

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CASE 35

# Endovascular Thoracic Aortic Repair

**Ronald A. Kahn, MD**

## QUESTIONS

1. What is the difference between conventional descending aortic reconstruction and endovascular aortic repair?
2. List the anatomic requirements and restrictions for endovascular aortic repair.
3. What are the recognized surgical complications of endovascular aortic aneurysm repair?
4. Discuss patient outcomes after thoracic endovascular aortic repairs compared with open repairs.
5. Which anesthetic technique is best for endovascular aortic repair?
6. What are the recognized potential complications of proximal graft deployment?
7. What are the advantages of transesophageal echocardiography monitoring during aortic thoracic endovascular repair?
8. Explain the relationship between spinal cord ischemia and endovascular thoracic aortic repair.
9. What is postimplantation syndrome?

An 83-year-old man with a past medical history significant for coronary artery disease, congestive heart failure, chronic obstructive pulmonary disease, hypertension, and previous abdominal aortic aneurysm repair presented with a 7-cm descending thoracic aortic aneurysm. The descending aortic aneurysm began 5 cm distal to the left subclavian artery and extended for 30 cm. Because of the patient's concurrent medical conditions, an endovascular repair was planned. Several self-expanding endograft devices were used.

Anesthesia and surgery progressed without incident. In the postanesthesia care unit, the patient became febrile and mildly hypotensive and developed oozing at the surgical sites.

### 1. What is the difference between conventional descending aortic reconstruction and endovascular aortic repair?

Endovascular aortic repair (EAR) is an alternative to conventional surgical repair of aortic pathology. Endovascular grafts are less invasive than conventional arterial reconstructions. Endovascular grafts are inserted through small openings from remote arterial access sites and do not require large abdominal incisions. This technique obviates the need for extensive and prolonged aortic occlusion, decreases blood loss, and avoids significant fluid shifts that occur with visceral manipulation, reducing the risk of significant hemodynamic changes perioperatively.

Because long-term outcome studies of EAR are lacking, younger patients with minimal or no medical comorbidities are frequently treated with open repairs because of their established track record and low complication rate. Patients with severe medical comorbidities may be better candidates for endovascular reconstruction.

### 2. List the anatomic requirements and restrictions for endovascular aortic repair.

Not all patients with aortic pathology have suitable anatomy for endovascular repair. For EAR to be successful, the device must form a tight seal between graft and native artery. The proximal neck (i.e., proximal "landing zone") must be at least 15 mm in length, and the aneurysm neck diameter should be no larger than the largest endograft available. Similarly, the distal attachment site must be nonaneurysmal and of sufficient length to accommodate a graft. No important aortic side branches, such as an accessory renal artery or inferior mesenteric artery, can be present in the aortic segment that is to be excluded. As a practical matter, excessive aneurysm neck tortuosity, severe calcification, aneurysmal necks >26 mm in diameter, and aneurysmal necks <10–15 mm in length may be relative contraindications for EAR. Finally, there must be at least one large, straight iliac artery that can accommodate passage (i.e., act as a conduit) of the endograft delivery system.

### 3. What are the recognized surgical complications of endovascular aortic aneurysm repair?

Although EAR is a less invasive technique compared with open repair, it is nonetheless associated with significant perioperative complications. Iliac or aortic anatomy and

pathology may preclude insertion of endovascular sheaths (delivery systems). The possibility always exists of iatrogenic arterial rupture, which may necessitate emergent resuscitation and immediate conversion to an open procedure, increasing the morbidity and mortality associated with the repair.

Injury to the aorta and end-organs may occur with guidewire insertion and device manipulation via either embolization or obstruction. Distal embolization of aortic material to the bowel, lower extremities, or other organs is common. Although the endovascular device may obstruct hypogastric artery flow, complications have not been reported. Retrograde thromboembolism as a result of graft manipulation, injection of large volumes of contrast material, vigorous flushing, or the passage of guidewires through a diseased aortic arch may result in cerebral injury. Inadvertent guidewire placement into the heart has occurred with injury to the aortic valve or pericardial tamponade with resultant hemodynamic collapse.

Segmental or total renal injury may occur as a complication of EAR. Graft migration, renal artery dissection, and improper placement of the proximal portion of the endovascular device can occlude the renal arteries. Renal artery occlusion may lead to renal insufficiency and the possibility of further procedures to correct the problem. A significant amount of contrast material is used during these procedures to define aortic anatomy, providing another possible mechanism for renal injury (Box 35-1).

## 4. Discuss patient outcomes after thoracic endovascular aortic repairs compared with open repairs.

EAR may be a viable option for surgical treatment of thoracic aortic pathology. Dake et al. (1994) reported 6-month, 1-year, and 2-year survival rates of 86%, 81%, and 73%, respectively, after endovascular thoracic aortic aneurysm repair. Predictors of death included the following: patients who were not open surgical candidates, the use of cardiopulmonary bypass (which was used in patients who underwent combined ascending aortic and arch surgery with endovascular thoracic aortic aneurysm repair), large aneurysms or large aneurysm neck diameters, and older patient age. The major complications of the procedure were early death (9%), neurologic conditions (10%), and pulmonary conditions (12%). The 9% mortality was not much different from the reported 11% mortality associated with open repair. However, 16% of the patients underwent emergency operations, and 60% of these patients were not candidates for open repair. Placed in context, the mortality rate is not unreasonable.

Dake et al. (1994) attributed this high incidence of stroke to catheter or sheath manipulations in the aortic arch and ascending aorta, excessive anticoagulation, or possibly surgical manipulation of the carotid or subclavian arteries. In more recent studies, meta-analyses provide evidence that EAR is associated with a lower incidence of early death, paraplegia, renal insufficiency, transfusions, reoperation for bleeding, cardiac complications, pneumonia, and length of stay compared with open surgery. Both endovascular repair and open repair after ruptured thoracic aortic aneurysms were associated with no differences in mortality or complications; however, uncomplicated discharge was more common after endovascular repair.

Long-term outcome has been better defined after endovascular repair of infrarenal aortic aneurysms. There is an initial earlier survival benefit after endovascular repair. With time, however, there is continued progression of the underlying aneurysmal disease with need for continued surveillance and interventions after EAR. Patients undergoing open repair have significantly greater rates of freedom from secondary interventions compared with patients undergoing EAR. After 2 years, there are no significant survival differences between groups; these comparable survival rates continue for at least 6 years postoperatively.

**BOX 35-1 Recognized Surgical Complications of Endovascular Aortic Repair**

- Insertion of endovascular delivery system precluded
  - Iliac artery anatomy or pathology
  - Aortic anatomy or pathology
- Artery rupture with hypotension
- Embolization of aortic material
  - Bowel
  - Lower extremities
  - Brain
  - Other organs
- Guidewire trauma
  - Aortic valve
  - Myocardial perforation with cardiac tamponade
- Graft malposition
  - Renal artery occlusion leading to renal impairment
  - Occlusion of intercostal or anterior spinal cord artery leading to paralysis
- Postimplantation syndrome

## 5. Which anesthetic technique is best for endovascular aortic repair?

Different anesthetic techniques have been described for aortic stent graft placement including local anesthesia, regional anesthesia, and general anesthesia. Because early procedures often required long surgical times, general anesthesia was usually administered to enhance patient compliance. With increasing operator experience and sophisticated devices, regional anesthetics (including epidural, spinal, and continuous spinal anesthetics) and local anesthetics supplemented by sedation are more common. Choice of anesthetic technique depends on the planned surgical interventions and the patient's comorbid conditions. Operations that require percutaneous catheter placement with limited incisions are well tolerated under local anesthesia and sedation. Either regional or general anesthesia is appropriate for extensive inguinal exploration and dissection or construction of a femoral artery-to-femoral artery conduit. Surgical dissection into the retroperitoneum requires a higher level of regional anesthesia or general anesthesia. Many of these procedures take a long time to perform. Patients undergoing local

anesthesia or regional anesthesia require intravenous sedation to treat agitation secondary to restlessness and discomfort from lying in one position for a prolonged period.

In a retrospective analysis of 91 patients undergoing EAR, local anesthesia was associated with reduced use of vasoactive agents, more favorable fluid balance, fewer intensive care unit admissions, and shorter hospital stays compared with regional or general anesthesia. In a prospective study of 239 patients undergoing EAR, no differences in all-cause mortality were observed among different anesthetic techniques. However, local anesthesia was associated with a lower incidence of respiratory complications compared with general anesthesia (0% versus 5%; $P < .01$) and a lower incidence of renal failure compared with general or regional anesthesia (0% versus 2% versus 1%; $P < .02$). Finally, in a larger multicenter retrospective study of 5557 patients undergoing EAR, the incidence of cardiac complications was significantly lower in both the local and the regional anesthesia groups compared with the general anesthesia group (1.0% vs. 2.9% vs. 3.7%). Similarly, the incidence of sepsis was significantly lower in the regional anesthesia group compared with the general anesthesia group (0.2% vs. 1.0%). Significant selection bias in these retrospective studies makes it difficult to extrapolate the results to clinical practice.

## 6. What are the recognized potential complications of proximal graft deployment?

Distal migration of the device occurring during proximal endograft deployment may result in inadequate exclusion of the aneurysmal sac with resultant endoleak. Older styles of endovascular stent grafts employed large balloon angioplasty catheters to expand and secure the proximal stent attachment system to the underlying normal vessel wall. These balloons have a large cross-sectional area, predisposing to distal aortic migration as aortic blood flow forces it forward. Device malposition secondary to migration may result in either occlusion of major arterial branches or incomplete aneurysm exclusion. Induced hypotension during device deployment has been successfully used to assist in proximal endovascular stent graft placement and may reduce the magnitude of migration. Hypotension is induced using short-acting vasodilators or ventricular quiescence. Ventricular quiescence can be achieved with adenosine or induced ventricular fibrillation. High-dose adenosine can produce sinoatrial and atrioventricular node inhibition. Nevertheless, significant endovascular stent graft movement can occur as continued aortic blood flow forces it forward. Most likely, no interventions are necessary for self-expanding devices.

## 7. What are the advantages of transesophageal echocardiography monitoring during aortic endovascular repair?

With the rapid evolution of ultrasound technology and the advent of transesophageal echocardiography (TEE), perioperative dynamic views of the cardiovascular system are now obtainable. These images have previously been unavailable by conventional transthoracic ultrasonography. With the esophagus in close approximation to the aorta, TEE has become an excellent tool for diagnosing pathology of the distal aortic arch, the descending thoracic aorta, and the proximal abdominal aorta. TEE can provide instantaneous views of guidewires and endografts before deployment, in relation to normal and diseased thoracic aorta. Long-axis views are used to aid placement of the angiography catheter and delivery device. Higher frequencies and transverse imaging plane views can help identify the catheter tip and delivery system within the aorta.

TEE has distinct advantages over perioperative angiography. TEE may provide exact vessel and lesion sizing and localization, which is difficult to obtain during single-plane angiography. Both endograft leakage (using Doppler color flow imaging) and iatrogenic dissections may easily be diagnosed with TEE, in contrast to angiography. TEE can also be used to estimate endograft sizing and evaluate the endograft location. Large intercostal arteries have been imaged, avoiding inadvertent obstruction by the aortic stent graft; however, consistent visualization of intercostal arteries is not possible in all patients. After stent graft placement, exclusion of flow from the aorta into the aneurysm can be easily confirmed using color Doppler flow imaging in most patients. Finally, because most of these patients have severe concomitant cardiac disease, perioperative TEE allows dynamic assessment of cardiac function.

## 8. Explain the relationship between spinal cord ischemia and endovascular thoracic aortic repair.

The reported incidence of postoperative neurologic injuries after endovascular thoracic aortic reconstruction is similar to open thoracic aortic repair. With descending aortic reconstruction, intercostal arteries that supply the anterior spinal cord may be sacrificed, resulting in spinal cord injury. Probable risk factors for paraplegia include the length of the thoracic endograft and a history of previous abdominal aortic aneurysm repair. Evidence for the usefulness of cerebrospinal fluid (CSF) drainage is extrapolated from the open thoracic aortic repair literature. During thoracic aortic surgery, when CSF pressure exceeds spinal venous pressure, a "critical closing pressure" is achieved, and the veins collapse independent of inflow pressure. Perioperative control of CSF pressure may reduce the incidence of spinal cord injury. Coselli et al. (2002) randomly assigned 145 patients undergoing thoracic abdominal aortic aneurysm repair with or without CSF drainage. Nine patients (13.0%) in the control group developed paraplegia or paraparesis compared with two patients (2.6%) in the CSF drainage group. These data are supported by meta-analysis and retrospective analysis. Anecdotal evidence also exists for the reversal of spinal cord symptoms by CSF drainage after endovascular thoracic aortic repair. The use of prophylactic lumbar CSF drainage catheters and induced hypertension may be warranted in high-risk patients undergoing endovascular thoracic aortic repair.

### 9. What is postimplantation syndrome?

Postimplantation syndrome is commonly observed after EAR. It is characterized by fever, elevated C-reactive protein levels, and leukocytosis in the absence of an infectious agent. It is usually mild and self-limited, lasting 2–10 days postoperatively, and responds to nonsteroidal antiinflammatory drugs. Occasionally, an exaggerated response may result in life-threatening distributive shock, respiratory failure, and disseminated intravascular coagulation. It is hypothesized that EAR induces a significant inflammatory response resulting in endothelial cell activation from intraaneurysmal device manipulation. Although rare, postimplantation syndrome may manifest as a consumptive coagulopathy. Endovascular exclusion of a large aortic aneurysm may result in significant thrombus in the excluded aneurysm sac, which can initiate fibrinolysis. Repeated instrumentation of the aorta, which occurs with difficult endograft placement, may produce endothelial damage resulting in stimulation of a procoagulant response.

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CASE 36

# Transurethral Resection of the Prostate

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## QUESTIONS

1. What is TURP syndrome, and what is the treatment?
2. What other complications can occur during TURP?
3. What types of irrigating fluids have been used for transurethral resection of the prostate?
4. What toxicities are associated with glycine?
5. What are the anesthetic options for a patient undergoing transurethral resection of the prostate?
6. If a regional anesthetic is selected, what level of anesthesia is required?
7. The patient's serum sodium level is 102 mEq/L 1 hour and 15 minutes into the procedure; how would you correct the sodium level to 135 mEq/L?
8. What surgical measures can minimize the incidence of TURP syndrome?
9. What other minimally invasive surgical modalities are available to treat benign prostatic hypertrophy?

A 74-year-old man with a past medical history of coronary artery disease with stable angina and hypertension was scheduled to undergo transurethral resection of the prostate (TURP) for benign prostatic hypertrophy. Current medications included metoprolol, 50 mg twice a day, and amlodipine, 10 mg once a day. The physical examination was unremarkable. Heart rate was 74 beats per minute, blood pressure was 160/75 mm Hg, and respiratory rate was 12 breaths per minute. The patient was 177.5 cm tall and weighed 72 kg.

### 1. What is TURP syndrome, and what is the treatment?

TURP syndrome is a collection of signs and symptoms that occur when excessive amounts of irrigating fluids are absorbed through the opened prostatic venous sinusoids. Absorption of fluids may result in water intoxication, hyponatremia, and hypoosmolality. Although most commonly associated with TURP, this syndrome may also occur with transurethral resection of bladder tumors, diagnostic cystoscopy, percutaneous nephrolithotomy, and endoscopic gynecologic procedures. The incidence of TURP syndrome is 0.78%–1.4%. The mortality rate in severe cases is 25%. The syndrome may be observed minutes after resection starts up to 24 hours postoperatively.

The decrease in serum sodium ($Na^+$) levels during TURP ranges from 3.65–10 mEq/L. Several mechanisms for this decrease in $Na^+$ have been postulated. Hyponatremia may be due to either simple dilution by the irrigating solution or diffusion of $Na^+$ into the irrigating solution at the surgical site or into the periprostatic or retroperitoneal spaces. The degree of hyponatremia is related to the rate of absorption of the irrigating fluid and not to the absolute amount absorbed.

Effects of TURP syndrome on the central nervous system include headache, restlessness, agitation, confusion, seizures, and eventually coma (Box 36-1). These findings are thought to be caused by cerebral edema, with a concomitant increase in intracerebral pressure. As the neurologic condition worsens, the patient may develop decerebrate posturing, clonus, a positive Babinski sign, brainstem herniation, and ultimately death. Ocular examination often reveals bilateral dilated and sluggishly reactive pupils and papilledema. Electroencephalography often shows low-voltage activity. If coma occurs, it usually resolves within hours to days, but it can be permanent. The incidence of neurologic injury is more closely related to the rate of $Na^+$ decrease rather than the degree of hyponatremia.

Hyponatremia and fluid overload have deleterious consequences on the heart. The initial cardiovascular effects of fluid overload include hypertension and bradycardia. However, serum $Na^+$ levels of 120 mEq/L are associated with negative inotropic effects on the heart causing hypotension, pulmonary edema, and congestive heart failure. Serum $Na^+$ levels of less than 115 mEq/L are associated with electrocardiogram (ECG) changes, such as a widened QRS complex, ventricular ectopy, and T-wave inversion. When serum $Na^+$ decreases to $<100$ mEq/L, respiratory and cardiac arrest may occur (Box 36-2).

If the patient develops signs and symptoms of TURP syndrome, surgery should be concluded as soon as possible. Treatment should be directed at increasing the serum $Na^+$ level and correcting volume overload by fluid restriction and administration of a loop diuretic, such as furosemide. In severe cases of hyponatremia, administration of a hypertonic saline solution (3%–5% sodium chloride) may be necessary. Rapid correction of hyponatremia has

**BOX 36-1 Central Nervous System Effects of TURP Syndrome**

- Headache
- Restlessness
- Agitation
- Confusion
- Seizures
- Coma
- Decerebrate posturing
- Clonus
- Babinski sign
- Sluggishly reacting pupils
- Papilledema

**BOX 36-2 Cardiovascular Effects of TURP Syndrome**

- $Na^+$ <120 mEq/L
  - Hypotension
  - Pulmonary edema
  - Congestive heart failure
- $Na^+$ <115 mEq/L
  - Widened QRS complex
  - Ventricular ectopy
  - T-wave inversion
- $Na^+$ <100 mEq/L
  - Respiratory arrest
  - Cardiac arrest

**BOX 36-3 Complications of Transurethral Resection of the Prostate**

- Bladder perforation
  - Extraperitoneal or intraperitoneal
- Bleeding
  - Related to size of gland and resection time
- Coagulopathy
  - Dilution of coagulation factors
  - Primary fibrinolysis
  - Disseminated intravascular coagulopathy
- Transient bacteremia and septicemia
- Toxicity of irrigating fluids
  - Hypervolemia
  - Hyponatremia
- Hypothermia
- Glycine toxicities
  - Transient blindness
  - Hyperammonemia
  - Nausea and vomiting
  - Coma
- Myocardial depression
- Electrocardiogram changes

been associated with cerebral edema and central pontine myelinolysis. All other treatment is dictated by the patient's symptoms. Supplemental oxygen should be considered, and the patient may require tracheal intubation and mechanical ventilation.

## 2. What other complications can occur during transurethral resection of the prostate?

Approximately 7% of all patients undergoing TURP experience a major complication. The 30-day mortality rate has been estimated to be 0.2%–0.8%. This is a marked improvement over studies performed in the 1960s, which showed a mortality rate of approximately 2.5%. Patients undergoing TURP are often elderly and have coexisting cardiopulmonary disorders making them more likely to experience complications. Because many patients are on long-term diuretic therapy, they are often dehydrated and present with electrolyte abnormalities preoperatively. Other complications associated with this procedure are described next (Box 36-3).

### *Bladder Perforation*

Bladder perforation occurs in approximately 1% of all TURP procedures. It may be caused by overdistention of the bladder with irrigating fluid or surgical instrumentation. An early sign of bladder perforation is decreased return of irrigating fluid. The abdomen becomes distended and often rigid. If the procedure is performed under regional anesthesia, patients may complain of pain or experience nausea and vomiting. Hypotension followed by hypertension is common.

Most perforations are extraperitoneal and benign in nature. This type of perforation causes pain in the periumbilical region. However, pain in the upper abdomen or referred pain to the shoulder may be a sign of intraperitoneal perforation, a potentially fatal complication. Diagnosis should be confirmed quickly by cystourethrography, and treatment should be with a suprapubic cystostomy.

### *Bleeding*

The prostate is a highly vascular organ. Because large amounts of irrigation fluid are used, blood loss is difficult to assess. Intraoperative blood loss corresponds to the size of the gland and resection time. Blood loss is generally considered to occur at a rate of 2–5 mL per minute of resection time and 20–50 mL/g of prostate tissue. Blood loss is linearly related to prostate size up to 35 g, at which point blood loss tends to exceed the linear correlation. Patients with resection times of greater than 90 minutes or a prostate size of >60 g have been found to have a significant increase in morbidity associated with bleeding.

### *Coagulopathy*

Subclinical coagulopathy occurs in approximately 6% of patients undergoing TURP, whereas clinical coagulopathy occurs approximately 1% of the time. This condition seems to correlate with the mass of resected prostatic tissue. It is a more likely event if the resected tissue is >35 g. Coagulopathy may be due to dilution of coagulation factors and platelets.

Primary fibrinolysis has also been implicated as a cause of coagulopathy. Plasminogen activator, which is responsible for converting plasminogen into plasmin, is released during these procedures. The treatment of choice for primary fibrinolysis is aminocaproic acid.

Secondary fibrinolysis may occur as a result of disseminated intravascular coagulopathy (DIC). DIC is caused by systemic absorption of prostate tissue, which is rich in thromboplastin. Consistent with this theory are the low levels of plasminogen activator, platelets, and fibrinogen that are commonly found in DIC and that frequently accompany TURP. If DIC is suspected, the

treatment is symptomatic. Fluid and blood products are administered as needed. Heparin administration may be beneficial.

### *Transient Bacteremia and Septicemia*

The prostate, rich in pathogens, may cause postoperative bacteremia via prostatic venous sinusoids. Indwelling urinary catheters enhance the risk. Approximately 6%–7% of patients go on to develop sepsis. Treatment consists of antibiotics and supportive care.

### *Toxicity of Irrigating Fluids*

The major toxicity of irrigation fluids used today is related to massive absorption causing fluid overload, hyponatremia, and hypoosmolality. The incidence of hypoosmolality and its associated neurologic sequelae has decreased since the use of nonelectrolyte isoosmotic irrigating solutions. However, fluid overload and hyponatremia still remain a problem. During TURP, 8 L of irrigating fluid may be absorbed causing an average weight gain of about 2 kg. Some of this fluid (20%–30%) is absorbed directly into the vascular space. The remainder is absorbed into the periprostatic and the peritoneal space (interstitial space). Several factors contribute to the rate of absorption of irrigating fluid, including prostate size, integrity of the prostatic capsule, and height of the irrigating fluid container. Greater amounts of irrigating fluid are absorbed when the prostate is large because of its richer blood supply and when the prostate capsule is violated.

Certain maneuvers can limit the amount of irrigating fluid absorbed. The first is to restrict the height of the fluid container above the surgical field; this decreases hydrostatic pressure driving fluid into sinuses. When the bag is >60 cm above the patient, absorption is greatly enhanced. The second maneuver is to limit resection times to <150 minutes because 10–30 mL of irrigation fluid is absorbed per minute of resection.

Sorbitol and mannitol, both sugar alcohols, have been associated with the development of lactic acidosis and hyperglycemia. Specific effects of glycine are discussed later.

### *Hypothermia*

Patients may develop hypothermia under either general or neuraxial anesthesia. The hypothermia can be exacerbated by using room temperature irrigating fluids. Using warmed irrigating fluid decreases heat loss and shivering. A theoretical concern exists that warming the irrigation fluids would cause vasodilation, increasing blood loss; however, this has not been shown to be a clinical problem. Because hypothermia may cause shivering, which increases venous pressure, there may be increased blood loss if the irrigating fluids are not warmed.

## 3. What types of irrigating fluids have been used for transurethral resection of the prostate?

The ideal irrigating fluid would be isotonic, electrically inert, nontoxic, and transparent; however, this type of solution does not exist. Originally, distilled water was used, but absorption of distilled water caused hyponatremia and hemolysis of red blood cells. This severe complication led to the use of isoosmotic solutions such as saline or lactated Ringers solution. However, because these solutions are highly ionized, they caused dispersion of high-frequency current from resectoscopes. The present generation of irrigating fluids is electrically inert and isotonic. These solutions include glycine and a mixture of sorbitol and mannitol (Cytal), which are the most commonly used, as well as glucose, mannitol, urea, and sorbitol.

## 4. What toxicities are associated with glycine?

Intravascular absorption of 1.5% glycine solution has been implicated as a cause for many neurologic manifestations associated with TURP, including transient blindness. Glycine, a nonessential amino acid, readily crosses the blood-brain barrier. It has a distribution similar to γ-aminobutyric acid, a naturally occurring inhibitory neurotransmitter. Transient blindness may result from inhibitory effects of glycine on the central nervous system or a direct inhibitory effect on the retina. Glycine retinal toxicity appears to be unrelated to its plasma concentration.

Glycine is metabolized to ammonia, which may lead to hyperammonemia in some patients. The mechanism by which hyperammonemia develops is unclear. One postulated mechanism is that ammonia is converted to urea in the liver via the ornithine cycle, in a reaction requiring arginine. This mechanism of action is supported by the fact that patients with arginine deficiency are more likely to develop hyperammonemia. Common signs and symptoms of ammonia toxicity include nausea and vomiting. As the ammonia level increases to >500 mmol/L, coma may occur. Coma typically resolves when the ammonia level decreases to <150 mmol/L. The cardiovascular effects of glycine are myocardial depression and nonspecific ECG changes, such as T-wave depression.

## 5. What are the anesthetic options for a patient undergoing transurethral resection of the prostate?

Regional anesthesia (Box 36-4) has long been considered the anesthetic of choice for TURP. Regional anesthesia allows for monitoring of mental status changes, irritability, and headache, the early signs of hyponatremia. If signs of hyponatremia occur, serum $Na^+$ levels are checked and treated expeditiously. Intraoperative irritability or combativeness could result from hyponatremia. If caused by hyponatremia or hypoxia, deepening the sedation level could be counterproductive.

**BOX 36-4 Benefits of Regional Anesthesia**

- Early detection of TURP syndrome
- Detection of bladder perforation
- Decreased blood loss
- Decreased incidence of deep vein thrombosis
- Postoperative pain control

As discussed earlier, another potentially fatal complication of TURP is bladder perforation. A T10 level of sensory blockade would allow the patient to complain of abdominal or shoulder pain, which are symptoms of bladder perforation.

As with other pelvic procedures, regional anesthesia has been shown to decrease blood loss and the incidence of deep vein thrombosis. The decrease in blood loss is most likely secondary to the decrease in blood pressure and in both central and peripheral venous pressure associated with neuraxial anesthesia. Many different reasons have been postulated for the decreased incidence of deep vein thrombosis. One reason may be the increase in peripheral blood flow resulting from sympathetic blockade. Other reasons include increased prothrombin time, a measure of the extrinsic pathway of coagulation, and a decrease in platelet count.

Another clear advantage of regional anesthesia is postoperative pain control. Good postoperative pain control also protects against sympathetic responses to pain, such as tachycardia and hypertension, which could increase the likelihood of myocardial ischemia in susceptible patients.

Comorbid conditions may necessitate general anesthesia. General anesthesia hides the early neurologic signs and symptoms associated with hyponatremia, hypoosmolality, or bladder perforation. When a general anesthetic is chosen, a smooth emergence is desirable. If the patient awakens coughing and "bucking" on the endotracheal tube, venous pressure increases, and bleeding may develop.

## 6. If a regional anesthetic is selected, what level of anesthesia is required?

The level of anesthesia required depends on the anatomy and sensory innervation of involved structures (Box 36-5). The structures that need to be blocked are the bladder, prostate, penis, and urethra. The dome of the bladder receives its sensory innervation via T11-L2, whereas the neck of the bladder receives its sensory innervation via S2-S4. The prostate receives its sensory innervation via T11-L2 and S2-S4. Finally, a sensory block of the penis and scrotum requires blocking S2-S4.

Based on this anatomy, a block to the level of T10 is usually sufficient for TURP. If a lower level is attained, bladder stretching from irrigation fluids would be uncomfortable. Because a block at the level of S4 is also required, spinal anesthesia is preferred over epidural anesthesia. Epidural anesthesia sometimes results in incomplete block of the sacral nerve roots.

**BOX 36-5 Sensory Innervation**

- T11-L2
  - Bladder dome
  - Prostate
- S2-S4
  - Bladder neck
  - Prostate
  - Penis
  - Scrotum

## 7. The patient's serum sodium level is 102 mEq/L 1 hour and 15 minutes into the procedure; how would you correct the sodium level to 135 mEq/L?

The $Na^+$ deficit must first be calculated using the following equation:

$$Na^+\text{deficit mEq} = TBW \times (Na^+\text{desired} - Na^+\text{observed})$$

TBW is total body water and constitutes 60% of lean body weight in the average man and 50% of lean body weight in the average woman. In this example, the patient's $Na^+$ deficit is:

$$1425.6 \text{ mEq} = (72 \text{ kg} \times 0.6) \times (135 - 102)$$

Hypertonic saline (3% sodium chloride) contains 513 mEq/L of $Na^+$. The volume of hypertonic saline required to replace a $Na^+$ deficit of 1425.6 mEq is 2.78 L. The maximum safe rate of increase in serum $Na^+$ is 0.5 mEq/L per hour. In this case, the serum $Na^+$ should be corrected over 66 hours. Thus, the hypertonic saline should run at a rate of 1425.6/66 = 21.6 mL per hour. In situations of significant hyponatremia associated with seizures or progressive neurologic deterioration, it may be necessary to correct the $Na^+$ deficit more rapidly (3 mEq/L per hour). This rapid correction should not exceed 2 hours and should be stopped if neurologic symptoms resolve sooner.

## 8. What surgical measures can minimize the incidence of TURP syndrome?

Several measures have been undertaken in an attempt to minimize TURP syndrome. The primary goal is to reduce the volume of irrigating fluid that is absorbed during resection; this may be achieved by one or a combination of methods:

- *Decreasing hydrostatic pressure within the bladder and prostatic venous pressure:* Using reduced pressure irrigation and lowering the fluid bag's height (although there is some controversy concerning whether the height of the bag is significant) decrease hydrostatic pressure. Patient positioning on the operating table also has an effect on irrigation absorption. Intravesical pressure needed to initiate absorption of irrigating fluid is lower in the Trendelenburg position compared with the horizontal position. Trendelenburg position increases the risk of TURP syndrome.
- *Limiting operative time to <90 minutes:* Operating times longer than 90 minutes have been shown to increase the incidence of TURP syndrome and intraoperative bleeding.
- *Restricting TURP to prostate glands <45 g:* Larger glands require longer resection times resulting in increased irrigant absorption and increased blood loss.
- *Injecting intraprostatic vasopressin:* Blood loss and amount of irrigant fluid absorbed are reduced with vasopressin injection.

### 9. What other minimally invasive surgical modalities are available to treat benign prostatic hypertrophy?

TURP has been considered the "gold standard" for the treatment of benign prostatic hypertrophy. Increasing numbers of patients present with concomitant cardiovascular disease or require oral anticoagulation, or both. Newer surgical laser modalities have been developed to address these concerns. Key advantages of these newer techniques are:

- Compatibility with physiologic saline as the irrigant solution
- Compatibility with oral anticoagulants preoperatively (GreenLight™ Laser technique, American Medical Systems, Inc., Minnetonka, MN.)
- Freedom from overnight admission

With the use of saline instead of a hypoosmolar solution, the risks of dilutional hyponatremia and TURP syndrome are eliminated. General anesthesia is preferable to neuraxial anesthesia in anticoagulated patients or patients with other contraindications to spinal anesthesia.

Two different laser techniques have been introduced in recent years: holmium laser enucleation of the prostate (HoLEP) and photoselective vaporization of the prostate (GreenLight™ Laser). HoLEP uses a holmium:yttrium-aluminum-garnet laser along with mechanical morcellation to remove prostatic tissue. This technique has been shown to decrease bleeding compared with traditional TURP, but no studies have investigated anticoagulated patients. The GreenLight™ Laser, in its current rendition, is a 120-watt potassium-titanyl-phosphate laser that uses laser light to penetrate and vaporize prostatic tissue without burning. The coagulated tissue that remains aids hemostasis, making this modality safe for use in patients who are at risk for bleeding.

Another more recent surgical modality that uses saline irrigation is plasma vaporization of the prostate. This technique consists of a bipolar mushroom-shaped (button) electrode or a specialized bipolar loop that is connected to a high-frequency generator that vaporizes and coagulates tissue. The primary surgical concern of this technique is that to be hemostatic, the electrode must be hovered and moved slowly through the tissue. By moving slowly, more heat is created that could damage healthy tissue. Because TURP syndrome is also avoided in this technique, general anesthesia may be considered instead of a spinal technique. Whether this technique can be safely used in anticoagulated patients has not been fully investigated.

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CASE 37

# Super Morbid Obesity

Ram Roth, MD

## QUESTIONS



A 32-year-old man, weighing 396 lb (180 kg) and standing 5 feet 7 inches (170 cm) tall, presented for laparoscopic sleeve gastrectomy. He had a past medical history of hypertension, diabetes mellitus, asthma, and gastroesophageal reflux disease. He used bilevel positive airway pressure (BiPAP) for obstructive sleep apnea (OSA) at night.

### 1. How is body mass index defined?

According to the World Health Organization, obesity is defined as abnormal or excessive fat accumulation that presents a risk to health. Differences in weight among individuals are due only partly to variations in body fat. Total body weight, although easy to obtain, is a limited measure of obesity. In 1832, Quetelet, a Belgian mathematician, defined the relationship between weight and height and created the Quetelet index, which eventually became known as the body mass index (BMI), so named by Keys in 1972.

BMI is an index of weight-for-height that is commonly used to classify obesity. It is defined as weight in kilograms divided by the square of height in meters ($kg/m^2$). Although also applicable to children, age is an additional factor. BMI values of ≥40 are commonly considered an indication for bariatric surgery. Patients with a BMI >35 and significant comorbidities (e.g., diabetes) are also candidates for bariatric surgery. Another indication for bariatric surgery is a desire to become pregnant in a nulliparous, obese woman.

Although several classifications of obesity exist, the most widely accepted is from the World Health Organization and is based on BMI (Table 37-1). More recently, with the increase of bariatric procedures, a slightly different classification has been introduced to the surgical literature (Table 37-2). The BMI of our patient is 62 (180 kg/1.7 $m^2$), and he is classified as super-superobese.

As noted earlier, in children, because of ongoing growth and differences in distribution of fat and muscle that is age dependent and gender dependent, the calculated BMI is measured against other children of the same age and gender (Figure 37-1). The calculated BMI is plotted on growth charts from the U.S. Centers for Disease Control and Prevention that are based on age and gender. A BMI percentile for age is determined. The percentile determines the classification of obesity (Table 37-3).

BMI calculations without taking into consideration body habitus may be misleading in certain patient populations. For example, in a muscular person, BMI may suggest obesity but in fact reflects additional muscle mass. Also, in a person with degenerative loss of skeletal muscle mass, BMI may not account for the relative increased percentage in fat. Calculation of body fat percentage may help differentiate between obesity from excess body fat and increased muscle mass. Body fat percentage is calculated as follows:

$$1.2\ (\text{BMI}) + 0.23\ (\text{age}) - 10.8\ (\text{sex}) - 5.4$$

Sex is assigned a value of 1 for males and 0 for females. Men who have a body fat percentage >25% are classified as obese (Table 37-4). Our patient's body fat percentage is 75.16%.

### 2. What cardiopulmonary changes occur with superobesity?

Superobesity affects multiple organ systems. Effects on the respiratory system involve the upper and lower airways and lung mechanics. Patients are prone to upper airway obstruction, particularly during sleep. OSA, defined by the number of apnea and hypopnea events per

**TABLE 37-1 World Health Organization Classification of Obesity by Body Mass Index (BMI)**

| BMI (kg/m²) | Classification |
|---|---|
| <18.5 | Underweight |
| 18.5–24.9 | Normal |
| 25–29.9 | Overweight |
| 30–34.9 | Class I obesity |
| 35–39.9 | Class II obesity |
| ≥40 | Class III obesity |

**TABLE 37-2 Classification of Obesity Based on BMI in the Surgical Literature**

| BMI (kg/m²) | Classification |
|---|---|
| 40–<50 | Morbid obesity |
| 50–<60 | Superobesity |
| ≥60 | Super-superobesity |

hour of sleep, occurs in approximately 3%–7% of all men and 2%–5% of all women (see Question 4 for details). However, the prevalence of OSA is >50% higher in obese individuals. Both chest wall and lung compliance are decreased secondary to fat accumulation over the thorax and abdomen. The decrease in lung compliance is also due to increased pulmonary blood flow secondary to increased cardiac output and polycythemia seen in chronically hypoxemic patients.

A decrease in lung compliance leads to a decrease in functional residual capacity (FRC), at the expense of expiratory reserve volume, vital capacity, and total lung capacity.

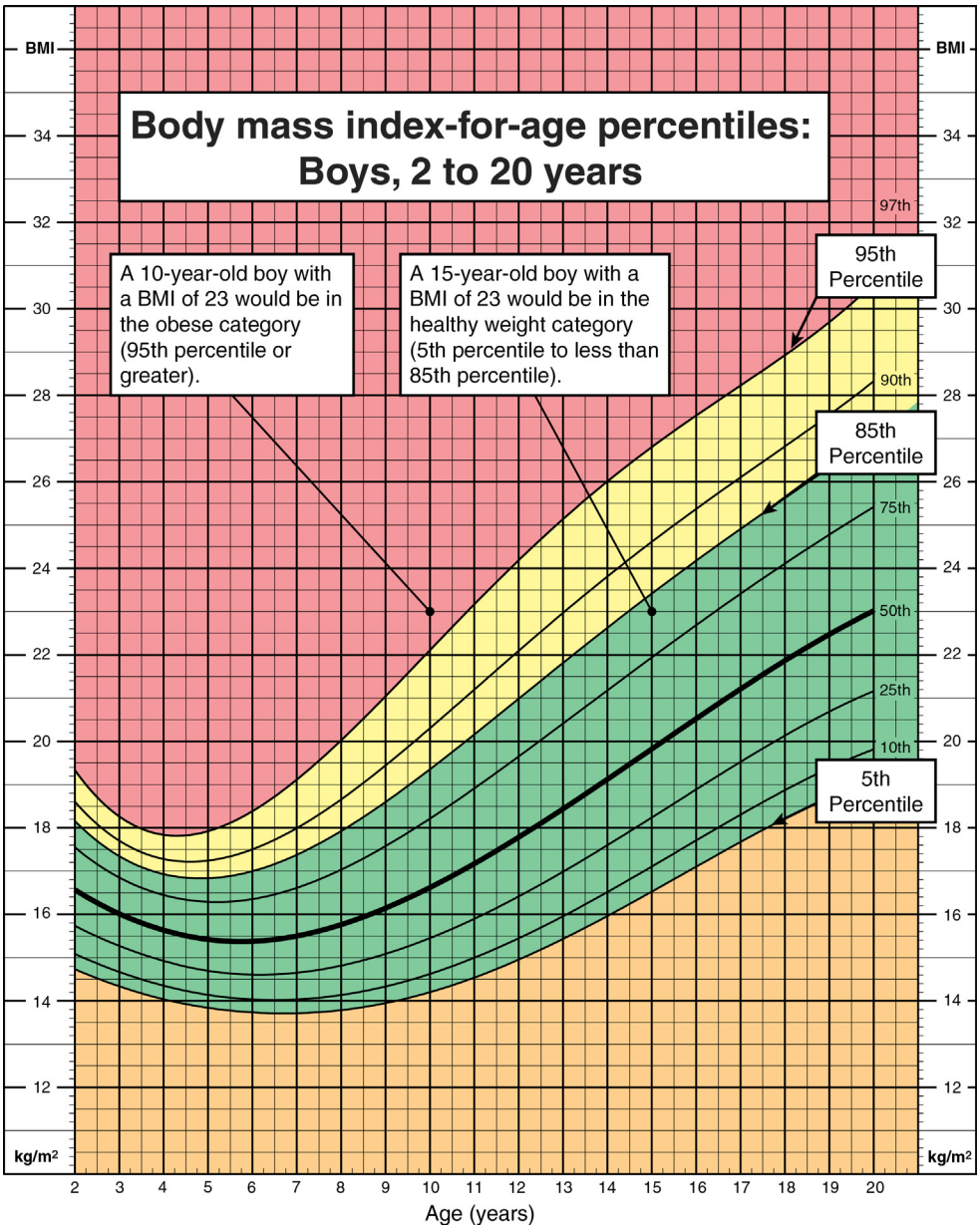


**FIGURE 37-1** ■ An example of BMI-for-age for a 10-year-old boy and a 15-year-old boy who both have a BMI of 23. (From the Division of Nutrition, Physical Activity, and Obesity, Centers for Disease Control and Prevention, Atlanta, GA.)

**TABLE 37-3 Classification of Obesity in the Pediatric Population by Body Mass Index Percentile**

| Percentile | Classification |
|---|---|
| <5 | Underweight |
| ≥5 | Normal weight |
| ≥85 | Overweight |
| ≥95 | Obese |
| >99 | Morbid obesity |

**TABLE 37-4 Comparison of Status with Body Fat Percentage**

| Description/Status | Women (Fat %) | Men (Fat %) |
|---|---|---|
| Normal fat | 10–13 | 2–5 |
| Athletic | 14–24 | 6–17 |
| Average | 25–31 | 18–24 |
| Obese | ≥32 | ≥25 |

Closing capacity is unchanged, but reduced FRC could result in normal tidal volumes occurring at lung volumes below closing capacity. Small airway closure, absorption atelectasis, ventilation/perfusion mismatch, and hypoxemia result. These changes are exacerbated during general anesthesia and in the supine position.

Total blood volume is increased, but the total blood volume per total body weight measurement is decreased (i.e., 50 mL/kg). As weight increases, so does cardiac output, with shunting to adipose tissue. The increase in cardiac output is the result of left ventricular hypertrophy and increased stroke volume. Ultimately, left ventricular hypertrophy, decreased left ventricular compliance, and impaired filling (i.e., diastolic dysfunction) occur. The endpoint is systolic dysfunction and left ventricular failure.

Right-sided heart changes are secondary to chronic hypoxemia, particularly in patients with OSA. Chronic hypoxemia and increased pulmonary blood volume lead to pulmonary hypertension, right ventricular hypertrophy, and ultimately right ventricular failure.

Development of atherosclerosis is accelerated. However, it is difficult to detect the presence of coronary artery disease by history alone because obese patients tend to have sedentary lifestyles. A high index of suspicion and diagnostic testing are indicated. Hypertension and arrhythmias are frequent complications.

## 3. What comorbidities are associated with superobesity?

Many comorbidities involving multiple organ systems occur in patients who are superobese (Table 37-5). The death risk is increased. The relative risk for coronary heart disease is 1.72 in patients with a BMI of 25–28.9 kg/m$^2$ and progressively increases with increasing BMI. Similar trends have been shown in the relationship between obesity and stroke or congestive heart failure. Overall, the estimated increase in cardiovascular mortality rate is fourfold and the estimated increase in cancer-related mortality rate is 2-fold in obese patients. The incidence of polycystic ovarian disease is also increased. As a group, people who are superobese have a 6-fold to 12-fold increase in all-cause mortality rates.

**TABLE 37-5 Comorbidities Associated with Superobesity**

| | |
|---|---|
| Cardiovascular | Coronary artery disease<br>Hypertension<br>Pulmonary hypertension<br>Congestive heart failure |
| Respiratory | Restrictive lung disease<br>Aspiration? Pneumonia? Asthma?<br>Obstructive sleep apnea<br>Obesity hypoventilation syndrome |
| Central nervous system | Cerebrovascular accidents<br>Idiopathic intracranial hypertension |
| Gastrointestinal | Hiatal hernia<br>Gastroesophageal reflux disease<br>Cholelithiasis<br>Fatty infiltration of the liver |
| Endocrine | Type 2 diabetes mellitus<br>Polycystic ovarian syndrome |
| Hematologic | Deep vein thrombosis<br>Pulmonary embolus |
| Musculoskeletal | Osteoarthritis |
| Immunology | ↑ incidence of malignancies<br>Breast<br>Ovarian<br>Endometrial<br>Esophageal<br>Colorectal<br>Gallbladder<br>Stomach<br>Pancreas<br>Liver<br>Prostate |

## 4. What is the pathophysiology of obstructive sleep apnea?

Although many patients with OSA are morbidly obese, nonobese patients have OSA as well. OSA tends to occur in middle-aged and older adults (most prevalent at age 55). Sedatives, hypnotics, alcohol, or muscle relaxants can exacerbate OSA. Young patients with craniofacial abnormalities can also have OSA.

Under normal circumstances, a breath is initiated by contraction of the diaphragm and intercostal muscles, increasing chest wall size. Negative pleural pressure is created and transmitted from lower airways to the pharynx. The pharynx consists of mucosa and soft tissues that lack bony attachments. When negative pressure is created in the pharynx, these tissues are drawn into the lumen, as if the pharynx were imploding. This inward movement is opposed by constriction of the upper airway dilator muscles, which maintain upper airway patency. Upper airway dilator muscles include the tensor palatine, which brings the soft palate off the nasopharyngeal wall, and the genioglossus, which advances the tongue off the oropharyngeal wall. However, during sleep, if the inward movement of pharyngeal tissue is unopposed, upper airway obstruction results. Adequate compensation by airway dilator muscles is lost in obese patients, and upper airway obstruction results causing hypercarbia

and hypoxia. The treatment for OSA consists of positive airway pressure, either continuous positive airway pressure (CPAP) or BiPAP, during sleep.

Hypoxic episodes during sleep lead to sympathetic discharge and arousal. When this cycle recurs several times per night, restful sleep is interrupted, and patients experience daytime somnolence, irritability, impaired cognition, and reduced concentration. Recurring episodes of hypoxia eventually cause pulmonary hypertension, right ventricular hypertrophy, and right-sided failure (cor pulmonale). Reactive polycythemia commonly develops.

## 5. How is obstructive sleep apnea diagnosed?

The first clinical indicator of OSA, loud snoring, is frequently reported by a sleeping partner. Definitive diagnosis is obtained by sleep studies, which look for the incidence of apnea and hypopnea. Apnea is defined as the total cessation of gas flow through the airway for at least 10 seconds followed by arousal or 4% decrease in oxygen saturation, despite attempts to breathe, or both. In patients with OSA, episodes of apnea occur at least five times per hour of sleep. Hypopnea is defined as a >50% reduction of gas flow through the airway for at least 10 seconds or decrease by 30% associated with arousal or a 4% decrease in oxygen saturation or both. In patients with OSA, hypopnea occurs at least 15 times per hour of sleep. The severity of OSA is based on the number of apnea-hypopnea events occurring during 1 hour (apnea-hypopnea index [AHI]). OSA is classified as follows:

- AHI 5–14: mild
- AHI 15–30: moderate
- AHI >30: severe

## 6. How is STOP-bang useful in screening patients?

The STOP-Bang questionnaire is an 8-item tool (Table 37-6) used to identify patients with sleep-disordered breathing (SDB). Each positive answer is assigned 1 point for a total of 8 points. Low risk for SDB is a score of ≤2, and high risk for SDB is a score of ≥3. STOP-Bang is 87% sensitive for detecting moderate SDB and 70.4% sensitive for detecting severe SDB.

## 7. What is obesity hypoventilation syndrome?

Obesity hypoventilation syndrome (OHS), commonly referred to as Pickwickian syndrome, is characterized by obesity (BMI >30 kg/m$^2$), daytime hypoventilation (arterial carbon dioxide tension [$PaCO_2$] >45 mm Hg, arterial oxygen tension [$PaO_2$] <70 mm Hg), and SDB in the *absence* of other causes of hypoventilation (e.g., neuromuscular disease, metabolic abnormalities). The presence of daytime hypercarbia differentiates OHS from OSA.

Causes of daytime hypercarbia may include one or more of the following mechanisms:

- *Abnormal respiratory mechanics secondary to obesity*—more energy is needed to breathe effectively because obese patients experience restrictive airflow. Restrictive air flow is due to excessive neck and airway tissue, decreased chest wall compliance secondary to substantial adipose tissue, impaired diaphragmatic movement, and early respiratory muscle fatigue.
- *Leptin resistance leading to central hypoventilation*—leptin is a hormone secreted by adipose tissue that binds to leptin receptors in the brain increasing ventilation. In patients with OHS, leptin levels are greater than in patients with similar BMI but without OHS. Over time, leptin resistance develops, and levels increase without enhancing ventilation.
- *Inadequate compensation of acute hypercapnia*—hypercapnia during airway obstruction while asleep is usually compensated by hyperventilation on arousal and by renal excretion of bicarbonate. In patients with OHS, these compensatory mechanisms are diminished, resulting in sustained elevation of $PaCO_2$.

Treatment strategies for patients with OHS include positive airway pressure during sleep (e.g., CPAP or BiPAP), supplemental oxygen, weight loss surgery, and respiratory stimulants. Supplemental oxygen must be used judiciously. Although supplemental oxygen can improve oxygenation, it could decrease minute ventilation and exacerbate hypercapnia in the most severe cases. This effect is of particular concern in postoperative patients who receive sedation or opioids or both. Weight loss surgery is described in Question 8.

Medroxyprogesterone is a respiratory stimulant. Studies have not shown a consistent benefit when this agent was administered to patients with OHS. An association with an increased risk of venous thromboembolism (VTE) limits its use in patients with OHS. Acetazolamide promotes renal excretions of bicarbonate inducing a metabolic acidosis that increases ventilation.

**TABLE 37-6 STOP-Bang Questionnaire**

| | | |
|---|---|---|
| S | Snore | Louder than talking or heard through closed doors |
| T | Tired | Feeling tired no matter how many hours of sleep received |
| O | Observed | Others have seen you stop breathing |
| P | Pressure | Treated for high blood pressure |
| B | BMI | >35 kg/m$^2$ |
| A | Age | >50 years old |
| N | Neck circumference | >40 cm |
| G | Gender | Male |

## 8. What are the most common weight loss surgical procedures?

There are four main types of bariatric surgery performed in the United States: biliopancreatic diversion/duodenal switch (BPD/DS), Roux-en Y gastric bypass, laparoscopic gastric sleeve (LGS), and laparoscopic adjustable gastric banding (Figure 37-2). The choice of technique depends on the size of the patient, surgical skill and experience, and patient choice after surgical consultation. Advantages of laparoscopic versus open procedures are decreased postoperative pain, parietal trauma, complication rates, and length of stay.

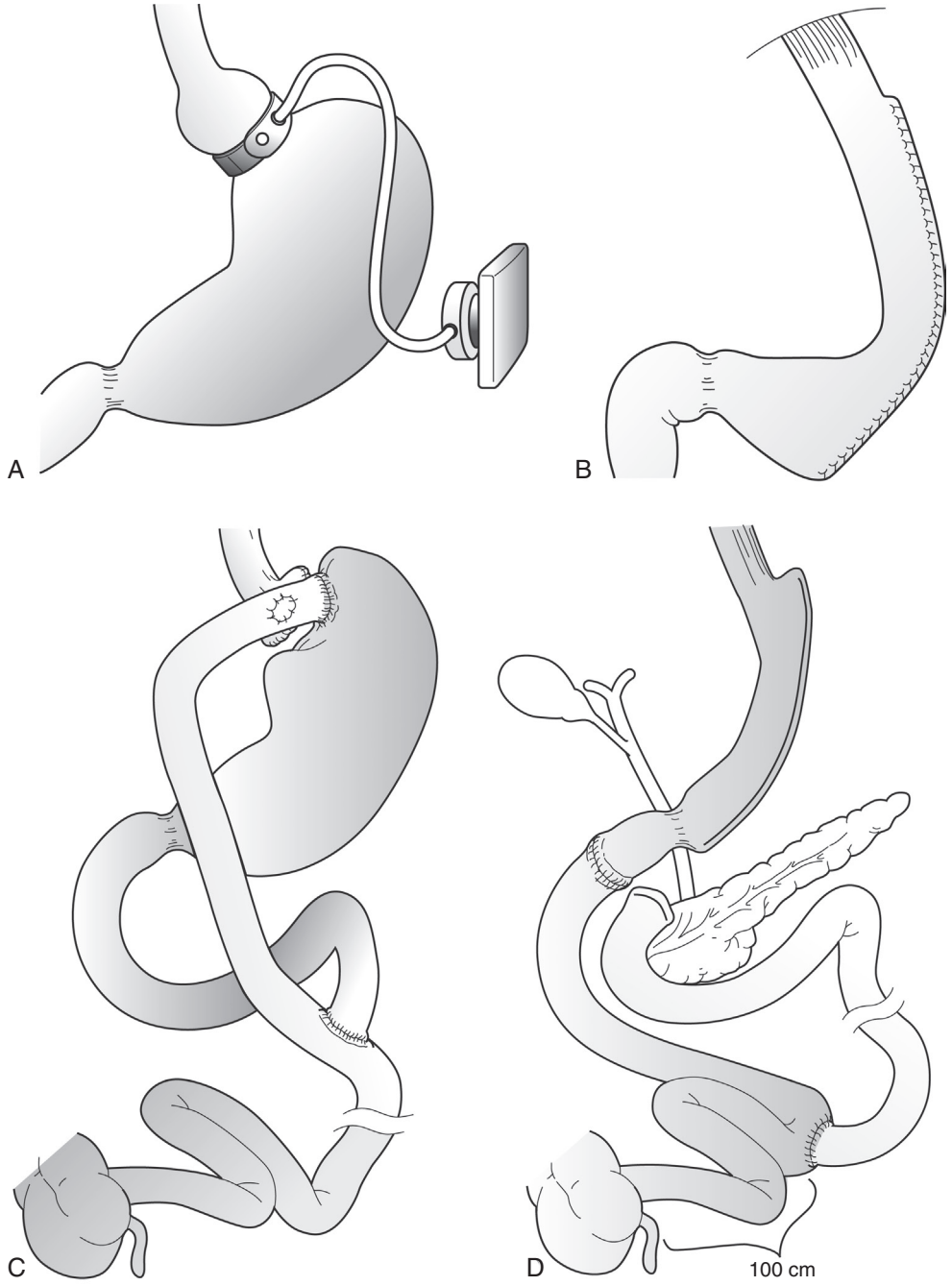


**FIGURE 37-2** ■ Operative procedures for weight loss that are performed laparoscopically. **A,** Adjustable gastric band. **B,** Vertical sleeve gastrectomy. **C,** Roux-en-Y gastric bypass. **D,** Duodenal switch operation. (From Miyano G, Garcia VF, Inge TH: Bariatric surgical procedures in adolescence. In: Holcomb GW III, Murphy JP [eds.]: Ashcraft's Pediatric Surgery, 5th edition. Saunders, Philadelphia, 2010.)

### *Biliopancreatic Diversion/Duodenal Switch*

BPD/DS surgery has both restrictive and malabsorptive components. The restrictive component involves removing approximately 70% of the stomach. The malabsorptive component requires rerouting the small intestine, creating two divergent intestinal loops that empty into a common channel. The shorter of the two pathways, the digestive loop, takes food from the stomach to the common channel. The longer pathway, biliopancreatic loop, carries bile from the liver to the common channel. In the common channel, contents of the digestive loop mix with bile from the biliopancreatic loop before emptying into the large intestine. This arrangement reduces the amount of time the small intestine has to absorb calories from ingested food and selectively limits absorption of fat. BPD/DS is less commonly performed because of nutritional complications and technical complexity.

### *Roux-en Y Gastric Bypass*

Roux-en Y gastric bypass involves dividing the stomach into two parts: a small pouch through which food passes

and a second pouch, which is not used in digestion. The smaller stomach pouch allows patients to feel "full" or "satiated" early in a meal. The small intestine is divided such that one end is connected to the nonfunctional stomach pouch, and the other end is connected to the small stomach pouch. The end connected to the new, smaller stomach is called the "Roux" limb because it is the route food takes.

### *Laparoscopic Gastric Sleeve*

In LGS surgery, the stomach is permanently reduced to approximately 25% of its original size. The reduced size stomach takes the form of a sleeve. Because LGS offers the opportunity for a second operation to be done later, it is commonly carried out as a first step before proceeding to BPD/DS.

### *Laparoscopic Adjustable Gastric Banding*

In laparoscopic adjustable gastric banding surgery, a nonpermanent reduction in stomach size is accomplished by placing an inflatable silicone device around the top portion of the stomach.

## 9. Is superobesity always an indication for awake intubation?

Not all superobese patients require awake intubation. Absolute body weight and BMI are not independent indicators for awake intubation. The determination of whether to intubate awake versus after induction of general anesthesia is based on the preoperative airway examination. However, this assessment may be impeded by a neck that is so large that thyromental, hyomental, and sternomental distances cannot be assessed. Awake intubation should be seriously considered when traditional predictors of difficult intubation exist (see Chapter 43). If there is any doubt as to the ease of intubation, an awake fiberoptic intubation remains the "gold standard" technique. Awake videolaryngoscopy-assisted intubation also may be considered.

Because many obese patients often prove to be difficult to ventilate by mask, alternative airway devices should be readily available if intubation is to take place after induction of general anesthesia. Supraglottic devices can provide oxygenation and ventilation if intubation fails and mask ventilation is ineffective. The ProSeal (Laryngeal Mask Co., Ltd, Le Rocher, Victoria, Mahe Seychelles) laryngeal mask airway offers the added benefits of diversion of regurgitated gastric contents away from the larynx and the ability to pass a gastric tube into the stomach. Supraglottic airways remain relatively contraindicated for elective use in superobese patients but are acceptable choices in an emergency.

## 10. What is the optimum patient position for intubation?

In superobese patients, visualization of the glottic opening is facilitated by placing the patient in the "ramped" position (Figure 37-3). The ramped position is achieved by placing blankets or a preformed wedge under the patient's head, shoulders, and upper body so that the sternal notch is aligned with the external auditory meatus. Ventilation is also facilitated in this position by unloading the excessive abdominal weight off the diaphragm.

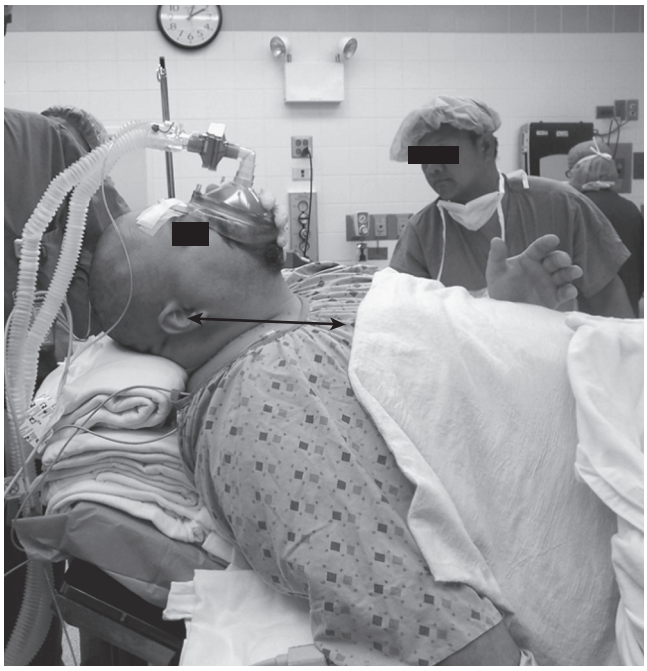

**FIGURE 37-3** ■ The "ramped" position, in which the upper body, neck, and head are elevated to a point where an imaginary horizontal line can be drawn from the sternal notch to the external ear *(arrow)*, not only improves the comfort of the patient but also improves the laryngeal view during intubation. When the endotracheal tube is safely secured, some of the blankets can be removed before surgery begins. (From Klowden AJ, Usharani N, Salter B: Perioperative and anesthesia management. In Friedman M [ed.]: Sleep Apnea and Snoring: Surgical and Non-surgical Therapy. Saunders, Philadelphia, 2009.)

## 11. What are anesthetic considerations?

### *Airway Management*

Preoperative assessment of the airway determines whether intubation of the trachea is performed on an awake patient or after induction of general anesthesia. This decision is made recognizing that superobese patients are at increased risk for oxygen desaturation and unanticipated difficult mask ventilation or intubation. These considerations are particularly important if rapid-sequence induction is deemed necessary. Contrary to classic teaching, obesity is not an independent risk factor for aspiration. Aspiration prophylaxis is indicated for patients at increased risk for other reasons. Before induction, alternative airway equipment (e.g., multiple sized laryngoscope blades, a videolaryngoscope, a fiberoptic scope) should be immediately available. At our institution, we recommend the presence of two anesthesia attending physicians to optimize successful airway management whenever a second person is available. Agents used for induction of general anesthesia and muscle relaxation should have a rapid recovery profile so that if difficulty is encountered, the patient can be awakened and resume spontaneous respirations quickly. Unless

contraindicated, succinylcholine is the classic choice for muscle relaxation. In the event that the "cannot intubate, cannot ventilate" situation is encountered, surgical access of the airway may be necessary.

### Positioning

Positioning the patient may require removal of "ramping" that was placed for intubation. The reverse Trendelenburg position improves ventilation by increasing FRC and pulmonary compliance. The legs are split into the "V" position, and footpads are used to prevent the patient from sliding off the bed. It is important to remember to release the footpads before adducting the legs. Shifting during surgery may have resulted in patient movement down toward the footpads. Approximating the legs without release of the footpads may cause untoward pressure on the knees and hips resulting in injury. All pressure points should be padded, and arms should be protected from nerve injury.

### Anesthetic Agents

An ideal anesthetic regimen has not been identified. However, pharmacologic principles are important for calculating the appropriate doses of medications administered. The volume of distribution of lipophilic and polar drugs is altered because of increased absolute body water content and lean body and adipose tissue mass. Whether dosing is based on total body weight or ideal body weight depends on the drug's lipophilic profile (Box 37-1).

Maintenance of anesthesia can be accomplished with inhalation agents (e.g., isoflurane, sevoflurane, desflurane), total intravenous anesthesia (e.g., propofol), or a combination of both. No one regimen is associated with a faster emergence. Monitoring of neuromuscular blockade is important to guide dosing of neuromuscular blocking drugs.

### Ventilatory Parameters

Tidal volumes should be calculated based on ideal body weight, and respiratory rates should be increased. Low levels of positive end expiratory pressure should be added (i.e., 5–10 cm $H_2O$). Alveolar recruitment (i.e., inspiratory pause at 40 cm $H_2O$ for 30 seconds) should be performed immediately after intubation and at least every half hour thereafter to improve oxygenation.

**BOX 37-1 Intravenous Drug Dosing**

**Total Body Weight**

Midazolam
Thiopental
Propofol (maintenance infusion)
Fentanyl
Succinylcholine
Cisatracurium

**Ideal Body Weight**

Propofol (induction)
Remifentanil
Vecuronium
Rocuronium

### Pneumoperitoneum

Pneumoperitoneum significantly decreases static respiratory system compliance and increases respiratory resistance. These changes may not be associated with an alveolar-arterial oxygen tension difference, which is larger in superobese patients. During the pneumoperitoneum phase, superobese patients have less efficient ventilation (i.e., a 100-mL increase of ventilation reduces $PaCO_2$ on average by 5.3 mm Hg in normal-weight patients and by 3.6 mm Hg in obese patients). $PaO_2$ is affected only by increased body weight.

### Infection and Venous Thromboembolism

Obese patients, especially patients with diabetes, are prone to infection and deep vein thrombosis. It is essential that both appropriate antibiotic and venous thromboembolism (VTE) prophylaxis are administered in a timely fashion.

### Hemodynamic Monitoring

Morbid obesity by itself is not an indication for invasive hemodynamic monitoring. As with other patients, coexisting diseases dictate the need for such devices. Inability to obtain reliable blood pressures by cuff is an acceptable reason to place an arterial catheter.

## 12. How can extubation be performed safely?

Superobese patients are especially vulnerable to complications in the early postoperative period, particularly adverse respiratory events. Although it is preferable to extubate the trachea at the end of the procedure, it should occur only when all extubation criteria are met. The most common reason for failed extubation and the need for reintubation is inadequate antagonism of neuromuscular blockade.

Extubation should be performed with the patient in the sitting position to maximize respiratory mechanics. Extubation criteria include the following:

- Awake, alert, and following commands
- Tidal volume of 5 mL/kg (ideal body weight)
- Negative inspiratory force >40 cm $H_2O$
- Head lift for 5 seconds

The anesthesiologist should be prepared for mask ventilation or reintubation with emergency airway equipment available, as was for induction. At our institution, two attending physicians (if available) are present at extubation for patients with a BMI of ≥60.

## 13. What are postoperative considerations?

Ideally, extubated patients should be observed for several minutes in the operating room. Once the patient is declared stable, teamwork is needed to transfer superobese patients safely from the operating table to a large bed. A mechanical lift or Hovermat (HoverTech International, Bethlehem, PA) may be necessary to move superobese patients safely.

In the postanesthesia care unit (PACU), patients should be nursed in the sitting position. Incentive spirometry is encouraged to prevent atelectasis. Some clinicians advocate CPAP or BiPAP to prevent airway obstruction and atelectasis in the postoperative period.

Pain management is important to reduce the incidence of postoperative respiratory complications. Inadequate deep breathing secondary to pain results in atelectasis. Additionally, adequate pain control facilitates the use of incentive spirometry and early ambulation; this contributes to improved respiratory mechanics and prevention of VTE. To reduce the incidence of opioid-induced sedation and respiratory depression, preoperative and postoperative multimodal approaches to pain management are beneficial. These may include intravenous acetaminophen, nonsteroidal antiinflammatory drugs, ketamine, local anesthetic infiltration of surgical wounds, and intravenous patient-controlled analgesia. If patient-controlled analgesia is provided, basal rates should be avoided to decrease the risk of opioid-induced respiratory depression.

Patient disposition after PACU discharge depends on the level of monitoring required. The use of BiPAP and oxygen saturation ($SpO_2$) monitoring are recommended whether or not patients have an official diagnosis of OSA. Patients receiving patient-controlled analgesia should be observed in a monitored setting. The Anesthesia Patient Safety Foundation encourages the use of end-tidal carbon dioxide along with $SpO_2$ on a continuous basis.

In patients with OHS, supplemental oxygen should be used judiciously because it may decrease minute ventilation (see Question 8).

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CASE 38

# Robotic Prostatectomy

**Daniel M. Gainsburg, MD, MS**

## QUESTIONS

1. What are the advantages of robotic-assisted laparoscopic radical prostatectomy over traditional open radical prostatectomy?
2. Briefly describe the surgical procedure.
3. What are the primary anesthetic concerns for robotic-assisted laparoscopic radical prostatectomy?
4. Describe the cerebrovascular, respiratory, and hemodynamic effects of pneumoperitoneum in steep Trendelenburg position.
5. What are possible complications of pneumoperitoneum and steep Trendelenburg position during robotic-assisted laparoscopic radical prostatectomy?
6. What are the preanesthetic concerns in patients presenting for robotic-assisted laparoscopic radical prostatectomy?
7. Discuss the anesthetic technique for robotic-assisted laparoscopic radical prostatectomy.
8. What are the concerns for positioning, ventilation, and fluid management of patients for robotic-assisted laparoscopic radical prostatectomy?

A 62-year-old, 77-kg man with prostate cancer presented for robotic-assisted laparoscopic radical prostatectomy (RALP). Past medical history included hypertension and hyperlipidemia. The procedure went smoothly with the patient receiving 2500 mL of intravenous fluid and experiencing a surgical blood loss of 50 mL. The patient's trachea was extubated, and he was transferred to the postanesthesia care unit (PACU). Shortly thereafter, he was noted to have difficulty breathing and decreasing oxygen saturation. It was decided to perform emergent reintubation, and on direct laryngoscopy, the patient was noted to have severe laryngeal edema.

### 1. What are the advantages of robotic-assisted laparoscopic radical prostatectomy over traditional open radical prostatectomy?

RALP is gradually supplanting open and laparoscopic techniques for the surgical treatment of prostate cancer. RALP offers the advantages of better visualization and increased precision manipulation of delicate nerves and vessels. RALP also provides enhanced ability to preserve the integrity of neurovascular bundles and reduced median recovery times for urinary continence and sexual function compared with open procedures. Other advantages are decreased intraoperative bleeding, reduced transfusion rates, less postoperative pain, shorter PACU stays, and shortened hospital stays.

### 2. Briefly describe the surgical procedure.

In RALP, after induction of general anesthesia, the patient is placed in lithotomy position, arms are carefully tucked at the side, and head-to-toe drapes are placed. Extensive draping limits the anesthesiologist's view of the patient and inhibits further examination of the patient. All catheters, monitors, and patient protective devices have to be placed and secured before draping. At this point, carbon dioxide ($CO_2$) pneumoperitoneum is initiated, and the patient is placed in 30-degree to 45-degree Trendelenburg position. During positioning, care is taken to prevent kinking or dislodging of the endotracheal tube. The surgeon places additional ports in the abdomen, and the robotic arms are "docked" (attached) to the ports. With the robot positioned over the patient and its arms attached to the ports, the patient cannot be moved. If cardiopulmonary resuscitation is required, the robot must first be detached and moved away.

The surgeon sits at the robot console. An assistant at the patient's side guides the robotic arms. Bladder neck, vas deferens, seminal vesicles, and prostate are dissected. As the prostate is dissected free, nerve-sparing is attempted when possible. When the prostate is freed up, it is placed elsewhere in the abdominal cavity, and the surgeon completes the vesicourethral anastomosis. Dissection of the pelvic lymph nodes is performed followed by placement of a perivesical drain. With the robotic phase of surgery completed, the robot is undocked and moved away from the patient.

The prostate is placed in a plastic specimen bag and removed from the patient through one of the port incisions. The patient is taken out of Trendelenburg position, the remaining ports are removed, incisions are closed, the patient's legs are taken out of lithotomy position, and the patient is awakened. Depending on surgical experience and difficulty of the case, mean operative times range from 160–296 minutes with mean blood losses of 50–287 mL.

### 3. What are the primary anesthetic concerns for robotic-assisted laparoscopic radical prostatectomy?

The primary anesthetic concerns for RALP are as follows:

- Physiologic effects of pneumoperitoneum in the Trendelenburg position
- Restricted access to the patient because of the massive equipment placed over the patient
- Prevention or treatment of complications secondary to inducing pneumoperitoneum and positioning the patient in exaggerated lithotomy and steep Trendelenburg

### 4. Describe the cerebrovascular, respiratory, and hemodynamic effects of pneumoperitoneum in steep Trendelenburg position.

Significant cerebrovascular physiologic changes may occur with the use of pneumoperitoneum and the steep Trendelenburg position (Box 38-1). Initiation of pneumoperitoneum increases intraabdominal pressure, which results in increased intracranial pressure (ICP). Placing patients in the Trendelenburg position also eventually increases ICP by elevating cerebral venous pressure, which hinders cerebral venous drainage and leads to increases in cerebral blood volume and potentially cerebrospinal fluid volume. Cerebral perfusion does not appear to be compromised during RALP. Disastrous consequences nevertheless may occur secondary to excessive increases in ICP, especially in patients with cerebral ischemia and cerebrovascular disorders.

Regional cerebral oxygen saturation ($rSO_2$) employing near-infrared spectroscopy cerebral oximetry has been used to evaluate cerebrovascular effects during RALP. Increases in $rSO_2$ have been observed with the use of pneumoperitoneum and the steep Trendelenburg position suggesting that RALP does not induce cerebral ischemia. The use of near-infrared spectroscopy to monitor $rSO_2$, a reflection of the balance between cerebral oxygen supply and demand, is limited because it measures only $rSO_2$ of the frontal cortex, not global cerebral oxygenation. $rSO_2$ was also found to increase with increases in arterial carbon dioxide ($PaCO_2$), but because hypercapnia also causes an increase in cerebral blood volume and eventually an increase in ICP, it is recommended that patients be maintained within normocapnic ranges.

Changes in respiratory homeostasis caused by pneumoperitoneum and steep Trendelenburg position are also significant. Pneumoperitoneum elevates intraabdominal pressure causing decreases in pulmonary compliance and tidal volumes along with increases in peak and plateau airway pressures. The addition of steep Trendelenburg position pushes abdominal contents against the diaphragm. The resulting pressure reduces functional reserve capacity, decreases pulmonary compliance, and predisposes to atelectasis. Further reductions in functional reserve capacity and pulmonary compliance are caused by increases in pulmonary blood volume and gravitational forces on mediastinal structures. To compensate for these effects, elevated peak airway pressures are required to maintain a constant minute volume. With ascending peak inspiratory pressures, the risk of barotrauma increases. This potential risk may be reduced by decreasing tidal volume, increasing the respiratory rate, and tolerating a minimal level of hypercarbia. Another potential concern of the steep Trendelenburg position is pulmonary interstitial edema, when much of the lung is below the left atrium.

Several observational studies have evaluated the hemodynamic effects of pneumoperitoneum in combination with the steep Trendelenburg position during RALP. In one large retrospective review comprising 1500 cases, mean arterial pressure, heart rate, and cardiac output all were noted to be decreased. Prospective studies with relatively small numbers of patients observed increases in mean arterial pressure, central venous pressure, and systemic vascular resistance with only the initiation of pneumoperitoneum. These changes are postulated to result from increased intraabdominal pressure compressing the aorta. Aortic compression results in increased afterload and may be enhanced further by humoral factors. Other studies found that central venous pressure did not change with insufflation but increased only with the addition of the steep Trendelenburg position.

Changes in heart rate and cardiac output have been variably reported as increased, no change, or decreased. Severe bradycardia, probably caused by vagal stimulation during peritoneal distention, has occurred on initiation of pneumoperitoneum in RALP cases. With the combination of pneumoperitoneum and steep Trendelenburg position, strain or workload on the heart, as measured by right-sided and left-sided stroke work index, is increased. The proposed mechanism for this phenomenon is increased filling pressures. In patients with sufficient cardiac reserve, these changes are probably well tolerated. Patients with compromised cardiac function could develop heart failure from increased preload.

**BOX 38-1 Cerebrovascular, Respiratory, and Hemodynamic Effects of Pneumoperitoneum in Steep Trendelenburg Position**

**Cerebrovascular**

↓ cerebral venous drainage →↑ CBV and ↑ CSF
↑ intracranial pressure

**Respiratory**

↑ peak and plateau airway pressures
↓ pulmonary compliance
↓ functional residual capacity

**Hemodynamic**

↑↓ mean arterial pressure
↑↓ or unchanged heart rate and cardiac output
↑ central venous pressure and systemic vascular resistance
↑ stroke work index

*CBV,* Cerebral blood volume; *CSF,* cerebrospinal fluid.

### 5. What are possible complications of pneumoperitoneum and steep Trendelenburg position during robotic-assisted laparoscopic radical prostatectomy?

Nonsurgical complications related to the use of $CO_2$ pneumoperitoneum and the steep Trendelenburg position range from mild subcutaneous emphysema (SCE) to ischemic optic neuropathy (Box 38-2). Other potential complications include corneal abrasions, laryngeal edema, brachial plexus injuries, and venous gas embolism.

$CO_2$ SCE is a common complication of laparoscopic surgery resulting from extraperitoneal insufflation. Identified risk factors include maximum end-tidal $CO_2$ of $\geq$50 mm Hg, six or more operative ports, operative time >200 minutes, and older patient age. $CO_2$ insufflation pressure determines the extent of SCE, and when insufflation is stopped, SCE quickly resolves. Although SCE is thought to be relatively harmless, severe cases may cause substantial hypercarbia. In mild cases, the anesthesiologist might notice a fullness or swelling of the patient's neck or chest after surgical drapes are removed. A common finding is crepitus, the characteristic crackling feel to the touch or sensation of air under the skin. In severe cases, swelling of the neck could potentially interfere with breathing after extubation; severely elevated hypercarbia may cause an excessive increase in the work of breathing. The recommended approach is to keep the patient mechanically ventilated until severe crepitus and hypercarbia resolve.

If high insufflation pressures are used, SCE may develop in prefascial planes leading to life-threatening complications of pneumothorax, pneumomediastinum, and pneumopericardium. Significant respiratory and hemodynamic disturbances may occur if these complications are not rapidly recognized.

Another potentially life-threatening complication of insufflation is venous gas embolism. Clinical presentation depends on the size of the gas bubbles and speed of entry into the circulation. This rare complication should be suspected whenever there is unexplained sudden cardiovascular collapse with changes in the capnography tracing. During RALP, $CO_2$ gas embolism has been associated with two distinct periods—initial insufflation of the peritoneum and dissection of the deep dorsal venous complex. In studies using transesophageal echocardiography, embolic events were detected only during transection of the deep dorsal venous complex and were subclinical in their effects. $CO_2$ is generally used to achieve pneumoperitoneum for RALP and is extremely soluble in the presence of red blood cells. Consequently, gas embolism during RALP tends to be less life-threatening than similar-sized air emboli.

If clinically significant gas emboli occur during RALP, treatment consists of immediate desufflation of the abdomen, undocking and removing the robot to allow patient access, maintaining steep Trendelenburg position, and tilting the patient left side down. Tilting the patient as described reduces the amount of gas that could advance through the right side of the heart and into the pulmonary circulation. Additionally, hyperventilation of the patient with 100% oxygen helps to correct hypoxemia, decrease the size of the gas embolus if nitrous oxide was being used, and increase $CO_2$ excretion. If these maneuvers are unsuccessful, aspiration of gas may be attempted through a central venous catheter, but this is unlikely to be successful. If required, cardiopulmonary resuscitation should be initiated.

Care must be taken in positioning the patient for RALP. As the operating table position changes from supine/lithotomy to steep Trendelenburg position, the patient could slide cephalad and possibly even off the table. Several methods are used to prevent this cephalad slide, but each has its drawbacks. Shoulder braces have been shown to cause brachial plexus injuries by compressing the upper trunk of the brachial plexus against the first rib or depressing the humerus into the axilla resulting in a stretch injury. Strapping the patient to the operating table with chest straps in a crossover ("x") pattern has been observed to decrease pulmonary compliance further in the steep Trendelenburg position with pneumoperitoneum. In the author's institution, horseshoe-shaped shoulder braces are carefully applied around the patient's acromioclavicular joints. This method prevents cephalad movement and brachial plexus injuries. Additionally, attention should be given to the pressure areas of the arms and legs to avoid ulnar neuropathy and lateral femoral cutaneous nerve injury.

Facial, pharyngeal, and laryngeal edema may also occur with the combination of steep Trendelenburg position and pneumoperitoneum. Increased amounts of intravenous fluid, reduced venous outflow from the patient's head secondary to pneumoperitoneum, and use of the steep Trendelenburg position may lead to pharyngeal and laryngeal edema. Restricting fluid and limiting time in the head-down position may help to avoid this complication.

**BOX 38-2 Complications of Pneumoperitoneum and Steep Trendelenburg Position during Robotic-Assisted Laparoscopic Radical Prostatectomy**

- $CO_2$ SCE
  - Crepitus
  - Hypercarbia
  - Pneumothorax
  - Pneumomediastinum
  - Pneumopericardium
- Venous gas embolism
  - Sudden cardiovascular collapse
  - Changes in capnography tracing
- Positioning
  - Sliding cephalad off the operating room table
  - Brachial plexus injuries
  - Peripheral nerve injuries
- Facial, laryngeal, and pharyngeal edema
  - Difficult extubation
  - May be difficult to reintubate
- Ocular injuries
  - Corneal abrasions
  - Ischemic optic neuropathy

*$CO_2$*, Carbon dioxide; *SCE*, subcutaneous emphysema.

If facial or conjunctival edema is observed at the end of surgery, airway edema should be suspected. In this instance, a cuff leak or breathe around test, although not always reliable, can be performed before attempting extubation. In extreme cases of edema, consideration should be given to leaving the patient tracheally intubated and nursed in the upright position. If the patient develops postextubation stridor or difficulty breathing, immediate reintubation is required, although this may be difficult because of airway edema. Extubation over an airway exchange catheter and other means of rapidly obtaining an airway should be considered.

Ocular injuries range from common corneal abrasions to rare cases of ischemic optic neuropathy. Corneal abrasion during RALP has a reported incidence of 3%–13.5% when using either eye or plastic tape. Causes range from chemosis (swelling or edema of the conjunctiva), exposure keratopathy (excessive drying of the lower portion of the cornea owing to incomplete eyelid closure), or direct contact trauma from equipment or the patient's own fingers. Symptoms are usually first reported by the patient while in the PACU, tend to be of short duration, and are easily treated. Recommended preventive measures include informing the patient concerning the risk of chemosis and corneal abrasion, instruction to avoid eye touching in the PACU, restricting intravenous fluid during the case, and the use of either eye patches or transparent occlusive dressings applied immediately after induction of general anesthesia to protect the eyes.

Ischemic optic neuropathy, an extremely rare and devastating complication of RALP, classically occurs in patients undergoing spine surgery in the prone position with significant hypotension and blood loss. One case of ischemic optic neuropathy during RALP has been reported in the literature. The patient experienced hypotension, blood loss, significant fluid administration, and blood transfusion and was in the Trendelenburg position for a prolonged period of time. Intraocular pressure has been observed to increase during RALP, with surgical duration and end-tidal $CO_2$ being significant predictors. The steep Trendelenburg position is postulated to increase venous pressure in the head and neck leading to interstitial fluid accumulation from capillary leak, decreased venous outflow, and decreased perfusion of the optic nerve. Increased end-tidal $CO_2$, which reflects increased $PaCO_2$, may result in choroidal vasodilation and elevated intraocular pressures. Injury to the optic nerve may be caused by several possible mechanisms, such as venous infarction from decreased venous outflow, ischemia caused by the small pial arteries supplying the nerve, and direct mechanical damage from elevated interstitial pressures.

## 6. What are the preanesthetic concerns in patients presenting for robotic-assisted laparoscopic radical prostatectomy?

The mean age of men undergoing RALP is approximately 60 years. A thorough preanesthetic evaluation should be performed along with optimization of cardiovascular, respiratory, metabolic, and other systems. This population of patients not only has an increased incidence of coronary artery disease but also may have renal abnormalities owing to prostatic hypertrophy.

Patients with known or suspected airway issues might be at increased risk postoperatively because of possible presence of airway edema. Preexisting peripheral neurologic deficits should be noted and, if necessary, the conscious patient should be placed in the lithotomy position prior to the induction of general anesthesia to verify freedom from neurologic exacerbation. Patients with glaucoma or other ocular diseases are currently at no known increased risk of ischemic optic neuropathy during RALP.

Patients with significant cardiac disease require further evaluation. Depending on the severity of disease, echocardiogram, stress test, and perfusion studies might be indicated. Special care must be taken in patients with drug-eluting stents because of the risk of stent thrombosis. Before discontinuing antiplatelet therapy, consultation with a cardiologist is necessary. It is generally safe to continue 81 mg of aspirin throughout the perioperative period.

Higher peak airway pressures are often required to ventilate these patients. Although higher peak airway pressures are not a contraindication, care must be taken in patients with severe chronic obstructive pulmonary disease. RALP is relatively contraindicated in patients with lung bullae or blebs because of the potential complication of rupture.

Obese patients (body mass index $>30$ kg/m$^2$) present additional challenges because of higher incidence of coronary artery disease, pulmonary dysfunction, and diabetes. Extra care should be undertaken when positioning these patients for the steep Trendelenburg position to avoid neurologic injury and cephalad sliding.

## 7. Discuss the anesthetic technique for robotic-assisted laparoscopic radical prostatectomy.

The combination of pneumoperitoneum and steep Trendelenburg position for RALP necessitates the choice of general endotracheal anesthesia with controlled ventilation. Because of tracheal shortening during pneumoperitoneum, the endotracheal tube should be carefully positioned to avoid endobronchial intubation. Although there is no specific recommended anesthetic drug regimen, appropriate choices should be based on the patient's cardiovascular status and other comorbidities. For optimal pneumoperitoneum to be achieved, complete muscle relaxation is essential. Epidural analgesia for postoperative pain control is not recommended because postoperative discomfort is substantially less in RALP compared with open procedures. Depending on the experience of the operative team and the patient's medical condition, additional monitoring and intravenous fluid access may be required. If needed, these items should be placed before docking the robot because of limited patient access afterward.

## 8. What are the concerns for positioning, ventilation, and fluid management of patients for robotic-assisted laparoscopic radical prostatectomy?

Positioning is a significant concern in patients undergoing RALP. One must ensure that the patient does not

slide cephalad or off the operating table when moved to the steep Trendelenburg position. Techniques that are commonly used to prevent this problem are chest binding in a crossover ("x") pattern, positioning on egg-crate foam or bean-bag mattress that is secured to the operating table, or placing shoulder braces of various kinds. The actual technique of positioning is usually one of surgical preference; however, careful application to prevent injury is of utmost importance.

As the intraabdominal pressure increases with insufflation, so does the patient's airway pressure. Ventilation may be difficult in patients with chronic obstructive or restrictive pulmonary disease. Several different ventilation modes may be tried for any one patient until best respiratory mechanics and gas exchange are achieved. Peak inspiratory pressures greater than 50–60 cm $H_2O$ might result in barotrauma.

Minimal (<2000 mL) intravenous fluids should be infused to avoid excessive urine output obscuring the operative field during vesicourethral anastomosis. Facial, pharyngeal, and laryngeal edema might also be reduced by fluid restriction. The author's recommendation is to infuse intravenous fluid up to 800 mL until the surgeon completes the vesicourethral anastomosis and then provide an additional 700–1200 mL of fluid to satisfy fluid deficits by the end of surgery.

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CASE 39

# Kidney and Pancreas Transplantation

**Andrew M. Perez, MD • Samuel DeMaria, Jr., MD**

QUESTIONS

1. What are the classifications of chronic kidney disease?
2. How are patients selected for combined kidney-pancreas transplantation?
3. What are the major anesthetic concerns for kidney-pancreas transplantation?
4. How is insulin administration managed intraoperatively for patients with a continuous subcutaneous insulin infusion?
5. Explain the relationship between acidemia and hyperkalemia.
6. Discuss the implications of fluid management in kidney-pancreas transplantation.
7. What is the role of transversus abdominis plane block for abdominal surgery?

A 44-year-old woman with type 1 diabetes mellitus (DM), hypertension, hypothyroidism, and stage 5 chronic kidney disease (CKD) presented for cadaveric kidney-pancreas transplantation.

## 1. What are the classifications of chronic kidney disease?

CKD is classified based on the presence of kidney damage and glomerular filtration rate (Table 39-1). Kidney damage is determined by either pathologic findings or abnormal markers found in blood, urine, or imaging. End-stage renal disease is termed stage 5 CKD.

## 2. How are patients selected for combined kidney-pancreas transplantation?

Pancreas transplantation alone is indicated for patients with severe and difficult-to-control type 1 DM without evidence of renal dysfunction. In rare circumstances, it may be indicated in patients with DM secondary to chronic pancreatitis or cystic fibrosis. Eligibility criteria, which can differ from institution to institution, include age, human immunodeficiency virus (HIV) status, and body mass index.

C peptide is generated during insulin biosynthesis and is released into the portal circulation along with insulin. Measurement of C peptide levels can confirm the absence or decreased production of insulin by the pancreas. C peptide levels <0.3–2 ng/mL are confirmatory evidence of the need for pancreatic transplantation. Additionally, a history of intolerance to insulin therapy and a history of recorded low glucose levels without the expected symptoms of hypoglycemia, such as diaphoresis, headache, and abnormal mentation or confusion, are indications for pancreas transplantation.

Kidney transplantation is indicated in patients with stages 4 and 5 CKD. In the United States at the present time, the most common etiology for CKD and subsequent need for kidney transplantation is diabetic nephropathy. When type 1 DM and CKD are present, as is the case in 50%–60% of patients, simultaneous pancreas-kidney (SPK) transplantation or pancreas transplantation after kidney transplantation may be performed. The best results with respect to graft survival appear to occur with SPK transplantation.

In 2010, >828 SPK transplantations were performed in the United States. Although there have been >40 cases of living related pancreas-kidney transplantations performed, most transplants are obtained from deceased donors. The United Network of Organ Sharing is responsible for cadaveric organ allocation. Organ matching is done based on major blood group (ABO) compatibility followed by human leukocyte antigen (HLA) profiling of the recipient. A crossmatch is performed between the recipient and the donor blood cells to determine if the recipient has antibodies against donor antigens. HLA matching previously was a high priority for organ matching; however, improved outcomes with newer immunosuppressant medications have diminished the importance of tissue typing.

## 3. What are the major anesthetic concerns for kidney-pancreas transplantation?

The anesthetic evaluation and management of patients undergoing SPK transplantation is directed at identifying and optimizing organ dysfunction or metabolic abnormalities that are associated with advanced DM and CKD. For a

**TABLE 39-1 Classification of Chronic Kidney Disease**

| Stage | Glomerular Filtration Rate (mL/minute/1.73 $m^2$) |
|---|---|
| 1 | >90 |
| 2 | 60–89 |
| 3 | 30–59 |
| 4 | 15–29 |
| 5 | <15 or dialysis |

full discussion of the preoperative evaluation and anesthetic management of patients with DM, see Chapter 26.

Preoperative evaluation generally includes history, physical examination, electrocardiogram (ECG), and laboratory studies. These assessments are sufficient to evaluate most patients undergoing surgery, but a more extensive cardiac evaluation is indicated for patients with type 1 DM and coexistent renal dysfunction because of accelerated plaque formation. In patients with coexistent type 1 DM and CKD stage 5, significant coronary artery stenosis was found in at least one coronary artery in 87% of patients. Dobutamine stress echocardiography may be particularly helpful in screening patients before SPK transplantation because many of these patients are unable to achieve the desired heart rate with treadmill stress testing. Coronary angiography is indicated in patients with positive results. At some centers, coronary angiography is routinely performed in all patients undergoing SPK transplantation who are >45 years old or who have had type 1 DM >25 years. This practice may detect patients with significant stenosis that may or may not be amenable to coronary intervention.

Laboratory studies that may be altered include serum sodium, potassium, and glucose levels, hematocrit, and pH. Timing of last hemodialysis, in addition to vital signs, is important preoperative information that can help determine the patient's volume status, degree of uremia, and platelet dysfunction.

Patients with type 1 DM, characterized by insulin deficiency, are at risk for hyperglycemia and ketosis without adequate insulin treatment. Poorly controlled DM can affect multiple organ systems and result in peripheral and autonomic neuropathy. Autonomic neuropathy may cause impaired gastric emptying, increasing the risk of aspiration during induction of anesthesia. Sodium citrate/citric acid, $H_2$ blockers, and metoclopramide before rapid-sequence induction and intubation may be indicated to reduce the risk of pulmonary aspiration. Neuropathy could render these patients unable to sense angina during periods of myocardial ischemia. Neuropathy can also result in either an extreme lability in heart rate and blood pressure or in a fixed bradycardia that does not change in the face of increased demand. These alterations can increase the risk of perioperative dysrhythmias and cardiovascular events.

Many patients have hypertension and may be taking different classes of antihypertensive medications to lower their blood pressure. Additionally, they may have anemia owing to decreased erythropoietin production and impaired platelet function from uremia. Figure 39-1 shows the multisystemic effects of diabetes and uremia and their relationship with each other.

SPK transplantation takes several hours to perform and requires profound muscle relaxation to allow for adequate exposure through a large midline incision. As a result, general anesthesia is nearly always employed. No one technique is superior to others. However, it is important to understand the implications of coexisting diseases, particularly renal failure, on the pharmacology and effects of various medications and adjuvants (Box 39-1). Intrathecal morphine, epidural catheter placement, or transversus abdominis plane (TAP) blocks may be performed to

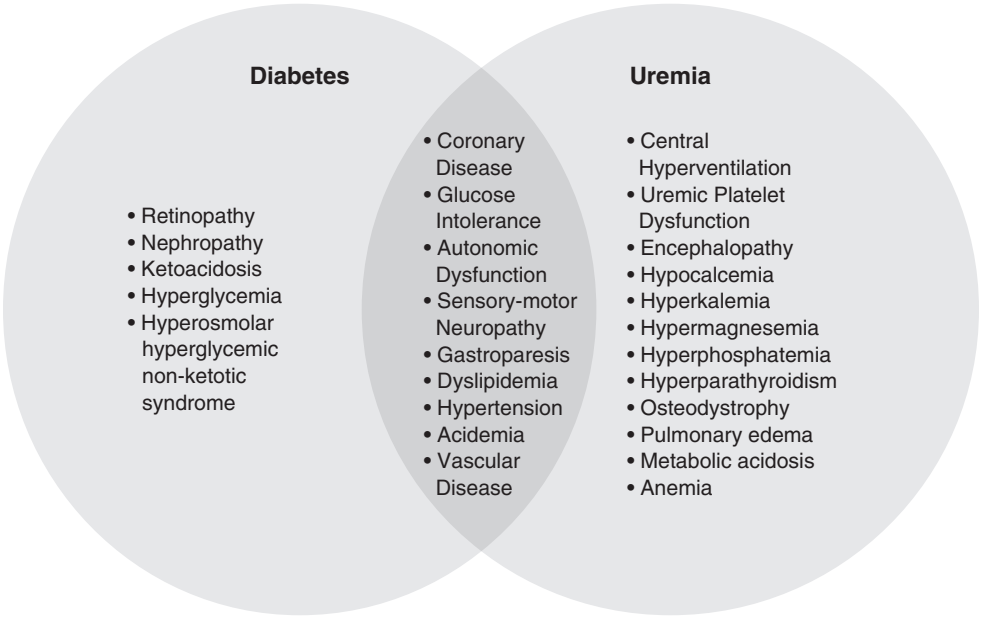


**FIGURE 39-1** ■ Multisystemic effects of diabetes and uremia.

## BOX 39-1 Major Anesthetic Concerns for Pancreas-Kidney Transplantation

### Preoperative Concerns

- Electrolyte abnormalities
  - Hyponatremia <131 mEq/L or hypernatremia >150 mEq/L
  - Hypokalemia <2.5 mEq/L or hyperkalemia >5.9 mEq/L
  - Hyperphosphatemia, hypermagnesemia, hypocalcemia
- Glucose
  - Medication history—insulin and oral hypoglycemic agents
  - Presence of pump, basal rate, 24-hour basal insulin requirement
  - Endocrinology consultation
- Anemia
  - Anemia is often chronic secondary to decreased erythropoietin
- Coagulopathy
  - Platelet dysfunction secondary to uremia; corrected with dialysis
- Dialysis
  - Knowledge of dry weight, recent dialysis can indicate relative hypovolemia
    - Potential hypotension on induction of anesthesia
  - Conversely, several days without dialysis may indicate hypervolemia
    - Potentially associated with cardiovascular overload, pulmonary edema
- Cardiovascular risk
  - Determine presence and degree of coronary artery disease

### Intraoperative Considerations

- Benzodiazepines
  - Effect potentiated by hypoalbuminemia
- Gastroparesis
  - Aspiration precautions and rapid-sequence induction
- Hyperkalemia
  - Levels >5.5 mEq/L may contraindicate use of succinylcholine
  - Prepare for treatment of hyperkalemic arrest
- Coagulopathy
  - May contraindicate neuraxial anesthetic
  - TAP block may be helpful to reduce postoperative pain
- Arterial catheter placement to guide fluid, insulin, and ventilatory settings
  - Allows for continuous blood pressure monitoring
- Intravenous access
  - Avoid sites of arteriovenous fistulas and shunts
  - Central access may be required in certain circumstances
- Intravenous fluids
  - Normal saline solutions may predispose to hyperchloremic acidosis
  - PlasmaLyte and lactated Ringer's solution as long as patient is not hyperkalemic
  - ½ NS with 75 mEq/L sodium bicarbonate
    - May improve pH and reduce base deficit
  - Benefits of colloid solutions are unknown but may include
    - Decreased total crystalloid administration
    - Decreased edema in the donor pancreas and improved microcirculation
- Induction agents
  - Propofol, etomidate, and barbiturates are protein bound
    - Dose may need to be reduced in patients with renal failure and hypoalbuminemia
- Volatile agents
  - Recommend isoflurane and desflurane
    - Desflurane may result in less residual anesthetic postextubation
  - Sevoflurane
    - Release of free fluoride ions does not result in clinical differences in renal transplant function
- Opioids
  - Meperidine
    - Accumulation of normeperidine, active metabolite; lower seizure threshold
  - Morphine
    - Accumulation of morphine-6-glucuronide, active metabolite
  - Fentanyl and remifentanil
    - Relatively unchanged pharmacokinetics
- Muscle relaxants
  - Succinylcholine
    - May increase potassium by 0.5–1.0 mEq/L
  - Cisatracurium
    - Hoffman elimination (does not accumulate in renal failure)
  - Rocuronium
    - Slightly prolonged duration; primarily hepatic excretion
  - Vecuronium
    - Slightly prolonged duration; primarily biliary and hepatic excretion
- Steroid
  - Methylprednisolone
    - Given before surgical incision, may result in hyperglycemia
- Immunosuppressant
  - Antithymoglobulin
    - Infused 1 hour after methylprednisolone is administered; anaphylaxis
  - Other immunosuppressant drugs administered after surgery include mycophenolate, sirolimus, cyclosporine, and tacrolimus
- Vasoactive agents
  - Norepinephrine, epinephrine, phenylephrine, ephedrine, vasopressin
    - Constrict blood vessels, may impair organ microcirculation, contribute to third spacing
    - Large studies do not support the use of a particular pressor over the other
  - Dopamine
    - Dilates renal arterioles, decreases renal vascular resistance, improves renal blood flow
    - No evidence demonstrating renal protection
  - Fenoldopam
    - Direct dopamine agonist, improves renal blood flow without β-adrenergic activity
  - Sodium nitroprusside
    - Contains cyanide, which is metabolized to thyocyanate; thyocyanate is excreted by the kidneys and is neurotoxic
- Fluid loading before vascular anastomosis
- Diuretics
  - Mannitol and furosemide
    - Use varies by surgeon and institution

*NS*, Normal saline; *TAP*, transversus abdominis plane.

decrease postoperative pain but are unacceptable as primary anesthetic plans. Epidural anesthesia could result in splanchnic hypoperfusion and excessive crystalloid administration leading to swelling of the donor pancreas. Colloid solutions may offer an advantage over crystalloid solutions by reducing pancreatic swelling and may reduce graft function complications.

In addition to standard American Society of Anesthesiologists (ASA) monitors, invasive arterial pressure catheters are recommended for closer observation of blood pressure and for serial arterial blood gas (ABG) sampling. Central venous catheters may be used for intravascular access, infusion of vasoactive medications, and trending central venous pressures.

Intraoperatively, serial ABG samples allow for monitoring of ventilation, oxygenation, acid-base status, electrolytes, hematocrit, and glucose. Glucose measurements can vary widely during the case, owing to methylprednisolone (hyperglycemia) and the newly anastomosed pancreas (hypoglycemia). In brittle diabetics (diabetic patients prone to glucose lability), glucose should be checked hourly, and after pancreatic anastomosis and release of the vascular clamp, it should be checked every 30 minutes. An important therapeutic goal is to maintain a physiologic pH, arterial oxygen ($PaO_2$), arterial carbon dioxide ($PaCO_2$), base deficit, sodium concentration, and potassium level.

In addition to methylprednisolone, antithymocyte globulin (ATG) or basiliximab is administered intraoperatively to prevent acute organ rejection. ATG is a rabbit pasteurized gamma globulin that possesses side effects including anaphylaxis and cytokine release syndrome. It is contraindicated in anyone with an allergy to rabbit protein or a history of adverse reaction to ATG. Basiliximab is a murine/human monoclonal antibody that blocks activity of the interleukin 2-receptor alpha chain on the surface of activated T lymphocytes. It is associated with anaphylaxis. However, basiliximab is frequently used in place of ATG because it has not been associated with cytokine release syndrome.

Anecdotal evidence points to postoperative complications in patients who have undergone renal transplantation, stemming from an acute combined metabolic and respiratory acidosis following tracheal extubation. For this reason, we recommend checking an ABG 30 minutes before extubation and giving serious consideration to continuing ventilatory support if the pH is $<7.25$ or the base deficit is $>7$ mEq/L. Other concerns regarding extubation include fluid overload, hemodynamic instability, hyperkalemia, hypoxemia, and hypercarbia. Patients with chronic obstructive pulmonary disease (COPD) and obstructive sleep apnea (OSA) are particularly vulnerable.

Common postoperative fluid management consists of 5% dextrose 0.45% normal saline (NS) at 40 mL per hour and NS 0.45% for hourly urine output replacement on a milliliter-for-milliliter basis. Patients undergoing renal transplantation may be oliguric, anuric, or polyuric. Hyperglycemia is an indication for removing dextrose from intravenous solutions until serum glucose levels are corrected. An insulin infusion is commonly continued throughout the initial perioperative period. Sodium bicarbonate (75 mEq) may be added to 1 L of NS 0.45% if acidosis exists. Third space losses are replaced with crystalloid or colloid boluses or both to maintain adequate end-organ perfusion pressures.

### 4. How is insulin administration managed intraoperatively for patients with a continuous subcutaneous insulin infusion?

These patients may present with varying levels of insulin requirements; some may self-administer intermittent short-acting and long-acting insulin, whereas others may opt for continuous subcutaneous insulin infusion (CSII) therapy (also termed insulin pump). Institutions vary in regard to the perioperative management of patients with CSII therapy undergoing surgery. For surgeries not involving pancreas transplantation, particularly short ambulatory procedures, some institutions permit continuation of the insulin pump, whereas others insist on pump deactivation. However, for SPK transplantation, discontinuing CSII affords the anesthesiologist improved control of insulin requirements, which may abruptly change throughout surgery. Also, turning off CSII eliminates the possibility of pump failure as a possible cause of hyperglycemia. Additionally, when the pancreas is transplanted and unclamping occurs, donor islet beta cells begin to produce insulin, and glucose levels can decrease by 50 mg/dL per hour. Blood glucose levels in conjunction with C peptide levels serve as indicators of graft function. Hyperglycemia and low C peptide levels are signs of graft nonfunction, whereas euglycemia and normal C peptide levels indicate adequate graft function. Most practitioners administer both dextrose and insulin throughout the procedure and into the postoperative period, avoiding ketosis and decreasing neo–beta islet cell activity. Some centers also use octreotide to decrease exocrine pancreas activity.

There are two strategies at the present time regarding insulin management after pancreas transplantation:

- *Complete replacement* by exogenous insulin to meet the body's insulin requirements to "rest" the donor beta islet cells for 3–4 days, followed by intermittent insulin dosing regimen.
- *PRN (pro re nata [as needed])* supplementation with exogenous insulin, allowing for a quick measurement of graft function while awaiting results of C peptide levels. After surgery, hyperglycemia commonly persists despite the production of endogenous insulin by the donor beta islet cells. This persistent hyperglycemia may be due to the insulin-resistant effects of immunosuppressive agents and the administration of high-dose glucocorticoids.

Regardless of the presence or absence of CSII, extreme vigilance regarding glycemic management during the perioperative period must be exercised. Glucose levels should be determined hourly and then half-hourly immediately after unclamping the vascular supply to the pancreas. Glycemic management is best accomplished with continuous insulin infusion intraoperatively that is continued into the postoperative period. Dextrose solutions should also be continued throughout the perioperative period because ketosis has been reported to occur even in patients who are euglycemic.

### 5. Explain the relationship between acidemia and hyperkalemia.

Patients with renal failure and concomitant type 1 DM are at significant risk for developing acidemia and hyperkalemia, particularly when there has been a lapse in hemodialysis. Because timing of dialysis and transplantation are difficult to coordinate, serum pH and potassium levels should be measured on the day of surgery. Abnormal values indicate the need for hemodialysis before transplantation.

Acidemia can occur secondary to ketoacidosis; administration of large amounts of chloride-containing crystalloids (see Question 6 for details); and retention of sulfates, phosphates, and uric acid. A low pH can potentiate the effects of sedative-hypnotics and opioids by increasing the nonionized fraction, resulting in impaired airway reflexes and respiratory depression. Monitoring and management of acid-base status are necessary to prevent the sequelae of acidemia. By assessing serial ABG measurements, the anesthesiologist can make appropriate changes in minute ventilation to compensate partially for a metabolic acidosis. However, after extubation, the seriousness of respiratory depression becomes a true challenge to the anesthesiologist; this is where combined effects of residual inhalation anesthetics, muscle relaxants, opioids, and restricted diaphragmatic movement owing to splinting can lead to rapid development of hypercarbia and acidemia. Patients with OSA and COPD are particularly vulnerable. Postoperative respiratory depression producing hypercarbia and acidosis is concerning in the postanesthesia care unit (PACU). Measures to improve respiratory function in the PACU include raising the head of the bed 30 degrees, pain control (balanced to prevent hypoventilation from splinting while avoiding respiratory depression), and continuous positive airway pressure for patients with OSA.

Interconnected with acidemia is the life-threatening metabolic disturbance of hyperkalemia. Extracellular acidosis increases serum potassium levels by 0.5–0.8 mEq/L for every decrease in pH of 0.1 unit; this occurs because as excess extracellular hydrogen ion moves intracellularly along its concentration gradient, potassium moves out of the cell to maintain electrical neutrality. As potassium levels increase, so does the likelihood of ECG changes, as follows:

- 6 mEq/L—peaked T wave
- 7 mEq/L—prolonged PR interval
- 8–9 mEq/L—absent P waves and widened QRS complex followed quickly by ventricular fibrillation

Intraoperative management of acute hyperkalemia is aimed at stabilizing cardiac membrane potentials and promoting intracellular potassium shifts (Table 39-2).

### 6. Discuss the implications of fluid management in kidney-pancreas transplantation.

The anesthesiologist's role in SPK transplantation is to temper the desires of two medical specialties, the nephrologists who want the kidney "wet" and the pulmonologists who want the lung "dry." Depending on the patient's preoperative volume status, intraoperative fluid administration may be limited by concerns for volume overload on pulmonary and cardiovascular function, which may result in hypoxemia and impaired contractility. Conversely, volume restriction and depletion are associated with hypotension after anesthetic induction, increased risk of delayed graft function, and end-organ hypoperfusion. This balancing act is complicated further by the wide selection of crystalloids and colloids available.

Factors for selecting appropriate fluid replacement include pH, potassium, and glucose content of various intravenous solutions. In the setting of hyperkalemia, it may be disadvantageous to administer PlasmaLyte electrolyte solution or lactated Ringer's solution because both contain potassium (5 mEq/L and 4 mEq/L, respectively). As a result, sodium chloride 0.9% (NS) is frequently used because it does not contain potassium. However, NS has a pH of 5.0 and a chloride content of 154 mEq/L and predisposes to hyperchloremic metabolic acidosis. At our institution, fluid management (Table 39-3) during kidney transplantation is designed to limit acid-base imbalances. Typically, 2.5–5 L of fluid is administered during these operations. At minimum, hourly ABG measurements should be obtained throughout surgery to monitor the patient's acid-base status.

More recently, researchers have looked into the effects of colloid solutions on pancreas transplantation. Early graft pancreatitis after reperfusion appears to be due to defects in the microcirculation, which may be caused by pancreatic swelling from aggressive crystalloid administration. Other causes of impaired microcirculation may be related to methods of organ preservation and medical management of the donor. Colloid solutions may decrease the total crystalloid volume administered; however, the short-term and long-term benefits of colloid solutions on graft function remain unknown.

The goals of fluid management should be aimed at optimizing cardiac performance to enable adequate blood flow to transplanted tissues. Vasopressors are to be used sparingly; however, they are indicated to maintain mean arterial pressure >65–70 mm Hg.

TABLE 39-2 **Management of Hyperkalemia**

| Mechanism of Action | Treatment |
|---|---|
| Stabilize cardiac membrane potentials | Calcium chloride 500–1000 mg intravenously |
| Promote intracellular shift of potassium | Hyperventilation<br>Sodium bicarbonate 1 mEq/kg<br>Insulin 5–10 units with D50 10–25 g |

*D50,* 50% dextrose solution.

TABLE 39-3 **Suggested Fluid Management Guidelines for Renal Transplantation**

| Laboratory Test | Result | Management |
|---|---|---|
| Base deficit | >3 mEq/L | 0.45% NS with 75 mEq/L of $NaHCO_3$* |
| | <3 mEq/L | Determine potassium level |
| Potassium | <4.5 mEq/L | PlasmaLyte or lactated Ringer's solution |
| | >4.5 mEq/L | 0.9% NS |

*$NaHCO_3$,* Sodium bicarbonate; *NS,* normal saline.
*An alternative in extreme acidosis or large base deficit is 5% dextrose in water (D5W) (1 L) with 150 mEq added $NaHCO_3$. $NaHCO_3$ for acidosis is controversial because it can impair oxygen delivery and result in respiratory acidosis if ventilation settings remain unchanged.

## 7. What is the role of transversus abdominis plane block for abdominal surgery?

Transversus abdominis plane (TAP) block is traditionally known as a landmark-guided block performed at the Petit triangle. The triangle landmarks include the iliac crest inferiorly, the latissimus dorsi muscle medially, and the external oblique muscle laterally. TAP block was originally described as a blind technique, performed based on obtaining characteristic "pops" as one traverses through fascial planes until the plane between the transversus abdominis and the internal oblique muscles is identified (Figure 39-2). The dermatomal level covered by the block is from T10 to L1, which is from just above the umbilicus to the superior iliac crest. SPK transplantations require large midline incisions, often extending above the T10 dermatome, whereas kidney transplantations are usually performed with a diagonal incision in the left lower quadrant. Such distinction is significant because SPK would require bilateral TAP blocks and these may not sufficiently cover the surgical incision, whereas incisional pain from kidney transplantation alone is usually prevented with a unilateral TAP block. The blind approach has been complicated by inadvertent needle placement into the liver, peritoneum, and bowel. Ultrasound-guided TAP blocks have decreased the incidence of complications by allowing real-time visualization of the spread of local anesthetic in the desired plane.

The area is prepared and draped in a sterile fashion. An ultrasound probe with sterile cover and sterile gel is placed over the Petit triangle, at the midaxillary line in a transverse plane to the lateral abdominal wall. After visualizing the various fascial planes and the peritoneum, the needle is directed in plane, crossing first the external oblique and then the internal oblique muscles. Saline or local anesthetic, 2 mL, is injected in the plane between the internal oblique and transversus abdominis muscles. When proper needle placement is confirmed, 20–30 mL of local anesthetic is administered. The volume, not the concentration, of local anesthetic used is the important factor. TAP blocks are "volume" blocks. Bupivacaine 0.25%–0.5% or ropivacaine 0.5%–0.75% provides longer duration of action. However, care should be taken to prevent exceeding the maximum recommended dose of the local anesthetic used. During local anesthetic injection, the extent of spread should be monitored continuously by scanning cephalad, caudad, medial, and lateral. Successful TAP blocks are associated with reduced postoperative morphine consumption for 48 hours.

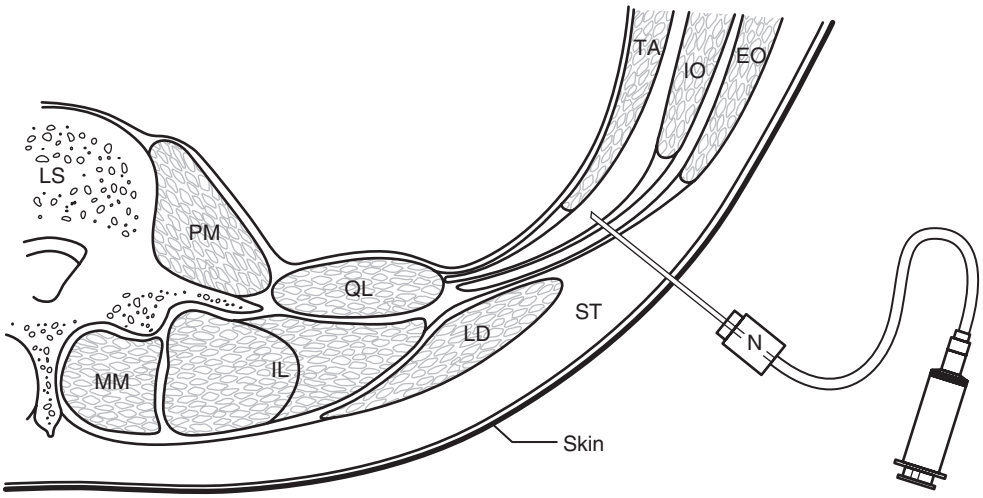


**FIGURE 39-2** ■ Fascial planes of TAP block. *EO,* External oblique; *IL,* longissimus iliocostalis; *IO,* internal oblique; *LD,* latissimus dorsi; *LS,* lumbar spine; *MM,* multifidus muscle; *N,* 50-mm blunt-tipped needle; *PM,* psoas major; *QL,* quadratus lumborum; *ST,* subcutaneous tissue; *TA,* transversus abdominis. (From McDonnel JG, et al. The analgesic efficacy of transversus abdominis plane block after cesarean delivery: a randomized controlled trial. Anesth Analg 106:186, 2008.)

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SECTION 7

# EYE, EAR, NOSE, AND THROAT

CASE 40

# Open Eye Injury and Intraocular Pressure

**Patrick L. Sittler, MD**

QUESTIONS

1. How is normal intraocular pressure maintained?
2. What are anesthetic the considerations for repair of open eye injuries?
3. Is succinylcholine contraindicated in open eye injury?
4. What nonanesthetic pharmacologic agents can decrease intraocular pressure?
5. How do you determine whether surgical repair of an open eye injury is emergent or urgent?

A 5-year-old boy was shot with a BB gun at a family barbecue. He is otherwise healthy and previously experienced an uncomplicated general anesthetic for bilateral myringotomy and tube placement.

## 1. How is normal intraocular pressure maintained?

Normal intraocular pressure (IOP) is 10–20 mm Hg with a difference of up to 5 mm Hg between the two eyes. Diurnal variation results in 2–3 mm Hg higher IOP each morning owing to mydriasis, supine position, and eyelid pressure during sleep. In addition, the supine position can increase IOP by 1–6 mm Hg. IOP is dependent on aqueous humor dynamics (most important factor), choroidal blood volume, central venous pressure (CVP), and extraocular muscle (EOM) tone.

### *Aqueous Humor Dynamics*

The eye is divided into anterior and posterior chambers by the iris. The eye has 250 μL of aqueous humor; one third of the aqueous humor is in the anterior chamber, and two thirds is in the posterior chamber. Aqueous humor is necessary for proper light refraction, allowing for vision. Additionally, it delivers oxygen and glucose to the avascular lens and cornea.

Aqueous humor is produced by diffusion, filtration, and active secretion from choroidal capillaries in the ciliary process located in the posterior chamber. It flows from the posterior chamber, around the iris, and into the anterior chamber. Elimination occurs through the space of Fontana and Schlemm canal at the iridocorneal angle. Changes in intraocular fluid dynamics can cause significant alterations of IOP because the globe is essentially noncompliant and surrounded by the rigid orbit. Decreases in cross-sectional area of the space of Fontana and Schlemm canal, as occur with mydriatic drugs, increase IOP. Even arterial pulsations cause measurable IOP changes.

### *Choroidal Blood Volume*

Sudden increases in systemic blood pressure and CVP increase choroidal blood volume, resulting in elevated IOP because of the comparatively slow elimination process. Although choroidal vessels do not autoregulate, the factors altering cerebral blood flow affect blood volume in the eye. Vasodilation occurs with hypercarbia, hypoxemia, and increases in metabolic rate. Similar to cerebral blood flow, there is a linear relationship between arterial partial pressure of carbon dioxide ($PaCO_2$) and blood flow. Hypoventilation, with the resulting elevation in $PaCO_2$, increases IOP.

### *Central Venous Pressure*

Significant increases in CVP can temporarily inhibit the flow of aqueous humor through the Schlemm canal causing an increase in IOP.

### *Extraocular Muscle Tone*

EOMs differ from skeletal muscles. Compared with skeletal muscles, EOMs can rapidly and precisely control contraction and relaxation and resist fatigue. Skeletal muscles are innervated by a single axon to the midbelly of each fiber. EOMs have single and multiple neuronal innervations allowing for focal contractions. Increased EOM tone increases IOP.

## 2. What are the anesthetic considerations for repair of open eye injuries?

The primary anesthetic goal for repair of open eye injuries is avoidance of sudden increases in IOP and the

resultant extrusion of vitreous humor. Increases in IOP may be seen with increased venous and arterial pressure, coughing, bucking, Valsalva maneuver, increased $PaCO_2$, and the supine position. The following maneuvers can reduce or prevent increases in IOP:

- Reduce IOP
  - Increase venous drainage by elevating the head
- Prevent increases in IOP
  - Minimize preoperative sedation to avoid increases in $PaCO_2$ secondary to sedation and hypoventilation
  - Minimize hemodynamic response to laryngoscopy and intubation by ensuring deep anesthesia before airway manipulation
  - Hyperventilate before intubation and during surgery
  - Minimize bucking and coughing during laryngoscopy and intubation by providing adequate depth of anesthesia and muscle relaxation
  - Use anesthetic techniques designed to provide smooth emergence without coughing or bucking while the endotracheal tube is still in place

To allow for unobstructed access to the surgical field, oral RAE tubes are popular choices for securing the airway. Supraglottic airways, such as flexible laryngeal mask airways, have also been used. Because airways are inaccessible during eye surgery, care should be taken to secure the artificial airway adequately.

Box 40-1 outlines considerations during various phases of general anesthesia.

**BOX 40-1 Anesthetic Considerations during Open Eye Surgery**

Aspiration precautions if "full stomach"
Elevate head of bed
Careful placement of anesthesia facemask
Ensure optimal intubating conditions to avoid coughing and bucking
Induction agents
  Propofol decreases IOP
  Ketamine
    Studies vary as to whether it increases IOP
    Blepharospasm and nystagmus may interfere with surgery
    Increased incidence of PONV
  Etomidate
    Decreases IOP
    Myoclonus may cause injury to eye
    Increased incidence of PONV
Neuromuscular blocking drugs
  Succinylcholine
    Probably does not increase IOP
    No evidence of vitreous extrusion
    Provides optimal intubation conditions in shortest time
  Nondepolarizing
    Rocuronium only drug approved for rapid-sequence induction
    Prolonged mask ventilation may predispose to eye trauma from mask
    Unprotected airway while awaiting for optimal intubation conditions
Laryngeal mask airway
  Not indicated if "full stomach"
  No access to airway
  Does not protect against laryngospasm from light anesthesia or aspiration
Maintenance
  Maintain deep anesthesia to decrease IOP
  Neuromuscular blockade to ensure motionless field
  Hypocapnia
  Hypoxia causes increased IOP by dilation of choroidal circulation
Emergence
  Reversal agents have no effect on IOP
  Smooth emergence (i.e., no coughing or bucking)
Prevention of PONV

*IOP,* Intraocular pressure; *PONV,* postoperative nausea and vomiting.

### 3. Is succinylcholine contraindicated in open eye injury?

Most open globe surgeries are performed emergently on patients subjected to trauma. All such patients are likely to be considered "full stomachs." Because most of these procedures are performed with general anesthesia, rapid-sequence induction (RSI) to minimize aspiration risk is usually the induction technique of choice. Either succinylcholine or double-dose rocuronium is approved for RSI. There are advantages and disadvantages related to both.

The use of succinylcholine has been a topic of considerable debate for years. Traditional concerns focused on a theoretic risk of intraocular contents extrusion after administration of succinylcholine. After eye trauma, patients reflexively press the eye with their hand and experience blepharospasm, both of which predispose to vitreous loss and extrusion. In other words, the damage is done before arriving in the operating room. To avoid succinylcholine based on a theoretic concern that extrusion of intraocular contents would occur fosters old teaching without scientific evidence. Previous reports of extrusion of vitreous occurred during "light" anesthesia. The greater preponderance of reports found no association between succinylcholine administration and vitreous expulsion.

Succinylcholine administration increases IOP within 1 minute, and IOP peaks at 9 mm Hg within 6 minutes. This peak pressure increase is significantly less than IOP elevations seen with crying, coughing, or bucking (e.g., during suboptimal intubating conditions). It may be that the IOP increase seen with succinylcholine is of no clinical consequence if intubation conditions are optimized.

Although the exact mechanism is unknown, there are many proposed theories for IOP increases seen with succinylcholine administration. One theory suggests the increase in IOP is caused by succinylcholine-induced tonic contractions of the EOMs. However, this idea was questioned by a study involving elective enucleation. After all EOMs were detached from the diseased eye, succinylcholine was administered, and IOP was measured. There was no difference in the IOP increase between eyes with detached EOMs and eyes with intact EOMs.

Further research in this area suggests that the increase in IOP may be a vascular event related to choroidal vascular dilation or decreased drainage as a result of elevated CVP. CVP elevation temporarily inhibits flow of aqueous humor through the Schlemm canal.

TABLE 40-1 **Pretreatments to Attenuate Intraocular Pressure Increases with Succinylcholine**

| | |
|---|---|
| Lidocaine | Blunts increase in IOP<br>Decreases airway reactivity and hemodynamic response to endotracheal intubation |
| Opioid | Attenuates increase in IOP seen with succinylcholine alone<br>Possible mechanism of action is by decreasing SVR or CVP or both |
| Nifedipine | Blunts IOP increase<br>Decreases SVR |
| Defasciculating dose | Potential benefit if fasciculations increased IOP<br>Studies have shown mixed results |

*CVP,* Central venous pressure; *IOP,* intraocular pressure; *SVR,* systemic vascular resistance.

The Kresge Eye Institute created an intubation algorithm for patients with open eye injury. This algorithm considers the difficulty of controlling the airway and the importance of RSI to determine if succinylcholine will be administered. In the algorithm, if a difficult airway is anticipated and RSI is needed, succinylcholine is administered with pretreatment to attenuate IOP increases that may occur. Pretreatment consists of one or more of the following: opioid, lidocaine, nifedipine, or defasciculating dose of a nondepolarizing neuromuscular blocking drug (NMBD) (Table 40-1). A retrospective review of all open globe surgeries performed using this algorithm showed no increase in vitreous extrusion or other complications owing to succinylcholine administration.

Rocuronium, a nondepolarizing NMBD, can be administered at a dose of 1.2 mg/kg for RSI. The advantage is that associated IOP increases are significantly less than increases seen with succinylcholine. The disadvantage is that the duration of action of rocuronium may outlast the length of surgery, and it may be problematic if intubation or mask ventilation prove to be difficult.

In situations where "full stomach" is not a concern, any one of multiple nondepolarizing NMBDs may be administered. However, significant increases in IOP can be seen if laryngoscopy occurs when intubating conditions are not optimized and from mask application during ventilation while waiting for peak effect of NMBDs. In the case of an unidentified "full stomach," there is an increased period of time with an unprotected airway.

Ultimately, the decision of which NMBD to administer depends on the following:

- NPO ("nothing by mouth") status of the patient
- Identification of difficult airway
- Optimal intubating conditions
- Minimizing increases in IOP that may occur with mask application

If succinylcholine is deemed to provide the best intubation conditions, it should not be avoided based on theoretic, unproved beliefs that it significantly increases IOP causing vitreous extrusion. The usual contraindications to its use (e.g., hyperkalemia, malignant hyperthermia) apply. Alternative NMBDs can be substituted as needed.

### 4. What nonanesthetic pharmacologic agents can decrease intraocular pressure?

Mannitol is an osmotic agent that increases plasma oncotic pressure and decreases aqueous humor formation. Acetazolamide, a carbonic anhydrase inhibitor, interferes with aqueous humor formation.

### 5. How do you determine whether surgical repair of an open eye injury is emergent or urgent?

Whether surgery is emergent or urgent depends on the ophthalmologist's evaluation of the viability of the injured eye. If the eye is not viable, it would be reasonable to delay surgery in the patient with a "full stomach" until the risk of aspiration is minimized. The same consideration should be given if the eye is viable. The ophthalmologist needs to weigh the risk of blindness against the risk of aspiration. If delaying surgery places eye viability at greater risk, surgery may need to proceed despite the risk of aspiration. It is important for anesthesia care teams and ophthalmologists to discuss the relative risks so that informed decisions can be made regarding the best timing for surgery.

Because many open eye injuries are part of more extensive traumatic events, a systematic review of the entire patient is necessary before proceeding to the operating room for repair of the eye injury. There may be other injuries requiring more immediate attention, and these would be prioritized accordingly. For example, if there was evidence of intracranial trauma, that would need to be addressed before the eye injury.

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CASE 41

# Retinal Detachment

Patrick L. Sittler, MD

## QUESTIONS

1. What are the different types of retinal detachment?
2. Briefly describe the different types of retinal detachment repairs.
3. Which patients are at risk for retinal detachment?
4. What are the advantages and disadvantages of general anesthesia versus regional anesthesia?
5. What are the different regional anesthesia options?
6. What are the considerations for general anesthesia?
7. What is the oculocardiac reflex, and how is it treated?
8. What is the implication of injecting a "gas bubble" into the eye?

A 36-year-old man presented for repair of right retinal detachment. He had been hit in the eye with a baseball. The patient was otherwise healthy, and he never had surgery.

### 1. What are the different types of retinal detachment?

There are three types of retinal detachments: rhegmatogenous, exudative, and tractional. Rhegmatogenous is the most common type and is caused by disruption of the retina, allowing fluid to enter the subretinal space. Exudative retinal detachment is rare and occurs when there is an accumulation of fluid in the subretinal space without an obvious disruption of the retina. Tumors in the layers beneath the retina, such as choroidal melanoma, produce exudative retinal detachment. The third type of retinal detachment is a tractional detachment that occurs when fibrous or fibrovascular tissue caused by injury or inflammation pulls the retina away from subretinal layers.

### 2. Briefly describe the different types of retinal detachment repairs.

Methods employed for repair of retinal detachments are scleral buckle, pneumatic retinopexy, or vitrectomy. In some instances, more than one method is necessary. The endpoint of all of these procedures is to repair the interruption of the retina, create an adhesion between the retinal pigment epithelium and the retina, and prevent recurrence of the detachment.

Surgical approaches vary depending on the method selected. Although pneumatic retinopexy and vitrectomy are intraocular procedures, scleral buckles are extraocular. Pneumatic retinopexy involves injection of a "gas bubble" into the vitreous cavity followed by cryopexy or laser photocoagulation to seal the retinal detachment. After the procedure is completed, the patient is positioned so that the "gas bubble" is abutting the repaired retina. For example, if the retinal detachment is in the 12-o'clock position, the patient would be required to remain in the upright position for 3–5 days.

The purpose of the scleral buckle is to change the internal contour of the globe by external manipulation. The inward displacement of the external tissue by the scleral buckle closes the retinal disruption, preventing the passage of liquefied vitreous into the subretinal space. It is controversial whether or not draining the subretinal fluid should be done during the procedure. Proponents of draining the fluid believe that the decreased intraocular volume allows for the inward displacement by the scleral buckle without increasing intraocular pressure; this also allows the detached retina to rest on the scleral buckle, facilitating reattachment.

Vitrectomies involve removal of vitreous gel, relieving traction on the detached portion of the retina. Sometimes the release of traction is insufficient to allow the retina to reattach. After vitrectomy, vitreous gel is replaced with silicone oil or a "gas bubble" to restore normal pressure in the eye. Depending on the size and location of the retinal detachment, pneumatic retinopexy may also be necessary.

### 3. Which patients are at risk for retinal detachment?

Several conditions predispose patients to retinal detachments. Among the ocular conditions associated with retinal detachments, high myopia (> 6.0 diopter) is associated with almost a threefold increase in incidence. Retinal detachment is a known complication of cataract surgery. Cytomegalovirus retinitis, most often seen with acquired immunodeficiency syndrome (AIDS), predisposes patients to retinal detachments. Ocular trauma is the cause of 10%–15% of retinal detachments and is the most common cause in children. Another common cause of retinal detachment in children is retinopathy of prematurity. Patients with a history of retinal detachment from intraocular pathology in one eye have a significant risk of retinal detachment in the other eye.

## 4. What are the advantages and disadvantages of general anesthesia versus regional anesthesia?

Selecting the appropriate anesthetic for any retinal surgery should be specific to each patient, the underlying medical conditions, and the intended procedure. Discussion with the ophthalmologist regarding surgical needs and patient expectations also helps in deciding what type of anesthesia would be best suited.

There are several methods of providing adequate operating conditions using regional anesthesia (retrobulbar, peribulbar, sub-Tenon block) with or without sedation. However, because some of these complex repairs may take >2 hours and patients may be unable to tolerate lying motionless, it may be necessary to provide general anesthesia to ensure patient safety, satisfaction, and the best opportunity for a good surgical outcome (Table 41-1).

Advantages of regional anesthesia include the following:

- Shorter time in the operating room
- Shorter postoperative recovery times
- Reduced stress response
- Avoidance of undesirable side effects (e.g., nausea and vomiting) of general anesthesia
- Minimized risk of exacerbating cognitive dysfunction in patients with preexisting cognitive deficits

Disadvantages of regional anesthesia include the following:

- Unsecured and inaccessible airway
- Uncooperative patient requiring escalating sedation that may result in respiratory depression
- Incomplete analgesia
- Surgery outlasting analgesic duration
- Ocular injury from patient movement

Regional techniques are not without risks. Minor risks include corneal abrasions and chemosis. More serious problems include permanent visual loss from perforation of the globe especially in myopic patients, injury to the optic nerve, and retrobulbar hemorrhage. Local anesthetic systemic toxicity (LAST) occurs from either direct vascular injection or spread of local anesthetic along the dural sheath of the optic nerve into the cerebrospinal fluid. Manifestations of LAST may result in drowsiness, temporary blindness of the contralateral eye, seizures, and respiratory and cardiac arrest. The management of LAST is described in Chapter 52.

Advantages of general anesthesia include the following:

- Provision of ideal operating conditions such that the patient remains motionless for the duration of the procedure
- Anesthesia can continue for as long as needed in cases where surgery is prolonged

Disadvantages of general anesthesia include the following:

- Inaccessible airway, although it is secured
- Disruption of the surgical repair
  - Coughing or "bucking" during emergence and extubation
  - Vomiting or retching in postoperative period
- Increased time to surgical start
- Increased time for emergence
- Increased time spent in the postanesthesia care unit (PACU)

## 5. What are the different regional anesthesia options?

Regional anesthesia options are retrobulbar, peribulbar, and sub-Tenon block. Retrobulbar and peribulbar blocks are most commonly performed. Retrobulbar and peribulbar blocks achieve anesthesia by a conduction block of the intraorbital sensory divisions of the ophthalmic branch of the trigeminal nerve. The difference between these blocks is needle placement. Retrobulbar blocks are performed posterior to the globe inside the cone comprising the extraocular muscles. Peribulbar injections are performed outside this muscle cone and are dependent on spread of the local anesthetic. Sub-Tenon block is performed by making a small entrance wound through the conjunctiva and Tenon capsule. A small amount of local anesthetic is injected intraocularly. The choice of block is based on personal preference. All three blocks are effective.

## 6. What are the considerations for general anesthesia?

No specific general anesthetic has been shown to be more beneficial than others for retinal surgery. Nevertheless, there are several issues to consider when planning the appropriate technique (Table 41-2).

TABLE 41-1 **Advantages and Disadvantages of General versus Regional Anesthesia**

| | Pro | Con |
|---|---|---|
| General Anesthesia | Motionless patient<br>Able to provide prolonged anesthetic | Inaccessible airway<br>Disruptions during surgical repair<br>Coughing and "bucking"<br>Vomiting or retching<br>↑ Time to surgical start<br>↑ Time for emergence<br>↑ Time in PACU |
| Regional Anesthesia | ↓ Time in operating room<br>↓ Stress response<br>Faster recovery<br>Avoid nausea and vomiting<br>↓ Risk of cognitive dysfunction in susceptible patients | Ocular injury from patient movement<br>Unsecured, inaccessible airway<br>Incomplete analgesia<br>Surgery outlasts block analgesia |

*PACU,* Postanesthesia care unit.

TABLE 41-2 **Issues to Consider for General Anesthesia**

| Issue | Complication | Suggestion |
|---|---|---|
| Access to surgical field | Obstructed view | Oral RAE tube or flexible LMA |
| Inaccessible airway | Disconnect or dislodgment | Ensure positioning of artificial airway<br>Secure airway well |
| $N_2O$ | Expansion of "gas bubble" | Consider TIVA with propofol |
| Coughing or "bucking" during emergence | Disruption of surgical repair | Consider TIVA with propofol |
| PONV | Disruption of surgical repair<br>Delayed discharge from PACU<br>Patient dissatisfaction | Consider TIVA with propofol<br>Multimodal antiemetic therapy |

*LMA,* Laryngeal mask airway; *$N_2O$,* nitrous oxide; *PACU,* postanesthesia care unit; *PONV,* postoperative nausea and vomiting; *RAE,* Ring-Adair-Elwyn; *TIVA,* total intravenous anesthesia.

### *Airway*

To allow for unobstructed access to the surgical field, oral Ring-Adair-Elwyn (RAE) tubes and flexible laryngeal mask airways (LMAs) are popular choices for securing the airway. Because the airway is inaccessible during surgery, care should be taken to secure the artificial airway correctly and adequately.

### *Nitrous Oxide*

In procedures where a "gas bubble" is to be injected, it is important to avoid using nitrous oxide ($N_2O$). (See Question 8 for detailed explanation.) According to some literature, $N_2O$ has been associated with postoperative nausea and vomiting (PONV). Avoiding $N_2O$ would be recommended in patients at high risk for PONV and in cases that may result in disruption of the surgical intervention from the physiologic consequences of increased intraocular pressure from vomiting.

### *Emergence*

Avoiding coughing or "bucking" during emergence and extubation (or removal of the LMA) is important because it may result in disruption of the surgical repair. There are many different strategies to accomplish this; total intravenous anesthesia (TIVA) with propofol may be of benefit.

### *Nausea and Vomiting*

Avoiding PONV is important in these cases. PONV not only results in delayed PACU discharge and patient dissatisfaction, but, more importantly, vomiting or retching may cause disruption of the surgical repair. Strategies for reducing PONV include administering multimodal antiemetic therapy and TIVA with propofol.

## 7. What is the oculocardiac reflex, and how is it treated?

The oculocardiac reflex consists of the following:

- Afferent limb—ophthalmic division of the trigeminal nerve
- Gasserian ganglion
- Efferent limb—vagus nerve

The reflex is typically triggered preoperatively or intraoperatively. Preoperatively, pressure on extraocular muscles during retrobulbar or peribulbar block can precipitate the reflex. Intraoperatively, pressure or traction on the globe can produce the reflex. The most common manifestation is severe bradycardia. However, cardiac dysrhythmias including junctional rhythm, ectopic atrial rhythm, atrioventricular blockade, ventricular bigeminy, multifocal premature ventricular contractions, wandering pacemaker, idioventricular rhythm, ventricular tachycardia, and asystole all have been described.

The oculocardiac reflex is treated either prophylactically or symptomatically with an anticholinergic. Additionally, surgical stimulation should cease until the arrhythmia has resolved.

## 8. What is the implication of injecting a "gas bubble" into the eye?

$N_2O$, because of its solubility, enters the "gas bubble" and causes an increase in volume; this results in an increase in intraocular pressure and may compromise retinal circulation. $N_2O$ should be avoided in these cases. Because the "gas bubble" may remain in the eye for 10–28 days, any subsequent general anesthetic during this time period should not include $N_2O$. Patients are given an identification bracelet delineating this information in the event they need surgery during this time.

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CASE 42

# Tympanomastoidectomy

**Cheryl K. Gooden, MD, FAAP**

## QUESTIONS

1. Why is tympanomastoidectomy performed?
2. What the preoperative anesthesia considerations are associated with tympanomastoidectomy?
3. What are the intraoperative requirements for tympanomastoidectomy?
4. Are inhalation or intravenous anesthetic agents preferred during tympanomastoidectomy?
5. Is nitrous oxide contraindicated during tympanomastoidectomy?
6. Should single or combination antiemetic therapy be administered to patients undergoing tympanomastoidectomy?
7. What are the postanesthesia care unit concerns after tympanomastoidectomy?

A 28-year-old woman with a history of chronic conductive hearing loss presents for right tympanomastoidectomy.

### 1. Why is tympanomastoidectomy performed?

When the eustachian tube malfunctions, a vacuum is created in the middle ear. This vacuum is usually associated with chronic upper respiratory infections and allergies. The vacuum causes suction on the tympanic membrane that is already weakened by recurrent infections. The result can be cholesteatoma, which is an abnormal growth of primarily skin cells that occurs behind a perforated tympanic membrane. Damage to nearby bone surrounding the ear is a likely consequence of cholesteatoma. Associated symptoms include progressive hearing loss, dizziness, facial nerve damage, and central nervous system infections with extension into the brain. Tympanomastoidectomy is performed to remove cholesteatoma and infected bone from the middle ear.

Surgical treatment consists of an incision made behind the ear, opening the mastoid and exposing the middle ear. Cholesteatoma or infected tissues or both are removed. The tympanic membrane is patched, and packing is placed in the external auditory canal.

### 2. What the preoperative anesthesia considerations are associated with tympanomastoidectomy?

Anesthesia assessment before tympanomastoidectomy does not differ much from basic anesthesia assessment. Issues specific to middle ear disease should be addressed. Decreased hearing acuity or use of hearing aids can make communication challenging. Common manifestations of middle ear–related disorders include nystagmus, vertigo, nausea, and vomiting. A history of motion sickness or postoperative nausea and vomiting (PONV) is an important issue to consider in the anesthetic plan.

### 3. What are the intraoperative requirements for tympanomastoidectomy?

Pertinent surgical anatomy is very small, necessitating magnification. Bleeding into the surgical field readily obscures the view through operating microscopes. Consequently, it is crucial to minimize intraoperative bleeding.

Because injury to the facial nerve is a major concern, facial nerve electromyography may be used during tympanomastoidectomy. This monitoring necessitates a motionless patient in the absence of neuromuscular blocking agents.

During surgery, the head of the operating room table is turned 90–180 degrees away from the anesthesia machine. In addition, the patient's head and neck are rotated to the opposite side from the operative field. It is important to ensure the following:

- Anesthetic circuit and monitoring cables are appropriately long
- Neck is not hyperextended
- Dependent ear and eye are free of excessive pressure

### 4. Are inhalation or intravenous anesthetic agents preferred during tympanomastoidectomy?

The choice of inhalation anesthetic agents versus total intravenous anesthesia (TIVA) and whether one is more advantageous than the other for middle ear surgery remain controversial. Similar intraoperative hemodynamics can be obtained with either intravenous or inhalation agents. The theoretic advantage of TIVA with propofol is the possibility of less nausea and vomiting.

### 5. Is nitrous oxide contraindicated during tympanomastoidectomy?

It is probably best to avoid nitrous oxide ($N_2O$) during tympanomastoidectomy. $N_2O$ is 31 times more soluble in

blood (blood gas coefficient 0.47) than nitrogen (blood gas coefficient 0.015). As a result, $N_2O$ diffuses into a closed air space (e.g., intestines, pneumothorax) more rapidly than nitrogen diffuses out, causing expansion of the air space. Because the middle ear is a natural air space, middle ear pressure increases when $N_2O$ is administered as part of the anesthetic technique; this is particularly problematic in the presence of a blocked eustachian tube. In this procedure, the tympanic membrane graft may become dislodged by increased middle ear pressure. Another consideration for avoiding $N_2O$ during tympanomastoidectomy is the loose association between it and PONV and postdischarge nausea and vomiting.

### 6. Should single or combination antiemetic therapy be administered to patients undergoing tympanomastoidectomy?

Antiemetic therapy has a crucial role in middle ear surgery because it is associated with PONV. All patients undergoing middle ear surgery benefit from prophylactic therapy. The risk of PONV depends on several factors, including the patient, the anesthetic, and the surgical procedure. The choice of antiemetic therapy varies from one institution to the next. Combination therapy has been shown to be effective for this procedure.

### 7. What are the postanesthesia care unit concerns after tympanomastoidectomy?

In the postanesthesia care unit (PACU), the most common problems encountered after tympanomastoidectomy are nausea, vomiting, and vertigo. Although patients may experience pain during recovery in the PACU, it tends to be less of an issue compared with PONV and vertigo. Most pain associated with tympanomastoidectomy occurs during the intraoperative phase as opposed to the recovery phase. Care in the PACU should be tailored to meet each patient's individual needs. Management may include hydration, drug therapy, quiet, and avoiding rapid elevation of the head of the patient's bed.

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CASE 43

# The Difficult Airway

**Allan P. Reed, MD**

## QUESTIONS

1. What are the predictors of difficult mask ventilation?
2. Discuss the risk factors for difficult intubation.
3. Are the risk factors for difficult intubation reliable predictors of difficult intubation?
4. How is an anticipated difficult intubation approached?
5. Describe the management options for a patient who, after induction of anesthesia, unexpectedly cannot be intubated with a Macintosh blade; the patient has a good mask airway.
6. After induction of anesthesia, ventilation by facemask and intubation are impossible; what maneuvers may help?
7. How is successful tracheal intubation verified?
8. After a difficult intubation, how is postoperative extubation managed?

A 76-year-old man presents for endoscopic vocal cord injections. He underwent general anesthesia many years ago without any known problems. The old records are unavailable. He has limited translation of the temporomandibular joint. Otherwise, his airway examination is within normal limits.

## 1. What are the predictors of difficult mask ventilation?

One of the most important predictors of a difficult airway is a history of a difficult airway. The opposite is not always true. A history of problem-free airway management is suggestive of future ease, but it is not a guarantee. Many factors that contribute to difficulty are progressive. Examples of such problems include rheumatoid arthritis and obesity. An airway history is recommended for all patients. Review of prior anesthesia records is frequently helpful. They may describe previously encountered problems, failed therapies, and successful solutions.

Difficult facemask ventilation occurs when a practitioner cannot provide sufficient gas exchange because of inadequate mask seal, large volume leaks, or excessive resistance to the ingress or egress of gas; this occurs with an incidence of 0.08%–5%. The wide range is probably due to conflicting definitions of difficult mask airway. Risk factors (Box 43-1) for difficult mask ventilation include a full beard, a massive jaw, edentulousness, skin sensitivity (burns, epidermolysis bullosa, fresh skin grafts), facial dressings, obesity, age >55 years, and a history of snoring. Other criteria that suggest the possibility of difficult facemask ventilation include a large tongue, heavy jaw muscles, a history of obstructive sleep apnea, poor atlanto-occipital extension, some types of pharyngeal pathology, facial burns, and facial deformities. Multiple types of pharyngeal problems can produce difficult facemask ventilation, including lingual tonsil hypertrophy, lingual tonsillar abscess, lingual thyroid, and thyroglossal duct cyst. Many of these problems cannot be detected by classic airway examination techniques. The presence of any one factor is suggestive of difficult mask ventilation. The more factors present at the same time, the greater the likelihood of difficulty. Increased mandibulohyoid distance has been associated with obstructive sleep apnea, the pathophysiology of which may be related to difficult mask ventilation.

Traditional facemask airway management is generally safe and effective. In the unusual instances when it is not, tracheal intubation remains the fallback option. Although this scheme works well in most cases, approximately 15% of difficult intubations are also difficult mask airways.

## 2. Discuss the risk factors for difficult intubation.

### *Sniffing Position*

The presence or absence of airway pathology does not influence the definition of difficult tracheal intubation. It occurs when multiple attempts at intubation are required. Traditional laryngoscopy is performed to visualize the laryngeal opening. The laryngoscopist is positioned outside the airway, above the patient's head. To see the airway, light must travel from the glottic opening to the laryngoscopist's eye. This technique requires an uninterrupted linear path between the larynx and laryngoscopist because light generally travels in straight lines. Most manipulations performed attempt to satisfy this criterion.

The airway contains three visual axes—the long axes of the mouth, oropharynx, and larynx. In the neutral position, these axes form acute and obtuse angles with one another. Light cannot bend around these angles under normal circumstances. To bring all three axes into better alignment, Magill suggested the "sniffing the morning air" position. True sniffing position requires both cervical flexion and atlanto-occipital extension.

**BOX 43-1 Predictors of Difficult Facemask Ventilation**

Obesity
Beard
Edentulousness
History of snoring
History of obstructive sleep apnea
Skin sensitivity (e.g., burns, epidermolysis bullosa, fresh skin grafts)
Massive jaw
Heavy jaw muscles
Age >55 years
Large tongue
Poor atlanto-occipital extension
Pharyngeal pathology
  Lingual tonsil hypertrophy
  Lingual tonsil abscess
  Lingual thyroid
  Thyroglossal duct cyst
Facial abnormalities
  Dressings
  Burns
  Deformities

Cervical flexion approximates the pharyngeal and laryngeal axes. Atlanto-occipital extension brings the oral axis into better alignment with the other two axes. Normal atlanto-occipital extension measures 35 degrees. With optimal alignment of the airway's visual axes, it becomes possible to look through the airway into the laryngeal opening. Reduced atlanto-occipital gap or prominent C1 spinous processes impair laryngoscopy if vigorous attempts at extension are performed because the larynx is forced anteriorly causing the trachea to bow.

Inability to assume the sniffing position is a predictor of difficult intubation. Examples of problems that prevent the sniffing position include cervical vertebral arthritis, cervical ankylosing spondylitis, unstable cervical fractures, protruding cervical disks, atlantoaxial subluxation, cervical fusions, cervical collars, and halo frames. Morbidly obese patients sometimes have posterior neck fat pads that prevent atlanto-occipital extension.

The ability to achieve the sniffing position is easily tested. The clinician has the patient flex the lower cervical vertebrae and extend at the atlanto-occipital joint. Pain, tingling, numbness, or inability to achieve these maneuvers predicts difficult intubation.

The benefits of the sniffing position have been dogma for >70 years. More recently, Adnet et al. (2001) and Chou and Wu (2001) have independently questioned its utility.

### Mouth Opening

Mouth opening is important because it determines the available space for placing and manipulating the laryngoscope and tracheal tube. A small mouth opening may not accommodate either one. Mouth opening also facilitates visualization of the uppermost part of the airway. Mouth opening relies on the temporomandibular joint (TMJ), which works in two ways. It has both a hingelike movement and a gliding motion, known as translation. Its hingelike movement allows the mandible to pivot on the maxilla. The more the mandible swings away from the maxilla, the bigger the mouth opening. The adequacy of mouth opening is assessed by measuring the interincisor distance. An interincisor distance of 3 cm provides sufficient space for intubation. This corresponds approximately to the width of two fingerbreadths. The two-fingerbreadth test is performed by placing the examiner's second and third digits between the patient's central incisors. If they fit, there should be adequate room to perform laryngoscopy. If they do not fit, laryngoscopy may be difficult.

Factors that interfere with mouth opening include masseter muscle spasm; TMJ dysfunction; and various integumentary ailments, such as burn scar contractures and progressive systemic sclerosis. Masseter muscle spasm may be relieved by induction of anesthesia and administration of muscle relaxants. TMJ mechanical problems remain unaltered by medications. Some patients demonstrate adequate mouth opening when awake but not after anesthetic induction. The problem often can be relieved by pulling the mandible forward. A mouth opening that was sufficient for a previous anesthetic may not be after temporal neurosurgical procedures.

### Dentition

Instrumentation of the airway places teeth at risk for damage. Multiple problems result from dental injury. Teeth may be dislodged or broken. Such teeth cannot be used for chewing, may be painful, and are costly to repair. Beyond these issues, broken teeth can fall into the trachea, migrate to the lung, and predispose to abscesses. Poor dentition is at risk for damage as the mouth is opened and as the laryngoscope blade is introduced. Teeth that can be extracted easily with digital pressure should probably be removed. During laryngoscopy in the presence of poor dentition, extra efforts are made to avoid placing pressure on the maxillary incisors. In doing so, the laryngoscope is manipulated into a less than ideal position resulting in poor visualization of the glottis.

Prominent maxillary incisors complicate laryngoscopy in another way. They protrude into the mouth and block the line of sight to the larynx. To overcome this problem, laryngoscopists must adjust their line of sight. To accomplish this, the laryngoscopist's eye is brought to a new position that is higher than the original one. The laryngoscopist looks tangentially over the protruding maxillary incisor; this creates two new points in the adjusted line of sight and a new straight line of sight. The new line of sight brings the laryngoscopist's view to a more posterior laryngopharyngeal position, resulting in a view that is posterior to the larynx. Consequently, the larynx is not visualized, and a difficult laryngoscopy is produced. In much the same way, edentulous patients tend to be easy intubations because the laryngoscopist can adjust the line of sight to a more advantageous angle.

### *Tongue*

The tongue occupies space in the mouth and oropharynx. The base of the tongue resides close to the glottic aperture. During traditional direct laryngoscopy, the base of the tongue falls posteriorly obstructing the line of sight into the glottis. Visualizing the larynx requires displacing the base of the tongue anteriorly so that the line of sight to the glottis is restored. The tongue is frequently displaced with a handheld rigid laryngoscope, to which Macintosh and Miller blades are most commonly attached. Laryngoscopes push the tongue anteriorly and in so doing, move it from a posterior obstructing position to a new anterior nonobstructing position within the mandibular space. The mandibular space is the area between the two rami of the mandible. Even with the tongue maximally displaced into the mandibular space, visualization of the larynx is sometimes inadequate.

Usually, a normal-size tongue fits easily into a normal-size mandibular space, whereas a large tongue would fit poorly. After filling the space, a large tongue still occupies some of the oropharyngeal airway causing obstruction. For this reason, a large tongue (macroglossia) is a predictor of a difficult intubation. Similarly, a normal-size tongue fits poorly into a small mandibular space. Consequently, it occupies some of the oropharyngeal airway, obstructing the line of sight. For this reason, a small mandible (micrognathia) is a predictor of difficult intubation. In essence, a tongue that is large compared with the size of the mouth, oropharynx, and mandible takes up excessive space in the oropharynx and interferes with visualization.

The base of the tongue resides so close to the larynx that inability to displace it adequately anteriorly creates another problem. The base of the tongue hangs down over the larynx, and the glottis is hidden from view. The glottic aperture is anatomically anterior to the base of the tongue—hence the term "anterior larynx." Under such circumstances, the larynx is anterior to the base of the tongue and cannot be seen because the tongue hides it. Glottic and supraglottic masses that force the base of tongue posteriorly can create difficult intubations as well. Some of the masses that may be encountered include lingual tonsils, epiglottic cysts, and thyroglossal duct cysts.

After filling the mandibular space with the tongue, additional pressure on the laryngoscope blade lifts the mandible anteriorly. In this setting, mandibular displacement is dependent on the TMJ. In addition to its hingelike motion, the TMJ works in a gliding (translational) movement. The gliding motion allows the mandible to slide anteriorly across the maxilla. If the joint does not translate, the mandible cannot be displaced anteriorly, and the tongue cannot be moved out of the line of sight.

Recognizing the implications of tongue size to successful laryngoscopy, Mallampati et al. in 1985 and Samsoon and Young in 1987 devised classification systems to predict difficult laryngoscopy using this concept. A difficult laryngoscopy occurs when it is impossible to visualize any portion of the vocal cords. Mallampati and Samsoon reasoned that a large tongue could be identified on visual inspection of the open mouth. Both classification systems relate the size of the tongue to the oropharyngeal structures identified. A normal-size tongue allows for visualization of certain oropharyngeal structures. As the tongue size increases, some structures become hidden from view. Consequently, both investigators proposed systems that reason backward from this premise.

Application of the Mallampati or Samsoon classification system is easy and painless. The patient is seated in the neutral position and asked to open the mouth wide and protrude the tongue as much as possible without phonation. Phonation is discouraged because it raises the soft palate and allows for visualization of additional structures. The observer looks for specified anatomic landmarks: the fauces, pillars, uvula, and soft palate. The Mallampati classification system uses three groups, and the Samsoon classification system uses four groups (Figure 43-1). Both systems suggest that as the tongue size increases, fewer structures are visualized, and laryngoscopy becomes more difficult. Mallampati scores tend to be higher in pregnant compared with nonpregnant patients.

Just as the size of the tongue can be estimated, so too can the size of the mandible. This estimation is accomplished by asking the patient to extend the head at the atlanto-occipital joint and identifying the mandibular mentum and thyroid cartilage. The thyroid notch (Adam's apple) is the most superficial structure in the neck and serves as a good landmark for the thyroid cartilage.

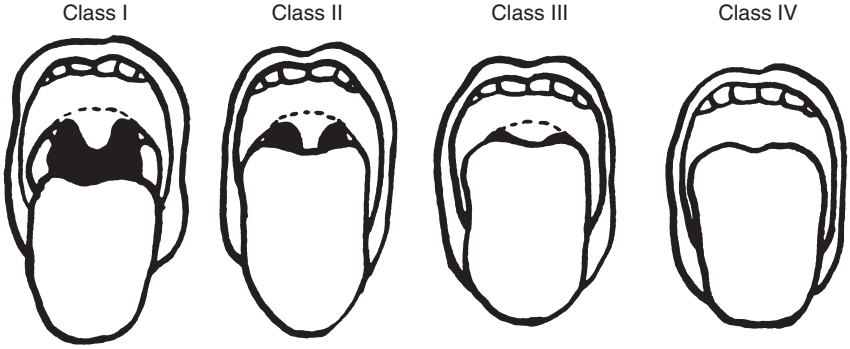



**FIGURE 43-1** ■ **Samsoon classification of pharyngeal structures.** (From Samsoon GLT, Young JRB: Difficult tracheal intubation: a retrospective study. Anaesthesia 42:487, 1987.)

The vocal cords lie just caudad to the thyroid notch. The distance between the thyroid cartilage and mentum (thyromental distance) is measured in one of three ways. The measurement can be made with a set of spacers, a small pocket ruler, or the observer's fingers. The normal thyromental distance is 6.5 cm. A thyromental distance >6 cm is predictive of an easy intubation. A thyromental distance ≤6 cm is suggestive of a difficult intubation. Rulers often are not present at the bedside. In the absence of a ruler, practitioners can judge the thyromental distance with their fingers. By knowing the width of one's middle three fingers, which frequently approximates 6 cm, the thyromental distance can be compared with the fingers' span. In this way, clinically relevant approximations can be taken into account when examining patients for the purpose of predicting difficult intubation. The usefulness of predicting difficult intubation based on thyromental distance has been challenged. Data from Rocke et al. (1992) and El-Ganzouri (1996) show that a decreased thyromental distance (receding mandible) offers a ≤7% probability of predicting difficult intubation. Chou (1993) and Brodsky et al. (2002) described patients whose thyromental distances were >6.5 cm and who were difficult intubations.

Similar measurements and predictions have been made using the hyoid bone and mandible as well as the sternum and mentum. Chou and Wu (2001) suggested that a long mandibulohyoid distance predicts a large hypopharyngeal tongue, which hides the glottis during laryngoscopy and produces a difficult intubation. They reasoned that the tongue is hinged to the hyoid bone so that a long hyomandibular length represents a caudad-lying tongue. With the base of the tongue positioned farther inferiorly, it occupies more space in the oropharyngeal airway. Consequently, it obstructs the laryngoscopist's line of sight. The hyoid bone is more difficult to feel than the thyroid cartilage and is often impossible to locate. The sternum and mentum are generally easy to find, but the sternomental distance has not been substantiated as a good predictor of difficult intubation by other investigators.

The ability to translate the TMJ is easily assessed before induction. The patient is asked to place the mandibular incisors (bottom teeth) in front of the maxillary incisors (upper teeth). Inability to perform this simple task is usually from one of two sources. First, the TMJ may not glide, predicting a difficult intubation. Second, some patients find it difficult to coordinate the maneuver, in which case there is no implication for a difficult intubation.

The upper lip bite test was proposed as a modification of the TMJ displacement test. The upper lip bite test is performed by asking the patient to move the mandibular incisors as high on the upper lip as possible. The maneuver is similar to biting the lip. Contact of the teeth above or on the vermilion border is thought to predict adequate laryngoscopic views. Inability to contact the vermilion border is thought to predict poor laryngoscopic views. Both the TMJ translation test and the upper lip bite test assess TMJ glide, which is an important consideration during laryngoscopy. Table 43-1 summarizes a quick, easy, bedside scheme for predicting difficult intubation.

**TABLE 43-1 Predictors of Difficult Intubation**

| Criteria | Factors That Suggest Difficult Intubation |
|---|---|
| History | History of difficult intubation |
| Length of upper incisors | Relatively long |
| Interincisor distance | <3 cm (<2 fingerbreadths) |
| Overbite | Maxillary incisors override mandibular incisors |
| TMJ translation | Inability to extend mandibular incisors anterior to maxillary incisors |
| Mandibular space | Small, indurated, encroached on by mass |
| Cervical vertebral range of motion | Cannot touch chin to chest or cannot extend neck |
| Thyromental distance | <6 cm (<3 fingerbreadths) |
| Mallampati/Samsoon classification | Mallampati III/Samsoon IV<br>Relatively large tongue<br>Uvula not visible |
| Neck | Short, thick |
| Palate shape | High arched or very narrow |

*TMJ,* Temporomandibular joint.

Adapted from American Society of Anesthesiologists Task Force on Difficult Airway Management: Practice guidelines for management of the difficult airway. Anesthesiology 118:251, 2013.

## 3. Are the risk factors for difficult intubation reliable predictors of difficult intubation?

Although it makes intuitive sense to perform and is consistent with best medical practices, airway evaluation frequently falls short of its intended goal. Numerous rating systems based on recognized prediction criteria have been investigated. Most have recurrent problems.

The first problem is nomenclature. A standardized definition of a "difficult airway" did not exist until 1993. At that time, it was explained as a situation in which a conventionally trained anesthesiologist experienced difficulty with mask ventilation, difficulty with tracheal intubation, or both. For years, individual investigators needed to establish their own definition of "difficult intubation" each time studies were conducted. Consequently, the endpoints of their work were not comparable with other investigations in the field, making comparative analysis of studies impossible. In 1993, the American Society of Anesthesiologists (ASA) Committee on Practice Guidelines for Management of the Difficult Airway offered a generally acceptable definition. The definition was altered slightly 10 years later. In 2013, "difficult tracheal intubation" referred to any intubation that required multiple attempts. This is a good clinical definition but lacks the precision required for scientific investigation. For example, some practitioners may perform a single laryngoscopy and, based on the view obtained, elect to

forego further attempts at laryngoscopy. Such cases may be handled with a supraglottic airway device, regional anesthesia, or other techniques. This situation does not meet the definition of difficult intubation, when in fact it would have if one more attempt at intubation was performed. The ASA definition serves as a good clinical understanding of difficult intubation but lacks the rigid, encompassing concerns required for scientific investigation. "Failed intubation" is an easier term to understand. A failed intubation exists when laryngoscopists give up and admit that traditional intubation techniques would not be successful. The endpoint is clear and occurs with an incidence of 1:280 in obstetric patients and 1:2230 in the general operating room population.

The second problem is identifying features that predict difficult intubation; this is frequently accomplished by attempting to recognize characteristics found in patients who have proven to be difficult intubations. The problem with such an approach is the lack of information about the same characteristics in patients who are easy intubations. As Turkan pointed out, we do not even know the normal values for many prediction criteria. A better method is to apply multivariate analysis to patient populations in a prospective manner. In that way, a single factor can be compared for difficult and easy intubations. Various rating systems attempt to combine multiple predictors into a formula. To date, none has been satisfactory.

The third problem is validating the tests once they are promulgated. Validation tests performed on the same patient population used to identify them are misleading. This is like counting the number of envelopes in a particular mailbox, predicting that all mailboxes contain that number of envelopes, and then validating the prediction by recounting the envelopes in that same mailbox. Validation must be performed by counting the envelopes in multiple different mailboxes. In the same way, validation of difficult intubation predictors must be performed in multiple different patient populations. The experimental patient sample cannot be used to validate experimental results. Different sample populations are needed for that.

The fourth problem is the experimental methods. Individual practitioners differ, and clinical practice has shown that a particular patient who is difficult to intubate in the hands of one laryngoscopist may be successfully intubated by another laryngoscopist. In this way, experimental designs using more than one laryngoscopist introduce a source of variation, which detracts from attempts to control experimental conditions. Relying on a single laryngoscopist obviates this problem but limits the number of patients that can be enrolled into a single study. Another source of experimental error is observer variation. Observations performed by different experimenters are subject to variations and introduce another source of erroneous data. The best way to prevent this problem is for all observations to be performed by a single experimenter. This too may limit the number of patients enrolled in a single study.

Statistical tests for assessing the usefulness of criteria include sensitivity and positive predictive value. Sensitivity is the ratio of correctly identified difficult intubation patients to all the difficult intubation patients within the entire patient population. For example, take a patient population in which five patients are difficult to intubate. If a particular predictor of difficult intubation correctly identifies all five patients, its sensitivity is 100%. If the test correctly identifies only two of the five patients, its sensitivity is 2/5 or 40%. Positive predictive value is the probability that difficult intubation patients identified by the test are in fact difficult to intubate. If the test predicts that five patients will be difficult to intubate and all five of those patients are difficult to intubate, its positive predictive value is 100%. If the test predicts that 10 patients will be difficult to intubate but only 5 of them are difficult to intubate, its predictive value is 5/10 or 50%. As Yentis (2002, 2006) pointed out on more than one occasion, statistical tests such as sensitivity and positive predictive value applied to classic prediction criteria have yielded disappointing results.

In 1984, Cormack and Lehane described a grading system for comparing laryngoscopic views as follows:

Grade I—the entire glottic opening
Grade II—the posterior laryngeal aperture but not the anterior portion
Grade III—the epiglottis but not any part of the larynx
Grade IV—the soft palate but not the epiglottis

Early evidence indicated good correlation between Mallampati/Samsoon classes and laryngoscopic grades. In other words, as the Mallampati/Samsoon classes increased in number, the prediction was that corresponding laryngoscopic grades would also increase in number for any given patient. This concept formed the basis for using Mallampati/Samsoon classes to predict difficult intubation. In 1992, Rocke et al. disproved that relationship. Rocke et al. investigated several classic predictors of difficult intubation and demonstrated that none of the ones they studied was reliable predictors of difficult intubation (Figure 43-2). More recently, Shiga and Langeron independently agreed. Classic prediction criteria essentially deal with surface anatomy. They screen for some factors that are associated with difficult intubation but fail to address others. Some potential problems are hidden from surface anatomy examinations. Subglottic, glottic, and supraglottic abnormalities, such as tracheal stenosis, lingual tonsil hypertrophy, or epiglottic prolapse into the glottic opening, cannot be diagnosed by standard physical examinations for predicting difficult intubation. Pathophysiologic factors such as mobile TMJ disks or disk fragments can produce severely limited mouth opening after induction of anesthesia, when none existed before. Precise measurements of atlantoaxial motion sometimes fail to predict difficult intubation. These factors and others may be unrecognized by standard tests but complicate intubation nonetheless. At the time of this writing, no single factor reliably predicts difficult intubation. The likelihood of a difficult intubation increases when multiple predictors are present in a patient at the same time.

### 4. How is an anticipated difficult intubation approached?

Anticipated difficult intubations with proven or suspected difficult mask ventilation are best approached

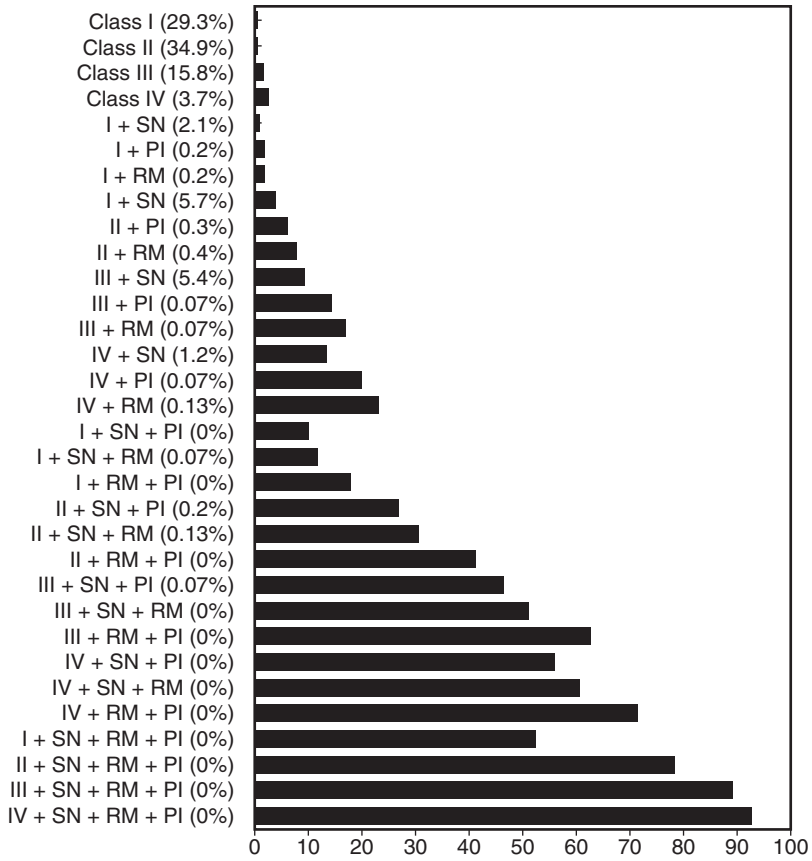



**FIGURE 43-2** ■ Probability of experiencing a difficult intubation for combinations of risk factors and their observed incidence (percentages). *PI,* Protruding maxillary incisors; *RM,* receding mandible; *SN,* short neck. (From Rocke DA, Murray WB, Rout CC, Gouws E: Relative risk analysis of factors associated with difficult intubation in obstetric anesthesia. Anesthesiology 77:67, 1992.)

with the patient awake and spontaneously breathing. Proper preparation of the airway before instrumentation is critical. Preparation begins approximately 1 hour before arrival in the operating room. At that time, antisialagogues are administered as premedication. Their use is intended to desiccate the mucosa before administration of topical local anesthetics. An intervening layer of secretions acts as a physical barrier preventing contact between local anesthetic and mucosa. Without direct contact of the two, inadequate airway anesthesia results and predisposes the patient to coughing, gagging, and withdrawal. Copious secretions impair the view through flexible fiberoptic laryngoscopes. Depending on the degree of preexisting airway compromise, preoperative sedation may be contraindicated.

After adequate antisialagogue effect, airway anesthesia is most easily achieved by nebulizing 4 mL of 4% lidocaine. Another equally effective option is to atomize the same solution. Superior laryngeal nerve blocks and transtracheal nerve blocks are sometimes required. If the nasal approach is planned, the risk of epistaxis can be minimized with topical application of 0.5% phenylephrine, 4% cocaine, or 0.05% oxymetazoline (Afrin). In the absence of local nasal pathology, flexible fiberoptic nasotracheal intubation is generally less difficult than the oral route.

After achieving satisfactory airway anesthesia, most intubation techniques progress well to successful completion. Blind techniques, retraction blades, and fiberscopes are commonly employed. Friable tumors, abscesses, and impending obstructive airway tumors often require awake tracheostomy.

### 5. Describe the management options for a patient who, after induction of anesthesia, unexpectedly cannot be intubated with a Macintosh blade; the patient has a good mask airway.

Having induced general anesthesia in a patient and then discovered a difficult intubation, it is imperative to maintain oxygenation and ventilation. This is generally accomplished with a facemask and 100% oxygen. Successful oxygenation during controlled ventilation and oxygen desaturation during intubation attempts are monitored with pulse oximetry. During traditional laryngoscopy, external posterior or lateral displacement of the larynx may bring it into view. Improved sniffing position may be helpful.

A multitude of retraction blades exist and vary in length and shape. They are used to displace the base of the tongue and epiglottis anterior to the line of sight. The most familiar types are the Macintosh and Miller blades. Difficulty with the Macintosh blade often arises when its tip fails to elevate the hyoid bone, which indirectly raises the epiglottis. Often, a straight blade elevates a floppy epiglottis when curved blades fail to

do so. Difficulty with the straight blade frequently comes from impacting on teeth. Upper airway edema or adipose tissue may sometimes encroach on the view of traditional retraction laryngoscopes, which are open on the right side.

Various stylets may be used. The hollow stylet, gummed elastic bougie, or similar devices should be available in all anesthetizing locations.

If a flexible fiberoptic laryngoscopy is not planned, blind spontaneously breathing nasotracheal intubation is an alternative offering a good chance of success. Vasoconstriction of the nasal mucosa, selection of a small nasal endotracheal tube (ETT) (6 mm), and generous lubrication of the tube's distal portion are highly recommended. If flexible fiberoptic intubation is planned, the risk of epistaxis may dissuade one from the nasal approach. Epistaxis might seriously impair mask ventilation and visualization by all means of laryngoscopy.

Compared with various retraction blades and stylets, flexible fiberoptic laryngoscopy has established a long and impressive success record with difficult intubations. Flexible fiberoptic laryngoscopy is applicable to anesthetized and awake patients. In an anesthetized patient, it can be performed with interrupted controlled ventilation by facemask, such as with traditional rigid laryngoscopy. Alternatively, it can be accomplished using simultaneous controlled ventilation via anesthesia facemasks equipped with a self-sealing diaphragm. Flexible fiberoptic intubation in a paralyzed patient is generally more difficult than in a spontaneously breathing patient because the anterior pharyngeal wall tends to collapse onto the posterior pharyngeal wall, obstructing the view. Also, the larynx assumes a more anterior position, hindering its identification. Copious blood or secretions seriously impair vision through a flexible fiberoptic laryngoscope (FFL). FFLs contain suction channels, but in contrast to suction channels in the pulmonologist's bronchoscope, the channel in the FFL is an inefficient one. Consequently, aspiration of blood and secretions is better accomplished with a standard large-bore suction device, such as the one normally used for traditional rigid laryngoscopy. Passing oxygen through the working channel of the FFL tends to push blood and secretions out of the way, prevents fogging, and enhances the patient's effective fraction of inspired oxygen ($Fio_2$). The sniffing position allows for further posterior displacement of the epiglottis, which could also obstruct the view. Consequently, cervical extension with the head flat on the bed is preferable for flexible fiberoptic laryngoscopy.

Various aids to FFL insertion exist. Care must be taken to seat oral airways exactly in the midline to prevent lateral displacement of the fiberscope, which adds to the difficulty of intubation. In cases for which it is especially important to do so, none of the presently available oral intubation airways adequately elevates the base of the tongue. Insertion of the nasotracheal tube before the fiberoptic scope risks epistaxis. Placing nasotracheal tubes too far eliminates adequate space for manipulating the scope between the nasotracheal tube and the larynx. Difficulty threading tracheal tubes into the larynx may arise if the tube's tip abuts the right arytenoid. To overcome this obstacle, the tracheal tube should be retracted 1–2 cm and rotated 90 degrees counterclockwise. This maneuver brings the tip anteriorly, away from the right arytenoid.

After exhausting one's personal repertoire of techniques, simply repeating methods that have already failed seems to have little chance of success. Additional instrumentation leads to laryngeal and pharyngeal edema predisposing the patient to airway obstruction. Alternative options are listed in Box 43-2. Initial tracheostomy is indicated for laryngeal fractures and for abscesses impinging on the airway. The ASA Difficult Airway Algorithm serves as a useful guideline (Figure 43-3).

## 6. After induction of anesthesia, ventilation by facemask and intubation are impossible; what maneuvers may help?

Inability to ventilate and intubate is a rare occurrence with a potentially tragic outcome. Several treatment options exist. Various oral and cricoid puncture methods have been described to assist with such situations.

Of the oral techniques, worldwide experience is greatest with laryngeal masks of various designs. The laryngeal mask is a tube attached to a mask. The mask has an inflatable balloon around its periphery. With the balloon deflated, the mask is advanced into the mouth and through the airway until obstruction to passage is encountered. At this point, the mask should be positioned cephalad to the esophagus and surrounding the larynx. The balloon is inflated in an attempt to create an airtight chamber around the larynx. The tube exits from the mouth and is connected to an anesthesia breathing circuit.

Laryngeal masks are available in adult and pediatric sizes. The mask works well in 90%–98% of cases. This 2%–10% failure rate is far greater than the incidence of inability to ventilate and intubate. Nevertheless, the LM has been successfully used for airway management in elective surgery as well as in cases of predicted and unanticipated difficult intubation. The laryngeal mask has been used to assist blind intubation and FFL-guided intubation in patients whose larynges could not be visualized by traditional rigid laryngoscopy.

If the inflatable balloon of the laryngeal mask is not positioned properly, a large gas leak occurs around the mask, impairing ventilation. This leak is exacerbated by

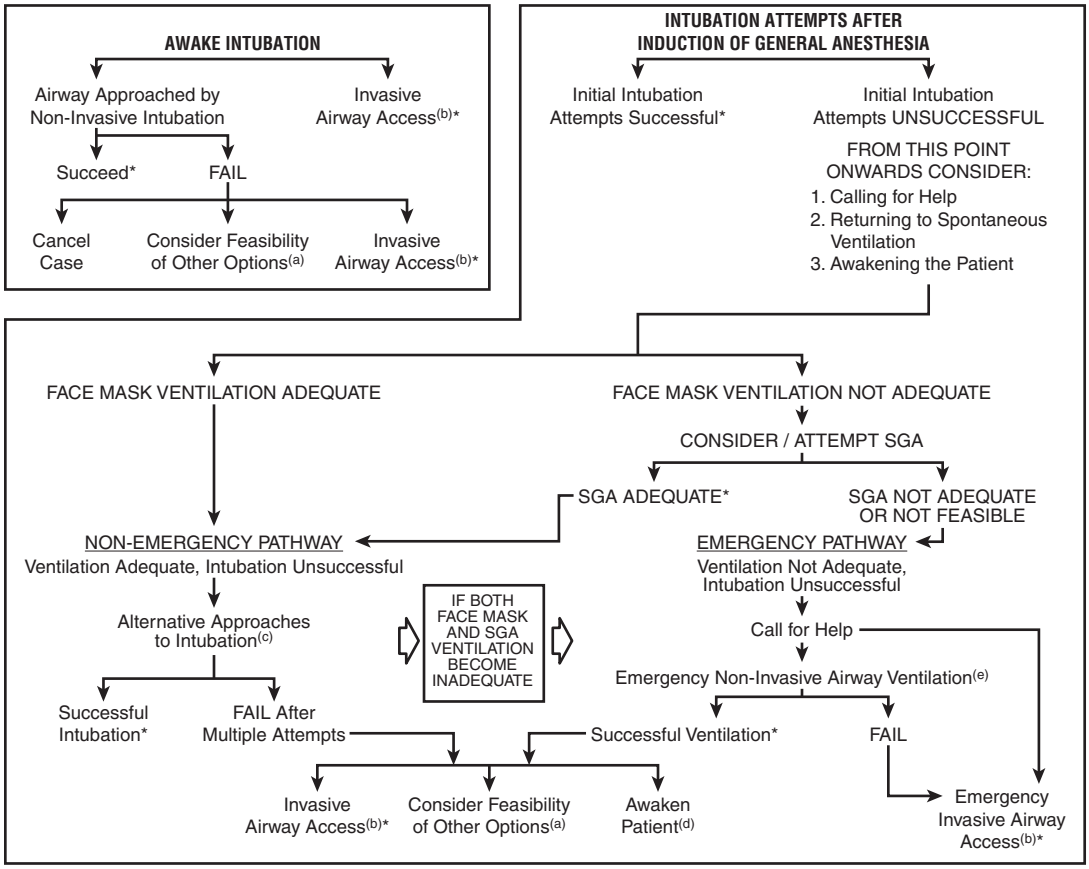
**BOX 43-2 Options for Failed Traditional Tracheal Intubation under General Anesthesia**

- Continue anesthesia by facemask
- Continue anesthesia with supraglottic device
- Regional anesthesia
- Awake spontaneous breathing (usually flexible fiberoptic intubation)
  - Same day
  - Several days later after resorption of airway edema
- Tracheostomy
- Cricothyroidotomy

AMERICAN SOCIETY OF ANESTHESIOLOGISTS

## DIFFICULT AIRWAY ALGORITHM

1. Assess the likelihood and clinical impact of basic management problems:
   - Difficulty with patient cooperation or consent
   - Difficult mask ventilation
   - Difficult supraglottic airway placement
   - Difficult laryngoscopy
   - Difficult intubation
   - Difficult surgical airway access
2. Actively pursue opportunities to deliver supplemental oxygen throughout the process of difficult airway management.
3. Consider the relative merits and feasibility of basic management choices:
   - Awake intubation vs. intubation after induction of general anesthesia
   - Non-invasive technique vs. invasive techniques for the initial approach to intubation
   - Video-assisted laryngoscopy as an initial approach to intubation
   - Preservation vs. ablation of spontaneous ventilation
4. Develop primary and alternative strategies:




* **Confirm ventilation, tracheal intubation, or SGA placement with exhaled $CO_2$**

a. Other options include (but are not limited to): surgery utilizing face mask or supraglottic airway (SGA) anesthesia (e.g., LMA, ILMA, laryngeal tube), local anesthesia infiltration or regional nerve blockade. Pursuit of these options usually implies that mask ventilation will not be problematic. Therefore, these options may be of limited value if this step in the algorithm has been reached via the Emergency Pathway.

b. Invasive airway access includes surgical or percutaneous airway, jet ventilation, and retrograde intubation.

c. Alternative difficult intubation approaches include (but are not limited to): video-assisted laryngoscopy, alternative laryngoscope blades, SGA (e.g., LMA or ILMA) as an intubation conduit (with or without fiberoptic guidance), fiberoptic intubation, intubating stylet or tube changer, light wand, and blind oral or nasal intubation.

d. Consider re-preparation of the patient for awake intubation or canceling surgery.

e. Emergency non-invasive airway ventilation consists of a SGA.

**FIGURE 43-3** ■ American Society of Anesthesiologists Difficult Airway Algorithm. This algorithm is intended as a practice guideline for difficult airway management. Practitioners are free to deviate from this algorithm as the need arises for each individual situation. (From American Society of Anesthesiologists Task Force on Difficult Airway Management: 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 118:251, 2013.)

high inflation pressures. Malposition of the balloon increases the risk of aspiration of gastric contents into the lungs. Obstruction to gas flow may occur if the tongue or epiglottis is pushed back over the larynx as the mask is inserted. Difficulty in positioning the laryngeal mask occurs 18% of the time, and failure to position properly occurs 3% of the time. The LM predictably offers little in cases of airway stenosis and gross anatomic distortion. Laryngeal masks are available in several varieties. The classic laryngeal mask airway (LMA) is shown in Figure 43-4. Multiple other models also exist. Advantages of disposable types include reduced cost for each one as well as elimination of cross-contamination from inadequately cleaned and sterilized, reusable models. An intubating laryngeal mask is designed to facilitate tracheal tube passage through the glottis. Although it works well to maintain upper airway patency, ideal alignment with the trachea can be problematic. Deviations from ideal positioning hamper tracheal tube passage. Many laryngeal masks come equipped with a distal port. The port is positioned just cephalad to the esophagus and allows egress of gastric contents that might otherwise collect in the pharynx. A tube connected to the port provides egress for pharyngeal contents. With proper alignment, a gastric tube can be inserted through this tube and into the stomach for elimination of gastric contents. Alternative supraglottic devices exist.

Of the more invasive techniques, cricothyroid puncture and transtracheal ventilation are well described. Successful use of transtracheal ventilation relies on preparation before the critical incident occurs. Equipment must be assembled and readily available. Devices are best stored in all anesthetizing locations and anywhere intubation might reasonably be anticipated. Basic equipment

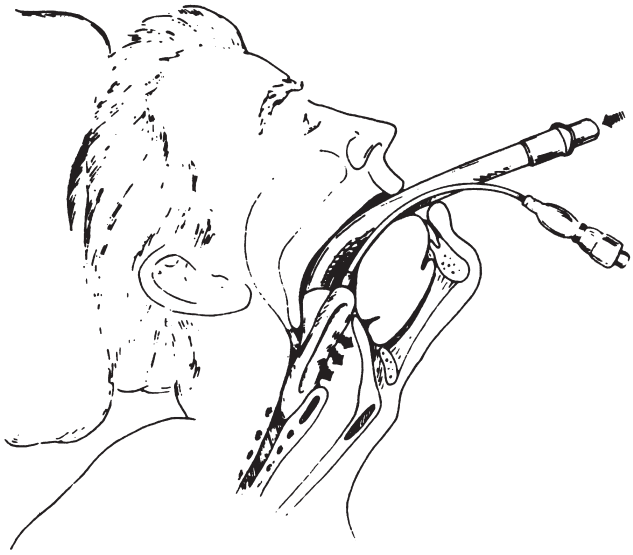


**FIGURE 43-4 ■ LMA positioned posterior to the larynx.** (From Cork R, Monk JE: Management of a suspected and re-suspected difficult laryngoscopy with the laryngeal mask airway. J Clin Anesth 4:231, 1992.)

consists of a 14-gauge over-the-needle catheter with Luer-Lok adapter, noncompressible oxygen tubing, standard 15-mm connector, and a source of pressurized oxygen (Figure 43-5). Such systems deliver gas at very high pressures and tend to disconnect at portions that are not securely fastened. Another configuration is required for anesthesia machines that do not provide easily accessible 15-mm adapters to common gas outlets. Figure 43-6 shows a system that screws into a 50 psi oxygen source

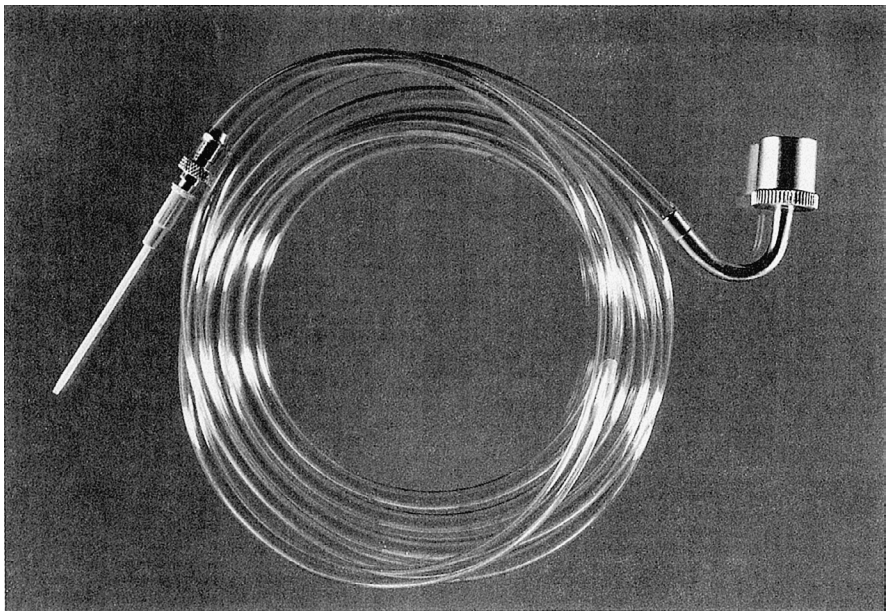


**FIGURE 43-5 ■** Cricothyroid puncture ventilation equipment (transtracheal ventilation). Most basic equipment adapts to common gas outlets on anesthesia machines or resuscitation bags. It consists of a 14-gauge over-the-needle catheter with Luer-Lok adapter, noncompressible oxygen tubing, standard 15-mm connector, and a source of pressurized oxygen. (Source of pressurized oxygen is not shown.)

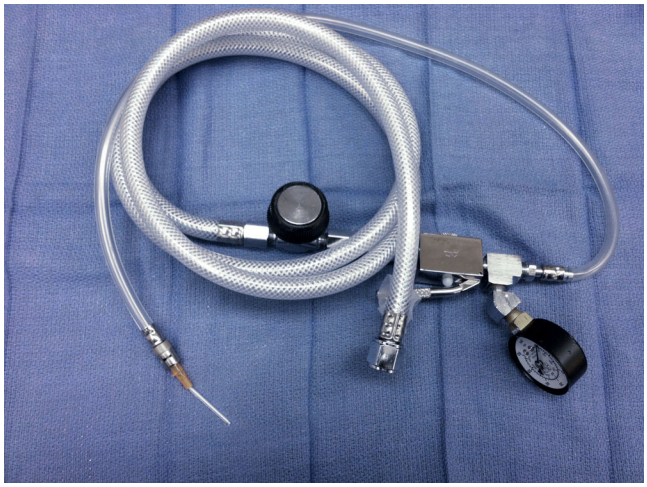


**FIGURE 43-6** ■ Cricothyroid puncture ventilation equipment (transtracheal ventilation). High-pressure system with screw adapter and pressure regulation valve.

and provides a step-down valve to reduce pressures to approximately 20 psi.

With the patient in the supine position, the head is extended to expose the anterior neck. The thyroid cartilage is palpated, and the finger is run inferiorly until a depression (the cricothyroid membrane) is felt. Another dense substance (cricoid cartilage) is appreciated just caudad to the depression. A 14-gauge needle is placed through the skin perpendicular to all planes and advanced until the cricothyroid membrane is punctured. Proper positioning within the trachea is confirmed by freely aspirating air through the needle. The needle is removed, leaving the catheter positioned in the lumen of the trachea. The device is attached to the intravenous catheter, and 100% oxygen is administered under positive pressure. Oxygen administration is most conveniently accomplished by attaching the 15-mm connector to the anesthesia machine's common gas outlet and controlling the flow of oxygen with the oxygen flush valve. Not all anesthesia machines that offer a common gas outlet function well in this circumstance. Ventilation systems using pressure step-down valves interposed between high-pressure oxygen sources, such as wall oxygen or oxygen tanks, can be attached to the same cricothyroid puncture catheter. The higher the pressure generated, the more likely the catheter will become dislodged, so a designated holder must be assigned to keep it in place. After insufflation of oxygen through the 14-gauge catheter, exhalation occurs through the natural airway. Consequently, it is important to ensure upper airway patency. If upper airway obstruction exists, gas cannot escape, and subsequent breaths stack, which risks pneumothorax.

If ventilation and intubation are impaired by tissues encroaching on the airway, rigid bronchoscopy may provide for immediate lifesaving ventilation and oxygenation. Alternatively, emergency tracheostomy can be performed. Emergency tracheostomy performed by the anesthesia care team has a high failure rate. Emergency tracheostomy performed by surgeons has a high success rate.

## 7. How is successful tracheal intubation verified?

The most reliable method of confirming successful tracheal intubation is by direct laryngoscopy with a traditional rigid laryngoscope and visualizing the tracheal tube between the vocal cords. External posterior displacement of the larynx may improve the view. Alternatively, a FFL can be advanced through the tracheal tube, and tracheal rings and carina can be identified. Two other methods of confirmation, expired carbon dioxide detection and esophageal indicator bulb inflation, are slightly less reliable. Expired carbon dioxide detection can be quantitative or qualitative. These methods frequently provide digital readouts, waveforms, or colorimetric indicators. Alternatively, the esophageal indicator bulb attached to an indwelling tracheal tube expands rapidly if the tube is located in the trachea. When positioned in the esophagus, it generally fails to inflate or expands slowly. Tertiary methods of verifying tracheal tube placement are less reliable than the above-mentioned methods and are listed in Box 43-3.

## 8. After a difficult intubation, how is postoperative extubation managed?

Extubation requires an estimate of postoperative airway edema. Repeated instrumentation during intubation and surgical manipulation independently and additively contribute to tongue base and laryngeal

**BOX 43-3 Methods to Verify Correct Tracheal Tube Placement**

**Most Reliable**

- Direct visualization of tracheal tube between the vocal cords
- Observation of carina via a flexible fiberoptic laryngoscope passed through the tracheal tube

**Very Reliable**

- Expired carbon dioxide detection by colorimetry or capnography
- Esophageal detector device

**Reliable**

- Auscultation of breath sounds
- Observation of chest expansion and contraction during inspiration and exhalation
- Epigastric auscultation and observation for gastric distention during respiration
- Tactile confirmation by assistant as ETT is passed
- Respiratory bag inflation and deflation during spontaneous respiration
- Respiratory bag compliance and spontaneous refilling
- Exhaled gas via the tracheal tube during chest compression
- Condensation and evaporation of water during respirations
- Tracheal tube cuff palpation at the suprasternal notch
- Endobronchial intubation
- Pulse oximetry
- Chest radiograph

swelling. Airway edema may culminate in respiratory obstruction after extubation.

Patients at risk for edema are best managed with prolonged tracheal intubation or tracheostomy. After edema has resolved, a trial of extubation or decannulation can be considered.

Before extubating a potentially edematous airway, the ETT cuff is deflated, and gas escaping around the tube is sought. The presence of escaping gas is encouraging but hardly pathognomonic of airway patency. Patients at substantial risk for reintubation can be extubated over a stylet. Stylets come in numerous styles. FFLs are a type of stylet that allows visualization of a portion of the airway during extubation. Oxygen can be administered through the working channel while observing for airway collapse. In the event of respiratory difficulty, airway patency can be reestablished by advancing the tracheal tube over the FFL, which is still positioned in the trachea. A jet stylet or tracheal tube exchanger may be used in a similar fashion. Jet stylets and tracheal tube exchangers share several potential complications. Both reside between the vocal cords and can produce laryngospasm, which predisposes to two problems. First, jet ventilation in the presence of upper airway obstruction results in breath-stacking because there is no egress for gas from the lungs, risking pneumothorax. Second, spontaneous respiratory efforts against a closed glottis can produce negative pressure pulmonary edema. This pulmonary edema is usually amenable to relief of the obstruction, supplemental oxygen, diuretics, and morphine. Both jet stylets and tracheal tube exchangers, if extended beyond the tracheal tube, can produce other problems. The posterior tracheal wall is membranous and is easily punctured leading to pneumomediastinum and mediastinitis. Stimulation of the carina produces hypertension, tachycardia, vigorous coughing, and retching. Even with these devices in place, the tracheal tube may not advance through the glottis. It can get caught on the base of the tongue, laryngeal cartilages, and vocal cords.

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CASE 44

# Laser Laryngoscopy

**Allan P. Reed, MD**

## QUESTIONS

1. Is postoperative voice quality worthy of consideration by the anesthesia care team?
2. What criteria are used to evaluate the airway?
3. Explain the special anesthesia requirements for laryngeal microsurgery.
4. Describe an anesthetic for laryngeal microsurgery.
5. What ventilatory modes are employed for endoscopic laryngeal surgery?
6. What are the special considerations for singers and other patients who use their voices professionally?
7. How does laser light differ from natural light?
8. What types of lasers are most frequently used for medical care?
9. What are the hazards of laser laryngoscopy?
10. How are laser airway fires treated?
11. Discuss the recognized postoperative problems that occur after laryngeal surgery.

A 50-year-old singer presents for laser laryngoscopy. She has vocal fold polyps but otherwise is in good general health.

### 1. Is postoperative voice quality worthy of consideration by the anesthesia care team?

The anesthesia care team generally focuses on major life-threatening issues. Preoperative and postoperative hoarseness is a secondary concern. However, in the minds of patients who use their voices professionally, voice problems assume great importance. Phonosurgery is dedicated to restoring voice quality. Singers, actors, teachers, clergy, lawyers, politicians, and many others use their voices professionally. These patients strive for the best quality sounds possible. Singers in particular are anxious about laryngeal instrumentation, especially tracheal intubation. They are acutely aware of instances in which patients could not sing after either brief or prolonged intubation. Intubation injuries to vocal folds are usually due to anatomic disruptions or neuromotor injury. Examples of anatomic disruptions include vocal fold tears, intubation granuloma, arytenoid dislocation, and vocal fold edema. Prolonged intubation can be complicated by laryngeal stenosis, intubation grooves, or cricoarytenoid arthrodesis and granulomas. Neuromotor injuries include vocal fold paralysis or paresis secondary to recurrent laryngeal nerve compression from a high-riding endotracheal tube (ETT) cuff. Postintubation vocal fold paralysis is uncommon given the numbers of procedures performed under general anesthesia.

Some patients whose voices are unintelligible desire to restore speech for communication. For these patients, a hoarse or soft voice is better than no voice at all. Consequently, anesthesia-related voice complications that prevent them from speaking can have substantial consequences and are worthy of our attention.

### 2. What criteria are used to evaluate the airway?

Anesthesia societies in multiple countries recommend airway evaluation focusing on history and physical examination of surface landmarks. However, these recommendations ignore many sources of airway problems. The location and size of pathologic airway lesions can have significant effects on airway management. For esophageal pathologies, such as obstructing lesions, and gastrointestinal bleeding, the potential for aspiration should be explored. Inspiratory stridor suggests airway stenosis approximately 4 mm in diameter. However, the absence of stridor does not always indicate a normal-size airway, and stridor may be absent despite a very stenosed airway. Exhausted patients may not generate enough airflow to produce stridor, even in the face of significant stenosis. Voice changes such as hoarseness are nonspecific and frequently result from small, nonobstructive lesions or potentially from mediastinal lesions. Dysphagia suggests the possibility of supraglottic obstruction. Inability to lie flat, the need to sit upright, and frequent position changes to breathe are symptoms of severe airway obstruction.

Supraglottic and glottic masses are evaluated by nasopharyngoscopy in an awake, spontaneously breathing patient. Subglottic and tracheal problems are investigated with chest x-rays, computed tomography, or magnetic resonance imaging. These problems often manifest with inspiratory and expiratory stridor. Ideally, airway imaging should be reviewed and discussed with the surgeon. Previous anesthesia records could

reveal prior problems with mask ventilation, laryngoscopy, bleeding, or extubation.

### 3. Explain the special anesthesia requirements for laryngeal microsurgery.

During laryngeal microsurgery procedures, surgeons and anesthesiologists occupy the same space at the same time. They must share the airway. The mouth and pharynx provide relatively little room for rigid suspension laryngoscopes and other tools, surgical visualization, and surgical manipulation. Millimeters of space can determine success or failure. Anesthesia equipment must take up as little room as possible. A small ETT or jet ventilation is generally used.

Airway surgery involves profound stimulation, requiring deep anesthesia for relatively brief periods. At the conclusion of surgery, stimulation quickly decreases to almost nothing, while patients remain deeply anesthetized. The goals for emergence are rapid awakening without coughing or bucking. Coughing or bucking abrades laryngeal incisions as vocal folds are forced against indwelling ETTs or the adjacent vocal fold. Coughing and bucking also can result in dislodgment of sutures and hemorrhage. Many patients are placed on voice rest postoperatively to prevent incision trauma that can impair healing. An opioid-based anesthetic with short-acting agents is desirable. An opioid-based anesthetic provides laryngeal sensory depression, allowing for smooth emergence.

Airway surgery is associated with the highest risk for postextubation airway compromise. It is of paramount importance to confirm adequate return of strength before extubation. It is the author's preference to extubate awake patients as opposed to deeply anesthetized or heavily sedated patients. Strong muscle tone is required for airway dilator muscles to maintain upper airway patency. Conscious efforts to maintain an open airway contribute to successful extubation.

### 4. Describe an anesthetic for laryngeal microsurgery.

Phonomicrosurgery usually requires general anesthesia. Surgical access to the airway and aerodigestive tracts is improved by using small ETTs and adequate muscle relaxation. In the absence of muscle relaxation, deep planes of anesthesia are required. Suspension laryngoscopy is highly stimulating and tends to produce hypertension and tachycardia. Sufficient anesthetic depth and agents that effectively blunt sympathetic stimulation, such as remifentanil or β-adrenergic blockers, or both, are commonly used. Most of these procedures are of short duration, so judicious use of muscle relaxants and short-acting anesthetic agents is helpful. The operating room table is generally turned 90 or 180 degrees from its usual position. Respiratory circuits and cables need to be sufficiently long to extend the additional distance. Laser surgery is associated with its own special risks and is discussed later.

Mobile supraglottic lesions can obstruct gas flow through the larynx during positive pressure ventilation and obscure the glottis during laryngoscopy. Classically, patients with epiglottitis receive general anesthesia followed by laryngoscopy and intubation. Nevertheless, some supraglottic lesions may indicate the need for awake intubation.

Laryngeal lesions, such as large vocal cord polyps and papillomas, have the potential to create partial airway obstruction after induction of general anesthesia. They rarely result in total airway obstruction but can make mask (or other supraglottic airway) ventilation difficult. Contrary to classic teaching, obstruction is frequently worse in anesthetized spontaneously breathing patients than in anesthetized patients receiving positive pressure ventilation by facemask. Spontaneous ventilation is negative pressure ventilation. As the diaphragm and intercostal muscles contract, intrathoracic pressure is reduced. Reduced intrathoracic pressure falls below barometric pressure and is frequently referred to as negative pressure. Negative pressure is transmitted to the upper airway, where it tends to draw pharyngeal tissues into the airway. It is as if soft tissues are imploding into the upper airway. Pharyngeal dilator muscles normally work to maintain airway patency, but general anesthesia reduces muscle tone, allowing soft tissues to collapse inward. Positive pressure ventilation tends to stent the airway open, and consequently it is more effective in these cases. If spontaneous ventilation is maintained, assisted ventilation with positive pressure and oral or nasopharyngeal airways could be beneficial.

Spontaneous ventilation is useful to evaluate airway dynamics. Tracheomalacia is a prime example. In this case, inhalation induction is performed with sevoflurane and 100% oxygen. When a sufficient depth of anesthesia is achieved, laryngoscopy to view the trachea during inspiration and expiration can proceed.

Subglottic lesions do not inhibit laryngeal visualization but can prevent advancing an ETT beyond the larynx and into the trachea. If subglottic lesions are present, a variety of small ETTs and a jet ventilation system should be available. Small-diameter ETTs are required to allow for optimal surgical visualization and manipulation. For adult patients, 5.5 mm internal diameter (ID) ETTs generally satisfy this requirement and allow for adequate gas exchange. Controversy exists over the use of such small ETTs in large adults. Adequate minute ventilation delivered through small ETTs is accompanied by high readings on inspiratory pressure monitors. This is generally of little clinical importance because small ETTs act as resistors. There is a substantial decrease in pressure across a small ETT. Actual intratracheal pressures approximate pressures seen with larger ETTs. Consequently, the risk of barotrauma is not substantially greater using small ETTs than it is with large ones. A common technique to reduce inspiratory pressures is to adjust the inspiratory-to-expiratory (I:E) ratio from 1:2 to 1:1; this provides more time for inspiration, reducing the inspiratory pressure required to achieve adequate tidal volumes. Alternative modes of ventilation, such as pressure-controlled volume guaranteed, are also applicable.

For nonobstructing airway lesions, standard techniques of induction, maintenance, and ventilation work well. It is common practice to administer topical local

anesthetic to the larynx and trachea during laryngoscopy. This practice is intended to reduce postoperative coughing and laryngospasm. Also, in the absence of muscle relaxants, anesthetized vocal folds help to provide vocal cord immobility. Lidocaine 2% or 4% solutions are commonly used for laryngotracheal anesthesia.

Vocal fold immobility is crucial for laryngeal surgery. Immobility is frequently achieved with muscle relaxants, but alternatives exist. For most short cases, reduced doses of commonly available intermediate-acting nondepolarizing neuromuscular blockers are appropriate. Loading doses of muscle relaxants should be avoided. Neuromuscular monitoring is required to determine the need for antagonism of the motor block and to determine sufficient return of strength for tracheal extubation. Airway surgery is associated with a relatively high risk of postextubation respiratory distress. Adequate muscle strength can reduce this risk.

An alternative to muscle relaxants is a deep plane of anesthesia; this is typically accomplished with total intravenous anesthesia using high-dose remifentanil (e.g., >0.2 μg/kg/min) or balanced anesthesia with remifentanil and volatile anesthetics. Relatively high doses of remifentanil render vocal cord movement unlikely. Avoiding muscle relaxants precludes anaphylaxis and residual neuromuscular blockade secondary to their use. High-dose opioids dampen the sympathetic response to laryngoscopy and intubation; however, they predispose to vocal cord adduction, which can impair mask ventilation and predispose to vocal cord trauma during intubation.

Anesthesia emergence can be accompanied by coughing and straining, both of which are potentially harmful after upper airway surgery. Forceful vocal cord adduction with or without an ETT in place exacerbates surgical tissue damage. The result is impaired healing, with vocal cord scarring and permanent adverse voice changes. Consequently, laryngeal topical anesthesia during airway manipulation and emergence from anesthesia and adequate opioid plasma levels are employed. Remifentanil offers intense analgesia and short duration of action, making it an excellent opioid choice. Alternatively, deep extubation can be considered to help reduce coughing on emergence. However, deep extubation risks aspiration of blood and debris that frequently accompanies airway surgery. High-dose opioids allow patients to awaken comfortably with the ETT in place, after which extubation can occur when they are able to protect their own airways (Box 44-1).

## 5. What ventilatory modes are employed for endoscopic laryngeal surgery?

Ventilatory techniques for laryngeal surgery are highly sophisticated. They are categorized as closed and open systems, and each one is associated with advantages and disadvantages (Table 44-1). Closed systems offer several advantages; they are familiar to the anesthesia care team, protect best against aspiration, allow positive pressure ventilation, and minimize operating room pollution. However, they also have certain disadvantages. They limit surgical visibility, interfere with surgical manipulations,

**BOX 44-1 Laryngeal Microsurgery**

**General Considerations**

- Operating room table turned 90 or 180 degrees
  - Expandable breathing circuit
  - Adequate length of monitoring cables
- Small ETT (5.5 mm ID)
- Ventilation
  - I:E ratio of 1:1 to decrease peak airway pressure may be required
  - Consider jet ventilation
- Blunt sympathetic stimulation
  - Deep plane of anesthesia
  - Opioids
  - β-adrenergic blockers
- Vocal cord immobility
  - Reduced doses of intermediate-acting muscle relaxants
  - Opioids
  - Deep plane of anesthesia
- Emergence
  - Avoid coughing and bucking

**Considerations by Pathology**

- Airway dynamics (e.g., tracheomalacia)
  - Maintain spontaneous ventilation for diagnostic purposes
- Laryngeal lesions
  - Less obstruction with positive pressure ventilation
  - Potentially difficult facemask or supraglottic airway ventilation
- Subglottic lesions
  - May be difficult to pass tracheal tube
  - Consider jet ventilation

TABLE 44-1 **Advantages and Disadvantages of Closed versus Open Anesthesia Systems**

| | Advantages | Disadvantages |
|---|---|---|
| Closed systems | Familiar to all anesthesiologists<br>Best protection against aspiration<br>PPV possible<br>Minimal OR pollution | Limits surgical visibility<br>Interferes with surgical manipulation<br>Risks ETT-related laryngeal trauma<br>Risk of fire during laser surgery |
| Open systems | Maximum surgical visibility<br>Maximum surgical manipulation<br>↓ risk of ETT-related tracheal trauma<br>↓ risk of fire during laser surgery | Requires special knowledge, training, and equipment<br>No aspiration protection<br>Cannot provide PPV |

*ETT,* Endotracheal tube; *OR,* operating room; *PPV,* positive pressure ventilation.

risk ETT-related laryngeal damage, and predispose to fire during laser applications depending on the type of ETT used.

Open systems maximize laryngeal visualization, reduce the risk of ETT trauma, and minimize the risk of laser fires. Some types of open system ventilation require special knowledge, training, and equipment. Also, open systems fail to protect against aspiration. Selection of open versus closed systems is based on the location, size, mobility, and vascularity of the lesion. Certain operations may require changing from one method to another. For example, a closed system with an ETT could be changed to an open system intraoperatively for a lesion that is rendered inaccessible by the ETT. A jet ventilation system may be changed to a closed system with an ETT for excessive blood or debris that could cause aspiration pneumonia.

Open techniques of ventilation include spontaneous ventilation, apneic oxygenation, and jet ventilation. During spontaneous ventilation, anesthesia maintenance is achieved with potent inhalation agents via facemask, nasopharyngeal airway, or laryngoscope or bronchoscope side port. Disadvantages of spontaneous ventilation with potent anesthetic gases include coughing, bucking, apnea, laryngospasm, vocal cord movement, hemodynamic fluctuations, inability to protect against aspiration, and operating room pollution with anesthetic gases. Intravenous agents help to overcome some of these problems. Remifentanil and propofol are frequently used adjuncts.

Apneic oxygenation is applicable to foreign body removal as well as nonobstructing glottic and subglottic lesions. Surgical manipulation occurs during apneic periods. Oxygenation can be provided by anesthesia facemask or ETT. This technique works best in patients with normal functional residual capacity. One administers 100% oxygen in an attempt to reach an end-tidal oxygen concentration of >90%. Apneic periods and surgical manipulation are allowed to proceed until oxygen saturations by pulse oximetry ($SpO_2$) decrease to the low 90s. Anesthesia is maintained with intravenous agents or potent inhaled anesthetics or both. Time for surgical manipulation is limited by oxyhemoglobin desaturation.

Jet ventilation requires administration of 100% oxygen under approximately 20 pounds/square inch (psi) pressure, via a catheter or blunt needle. Jet ventilation systems do not accommodate potent inhaled anesthesia vaporizers. Consequently, total intravenous anesthesia is required. Remifentanil, 0.05–0.2 μg/kg/min, and propofol, 50–100 μg/kg/min, are commonly employed.

Supraglottic (proximal) jet ventilation is performed by fixing a jet needle to a suspension laryngoscope or rigid bronchoscope. The jet needle is aimed at the larynx so that oxygen enters the trachea. Advantages of supraglottic jet ventilation include an unobstructed surgical view and limited risk of laser fires. The risk of laser fire is limited by eliminating polyvinyl chloride (PVC) ETTs and by diluting delivered oxygen jets with room air. Room air entrainment is explained by the Venturi principle. Potential problems include poor oxygenation; gastric insufflation; aspiration of blood, smoke, and debris; vocal cord movement; and barotrauma.

Subglottic jet ventilation involves placing a 2–3 mm diameter jetting catheter into the trachea. Oxygen is delivered directly into the trachea. A major advantage of subglottic jet ventilation over proximal jet ventilation is vocal cord immobility. Disadvantages of subglottic compared with proximal jet ventilation include slight obstruction of the surgical field and barotrauma.

Both proximal and subglottic techniques provide adequate oxygenation and ventilation. Sanders' manual ventilator valves are applicable to normal respiratory rates. High-frequency jet ventilators are set to deliver approximately 110 breaths per minute. High-frequency jet ventilation provides for continuous gas flow out of the airway, which tends to carry away small amounts of blood and debris as well as reducing peak and mean airway pressures, which could minimize ventilator-related hypotension. Ventilator rate, percent inspiratory time, and driving pressure affect arterial carbon dioxide tension ($PaCO_2$). Continuous positive airway pressure and fraction of inspired oxygen ($FiO_2$) contribute to oxygenation.

Jet ventilation requires airway patency for air entrainment and gas egress. Upper airway obstruction that does not allow escape of gas from the lungs predisposes to pneumothorax and pneumomediastinum. Airway patency can be achieved with chin lift, jaw thrust, or placement of a laryngoscope.

The Venturi principle draws large volumes of gas into the lungs, augmenting the small oxygen pulses delivered directly by high-frequency jet ventilation. Adequacy of oxygenation is monitored by pulse oximetry. Ventilation is monitored noninvasively by capnometry. Open systems are amenable to qualitative measurement of end-tidal carbon dioxide ($ETCO_2$), which demonstrates that ventilation is occurring. Quantitative measurement of $ETCO_2$ from open systems is of little clinical value. Chest wall undulations and breath sounds are clinical evidence of ventilation.

## 6. What are the special considerations for singers and other patients who use their voices professionally?

Most patients experiencing postoperative voice changes find it annoying. Patients who use their voices professionally find it devastating. Scrupulous attention to detail and superior skills are required in these patients. Induction of anesthesia must provide optimal intubating conditions. The requirements are deep anesthesia and profound muscle relaxation. The combination of both deep anesthesia and profound muscle relaxation allows the glottic opening to fall posteriorly for ease of visualization and provides vocal cord abduction. Vocal cord abduction moves the cords away from the glottic midline, reducing the risk for trauma during ETT passage. Adducted vocal cords are subject to laceration and hematoma formation as the ETT is inserted. The ETT should be passed through the posterior glottis, between both vocal cords without touching either one. Stylets are avoided if possible. Intubation over fiberscopes risks contact with vocal cords during ETT advancement. Blind intubation is similarly discouraged. When inserting the laryngoscope blade, it is best to look for the glottis from a proximal to distal direction to avoid arytenoid injury from the laryngoscope blade. Emergence should be free from coughing

and bucking. At extubation, the ETT cuff is completely deflated, and the tube is removed during inspiration.

For brief procedures, 5.5 mm ID ETTs provide minimal laryngeal trauma, good gas exchange, and excellent surgical visualization. For longer operations, 6.0 mm ID and 6.5 mm ID ETTs work well for most adults.

Supraglottic devices, such as laryngeal masks, avoid tracheal intubation and its inherent risks. However, they are not without potential problems. Supraglottic devices do not protect against aspiration, expose laryngeal mucosa to desiccation from dry anesthetic gases, and have been associated with arytenoid dislocation and nerve damage.

### 7. How does laser light differ from natural light?

The acronym "laser" stands for *l*ight *a*mplification by *s*timulated *e*mission of *r*adiation. Laser light is a single frequency of radiation emitted in parallel beams. Its spot size does not vary over distance. Natural light diverges as distance from its source increases. Laser light is monochromatic. Natural light is composed of a spectrum of wavelengths representing many colors.

### 8. What types of lasers are most frequently used for medical care?

Carbon dioxide ($CO_2$) lasers are most commonly used for laryngoscopy. The laser energy is absorbed by water with a spread of only a few cell layers. $CO_2$ lasers create precise vaporization with little peripheral damage. $CO_2$ laser light is invisible, so an aiming beam of helium-neon is used to demonstrate where the laser is pointed. Neodymium:yttrium-aluminum-garnet (Nd:YAG) lasers are used for thermocoagulation of hemorrhagic lesions. They are used for respiratory tumors and gastrointestinal tract varices. Ruby and argon lasers are absorbed by pigmented cells such as hemoglobin.

### 9. What are the hazards of laser laryngoscopy?

The most well-known hazard of laser laryngoscopy is airway fire. Anesthetic management is designed to minimize the potential for fire. Gas mixtures are formulated to reduce the probability of combustion, while simultaneously providing adequate oxygenation. Oxygen and nitrous oxide ($N_2O$) individually support combustion. $FiO_2$ is supplied at 30% and increased only if required to improve oxyhemoglobin saturation. $N_2O$ is avoided during laser laryngoscopy. ETT cuffs that form a poor seal or that are deflated by laser beams leak inspired gases into the larynx. Delivered high oxygen concentrations or $N_2O$ migrates to the larynx, so fire is a risk with continued laser use. Many laser ETTs are equipped with two cuffs. If the upper cuff is unintentionally deflated, the lower cuff should still provide an airtight seal.

Additional problems related to lasers include atmospheric contamination, perforation of unintended adjacent tissues, inappropriate energy transfer, and embolic events (usually occurring during gynecologic procedures). Atmospheric contamination is the most commonly occurring complication of laser surgery. Laser light vaporizes intracellular water and emits a plume of smoke. The smoke could contain carcinogens and viral particles. When released into the atmosphere, these contaminants contact exposed skin of patients and operating room personnel. They could also be inhaled by individuals in the room. Total body draping for patients and special masks that resist laser plume contaminants for personnel should be used. Smoke evacuators are also helpful. Perforation of the esophagus can occur during laryngeal surgery. Inappropriate energy transfer has the potential to injure patients and operating room staff. Examples include ignition of an ETT or surgical drapes. These hazards are minimized by aiming the beam before activating it.

The potential for eye damage can be reduced by taping the eyelids shut and covering them with moist gauze, metallic eye shields, or both. Wet towels are placed around the patient's head, face, and neck to decrease the risk of fire from an errant laser beam. Wraparound goggles are used to protect patients and personnel from eye damage. Clear plastic or glass goggles block $CO_2$ lasers, but specific colored goggles are required for other types of lasers, such as Nd:YAG and argon lasers.

Lasers place anesthesia equipment at risk for damage. Lasers have ignited ETTs. PVC ETTs are readily penetrated by lasers. When penetration occurs, flames are created, and PVC degrades to toxic substances. Flames are directed toward the lungs, resulting in tracheal damage and pulmonary burns. When these conditions are duplicated in a laboratory, flames exiting the ETT are reminiscent of a blowtorch. Metal ETTs reduce the hazard but are laser resistant, not laser proof. The cuffs on metal ETTs are highly susceptible to fire from laser damage. For this reason, cuffs are filled with water. The hope is that a small fire would be extinguished by water escaping from the perforated cuff. Packing the ETT cuff with saline-soaked gauze helps to reduce the risk of perforation and fires. Box 44-2 lists the components of a typical anesthetic for laser laryngoscopy.

### 10. How are laser airway fires treated?

Precautions to minimize the risk of airway laser fires do not prevent all of them. Surgeons are most likely to identify the

**BOX 44-2 Components of a Typical Anesthetic for Laser Laryngoscopy**

**Gas Mixture**
- Avoid nitrous oxide
- Use lowest $FiO_2$ patient will tolerate (goal 30%)
- Preferable mixtures are air/oxygen or helium/oxygen

**Total Intravenous Anesthesia**
- Propofol infusion
- Remifentanil infusion

**Ventilation Systems**
- Closed circle system
- Low-frequency (handheld) jet ventilation system
- High-frequency jet ventilation system

*$FiO_2$,* fraction of inspired oxygen.

fire first. As soon as the fire is recognized, oxygen administration should be stopped, and a burning ETT or cottonoid should be removed. Oxygen administration is interrupted first to prevent additional airway damage from a flame that is drawn into the uppermost portions of the airway as the burning object is removed. If tissues continue to burn, water should be poured down the airway to extinguish the fire. An easily accessible bowl or bottle of water should be kept on the operating room nurse's table for this purpose. When the fire has been extinguished, oxygenation can be resumed by facemask or a new ETT. Examination of the airway is then performed. Prophylactic tracheal intubation against future airway edema and resulting obstruction is probably prudent but may be difficult. If pulmonary burns are anticipated, tracheal intubation is also recommended. If the original tracheal intubation was difficult, extubation may not be the best choice. It is possible that tracheal reintubation would be more difficult after instrumentation and fire. Sometimes it may be best to leave the original ETT in place if it is functioning well. Tracheostomy may be necessary. When airway control is confirmed, bronchoscopy and laryngoscopy for diagnosis of airway burns should be performed. Evidence of inhalation or smoke damage may require lavage, high-dose steroids, antibiotics, and positive pressure mechanical ventilation.

### 11. Discuss the recognized postoperative problems that occur after laryngeal surgery.

Laryngeal surgery is frequently accompanied by postoperative upper airway problems. After tracheal extubation, blood, secretions, debris, or pain in the distribution of the superior laryngeal nerve can produce laryngospasm. It can result in partial or total airway obstruction. Attempts to prevent laryngospasm include topical local anesthesia, intravenous lidocaine, and adequate analgesia. Treatment includes suctioning the airway, administration of 100% oxygen by facemask, positive pressure to splint the airway open, and small doses of succinylcholine (10–20 mg). Alternatively, induction agents such as propofol may help. Other causes of postextubation stridor include laryngomalacia, tracheomalacia, vocal cord paralysis, airway edema, hematoma, soft tissue obstruction, and retained foreign body (e.g., cottonoid, throat pack). Fiberoptic laryngoscopy can help make the diagnosis.

One sign of upper airway obstruction is stridor. Stridor is usually a high-pitched inspiratory noise emanating from the airway. It can result from partial obstruction or near-complete obstruction. Treatment options are 100% oxygen by facemask, sitting position, and steroids. Some patients may benefit from nebulized racemic epinephrine. For selected patients, heliox, a helium/oxygen mixture, can improve gas flow through a narrowed airway. Stridorous noise can diminish because the airway diameter is improving or because it is getting worse and less gas is passing through it.

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CASE 45

# Functional Endoscopic Sinus Surgery

**Alan J. Sim, MD • Adam I. Levine, MD**

## QUESTIONS

1. What is functional endoscopic sinus surgery?
2. To what are complications associated with functional endoscopic sinus surgery attributed?
3. List anesthetic considerations and goals.
4. What information should be obtained during the preoperative assessment?
5. Describe Samter's triad and the anesthetic implications.
6. Explain the concept of "controlled" or "deliberate" hypotensive anesthetic technique.
7. Explain the risks and benefits of deliberate hypotension.
8. Describe the various techniques and medications used to improve the quality of the surgical field by both surgeons and anesthesiologists.
9. What techniques are available to decrease postoperative pain and minimize recovery time after functional endoscopic sinus surgery?

A 25-year-old woman with chronic sinusitis presents for functional endoscopic sinus surgery (FESS). She has a history of asthma, nasal polyps, and recurrent sinus infections that are unresponsive to multiple treatments with steroids and antibiotics. She reports a severe allergy to aspirin and is anxious about postoperative pain. After induction of general anesthesia, her blood pressure monitor reads 70/40 mm Hg. The surgeon complains of increased bleeding in the field and asks to decrease the blood pressure further to improve visualization.

### 1. What is functional endoscopic sinus surgery?

FESS is a nasal endoscopic technique that allows visualization of the paranasal sinuses and nasal cavity without a skin incision. Described in the late 1970s by Messerklinger and Stamberger, FESS has become increasingly popular in the last 30 years and is now one of the most commonly performed ambulatory surgical procedures in otolaryngology. Combined with its low risk of major complications and high success rate, it is the mainstay in the surgical treatment of sinusitis; nasal polyps; epistaxis; and bacterial, fungal, recurrent, acute, and chronic sinus problems. Across gender, ethnicity, and age groups, chronic sinusitis affects approximately 35 million Americans annually and accounts for 11.6 million physician visits each year. Chronic sinusitis has been shown to have a dramatic effect on quality of life, comparable with that seen in conditions such as coronary artery disease and asthma. More recently, functional sinus endoscopy has expanded to provide a relatively low-morbidity approach to various other surgical procedures, including skull base surgery, transsphenoidal pituitary tumor resection, and treatment of vascular malformations.

### 2. To what are complications associated with functional endoscopic sinus surgery attributed?

FESS generally is a low-risk procedure and carries with it a large safety profile. However, many catastrophic complications, including death, have been reported in patients undergoing FESS. These complications include massive hemorrhage, direct brain injury, blindness from ocular and optic nerve damage, anosmia (impaired sense of smell), cerebrospinal fluid leak, and intracranial infection. These complications are listed in Table 45-1, and they are categorized into three major groups: orbital, intracranial, and nasal. These complications have been attributed to the location of the paranasal sinuses and nasal cavity within the skull and their close proximity to numerous major and significant anatomic structures, such as the internal carotid arteries, orbits, optic nerves, and intracranial cavity (Figure 45-1).

Because of the limited field of view through endoscopes, the risk of major complications is thought to increase when uncontrolled or excessive intraoperative bleeding into the surgical field impairs visualization of important anatomic structures. Intraoperative bleeding and poor surgical conditions not only increase complications but also can prolong total surgical time and lead to incomplete resection of tissue or tumors, which may require reoperations. Numerous factors related to the patient's comorbidities and medications,

TABLE 45-1 **Major Complications Associated with Functional Endoscopic Sinus Surgery**

| Orbital | Intracranial | Nasal |
|---|---|---|
| Orbital hemorrhage | Cerebrospinal fluid leak | Adhesions |
| Abscess (infection) | Meningitis | Anosmia |
| Blindness (damage to optic nerve) | Brain abscess | Hyposmia |
| | Intracranial hemorrhage | Injury to lacrimal duct |

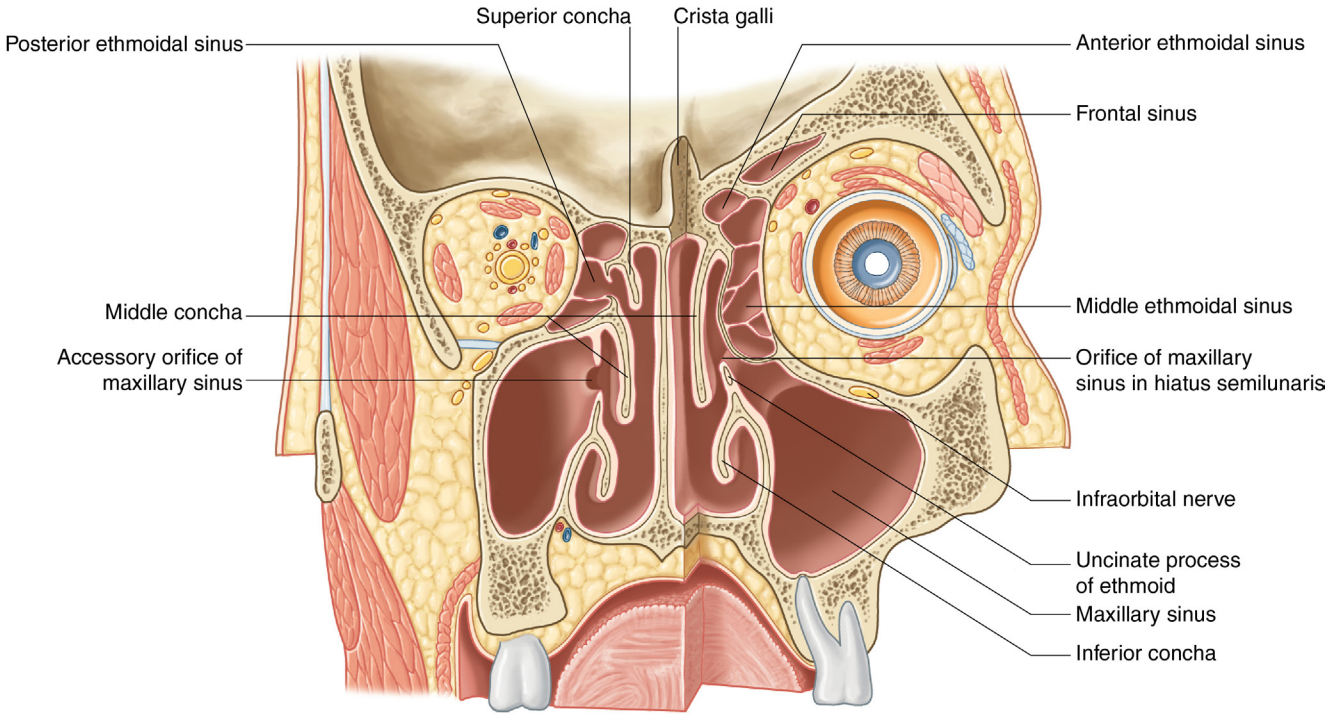


**FIGURE 45-1** ■ **Proximity of sinuses and surgical field to critical structures, including the brain and orbit.** (From Standring S [ed.]: Gray's Anatomy: The Anatomical Basis of Clinical Practice, 40th edition. Churchill Livingstone, Philadelphia, 2009.)

the type of procedure performed, and the anesthetic technique can contribute to a poorly visualized surgical field secondary to excessive intraoperative bleeding.

### 3. List anesthetic considerations and goals.

In highly motivated patients with minimal or limited sinonasal disease, simple sinus surgery can be performed with infiltration of local anesthetic, nerve blocks, and vasoconstrictors alone or with monitored anesthesia care. In such instances, excellent communication between all parties involved (i.e., surgeon, anesthesiologist, and patient) is necessary to create optimal surgical conditions. However, monitored anesthesia care should be used with caution in patients who may be uncooperative (e.g., children, developmentally disabled adults), possess potentially difficult airways (e.g., patients with obstructive sleep apnea, obesity, airway pathology), have a risk of aspiration (e.g., patients with gastroesophageal reflux disease), or require longer operative times. Active infections, extensive sinusitis, and large tumors may be associated with increased blood loss. In addition, the applications of FESS as a surgical technique are constantly broadening, including skull base surgery. Providing a secure airway and motionless surgical field via general anesthesia is likely to be preferred for most procedures.

For reasons stated earlier, facilitation of a "bloodless" surgical field should be a principal concern. Other important anesthetic considerations and goals for FESS are listed in Table 45-2. These include airway protection and prevention of aspiration of blood and tissue, patient immobility, and emergence from anesthesia without bucking on extubation. Coughing or straining can increase postoperative bleeding. In addition, because FESS is often performed as an outpatient ambulatory procedure, a rapid recovery profile is highly desired. Avoiding postoperative nausea and vomiting (PONV) (postoperative retching can also promote postoperative bleeding)

TABLE 45-2 **Summary of Goals for Functional Endoscopic Sinus Surgery**

| Otolaryngologist | Anesthesiologist | Patient |
|---|---|---|
| Increased visualization | Secure airway and prevent aspiration | Good pain control |
| Minimal bleeding | Safely achieve hypotension | Decreased nausea and vomiting |
| Motionless field | Smooth emergence from anesthesia | Early discharge from PACU |
| Access to nasal passages | | |

*PACU,* Postanesthesia care unit.

while providing sufficient postoperative analgesia is also desirable.

## 4. What information should be obtained during the preoperative assessment?

Anesthesiologists caring for patients undergoing FESS must constantly negotiate between the patient's various comorbidities and the risks incurred by optimizing the surgical field (i.e., reduced intraoperative bleeding) via induced physiologic derangements (i.e., reduction in cardiac output [CO] and hypotension). A thorough yet directed evaluation done in accordance with current American Society of Anesthesiologists (ASA) practice advisory guidelines on preanesthetic evaluation should be performed in all patients undergoing FESS.

"Controlled hypotension" is not without risk, and patients with significant cardiac or vascular disease, including valvular pathology, congestive heart failure, and atherosclerotic disease may not tolerate significant decreases in mean arterial pressure (MAP). Significant end-organ damage can result. Assessment of physiologic reserve and tolerance of "deliberate hypotension" can be obtained with a history focusing on exercise tolerance and symptoms with physical exertion. Complaints of dyspnea, chest pain, palpitations, or dizziness with climbing two or more flights of stairs (i.e., >4 metabolic equivalents or METS) or occasionally during rest may indicate the need for further cardiovascular testing, such as an electrocardiogram (ECG), echocardiogram, stress test, or coronary angiography.

Local vasoconstrictors such as cocaine or epinephrine are commonly applied in FESS. Patients with significant coronary artery disease or cardiac arrhythmias may not tolerate the tachycardia and hypertension associated with increased circulating catecholamines. Cocaine and epinephrine should be used with caution in these patients. Antiplatelet or anticoagulation therapy should be discontinued before surgery in concordance with current practice guidelines, particularly in the setting of coronary stents. As of 2010, patients with drug-eluting stents taking clopidogrel and aspirin should avoid elective surgery and cessation of antiplatelet therapy until at least 1 year after placement of the stent, and resumption of these medications should be coordinated carefully with the patient's cardiologist. The American College of Cardiology/American Heart Association (ACC/AHA) further recommended that, if possible, aspirin should be continued into the perioperative period even after 1 year has passed since placement of a drug-eluting stent. It is important that the perioperative management of anticoagulation therapy in these patients is discussed between the surgeon, the anesthesiologist, and the patient's cardiologist before the day of surgery. Helpful preoperative studies include prothrombin time, activated thromboplastin time, platelet count, and complete blood count.

## 5. Describe Samter's triad and the anesthetic implications.

Patients undergoing FESS tend to share certain comorbidities that may be of particular concern to anesthesiologists (Table 45-3). Preoperative diagnoses and indications for FESS include nasal polyps, chronic sinusitis, recurrent sinus infections, benign and malignant tumors, and management of previous surgical procedures (e.g., cerebrospinal fluid

TABLE 45-3 **Summary of Common Comorbidities in Patients Presenting for Functional Endoscopic Sinus Surgery**

| Cardiac | Respiratory | Endocrine |
|---|---|---|
| Coronary artery disease | Chronic sinusitis | Long-term steroid use |
| Atrial fibrillation (on long-term anticoagulation) | Nasal polyposis and atopy | Diabetes |
| Valvular disorders (e.g., aortic stenosis) | Asthma or reactive airways disease | Hyperthyroidism |
| | Obstructive sleep apnea | Pituitary lesions (skull base surgery) |
| | COPD | |

*COPD,* Chronic obstructive pulmonary disease.

leak, scar tissue formation). The coexistence of asthma or reactive airways disease and nasal polyposis in patients is roughly 20%–30%. Samter's triad, or aspirin-exacerbated respiratory disease, is the combination of reactive airways disease, chronic rhinitis and nasal polyps, and sensitivity to aspirin. The disease is produced by an abnormality in the arachidonic acid cascade resulting in overproduction of leukotrienes. Aspirin blocks the production of prostaglandins and shifts the cascade toward the production of leukotrienes, precipitating allergylike effects, such as bronchospasm, urticaria, or anaphylaxis. Other nonsteroidal antiinflammatory drugs (NSAIDs), such as ketorolac or ibuprofen, similarly block prostaglandin formation and should be avoided in these patients, although acetaminophen is generally considered safe.

Patients with a history of poorly controlled asthma or reactive airways disease commonly present for FESS. These patients should be seen and medically optimized before surgery as indicated by history and symptoms. Preoperative use of oral or inhaled $\beta_2$-adrenergic agonists (e.g., albuterol), anticholinergics (e.g., ipratropium bromide), antileukotrienes (e.g., montelukast), corticosteroids, and antibiotics may be necessary. Achieving controlled hypotension through the use of intraoperative β-adrenergic blockers, including $\beta_1$-selective agents (e.g., metoprolol, esmolol), should be approached with caution because of increased likelihood of bronchospasm.

Long-term steroid use is also prevalent among patients undergoing FESS. Although routine use of steroids for treatment of chronic sinusitis is controversial, preoperative steroids have been shown to improve surgical conditions in patients with rhinosinusitis and polyposis owing to their antiinflammatory and antiedema effects. In addition, perioperative use of steroids is particularly advantageous because steroids have effective antiemetic properties. Adrenal or pituitary insufficiency may be a concern in these patients; however, as long as patients receive their usual daily maintenance dose preoperatively or are administered equivalent intravenous doses during the intraoperative period, it generally does not pose a problem.

## 6. Explain the concept of "controlled" or "deliberate" hypotensive anesthetic technique.

Assuming normal platelet function and barring any frank coagulopathy, intraoperative bleeding in FESS primarily depends on the extensive vascularity of nasal and sinus mucosa. Intraoperative bleeding is also a function of the intensity of blood flow through the major vessels and capillaries within the nasal cavity. This intensity is influenced greatly by the relationship between MAP and regional or central venous pressures. "Controlled" hypotension is an anesthetic technique aimed at "deliberately" significantly decreasing the MAP and has long been advocated to aid in the reduction of blood loss and improve visualization in sinus surgery.

It is generally accepted that one can safely achieve a 30% decrease from baseline MAP or an absolute value of 50 mm Hg in healthy patients with ASA class I status. However, deliberate hypotension itself cannot be defined by an exact number, percentage, or blood pressure measurement. The degree of deliberate or controlled hypotension must be individualized to each patient and should be tailored until the desired effect is obtained (i.e., dry or bloodless surgical field) as opposed to a predetermined value. The benefit of achieving a "bloodless field" must always be counterbalanced by the necessity to provide adequate oxygen delivery to tissues by maintaining acceptable cerebral and coronary blood flow.

MAP is defined as the product of systemic vascular resistance (SVR) and CO, as follows:

$$\text{MAP} = \text{SVR} \times \text{CO}$$

A reduction in SVR, CO, or both can be implemented to achieve a lower MAP. However, more recent evidence has suggested that interventions that aim at reducing CO have been demonstrated to be more effective in improving surgical conditions in FESS compared with interventions reducing SVR. Reduction of SVR is often achieved through the use of vasodilating agents, such as calcium channel blockers, nitrates, hydralazine, or potent inhaled anesthetics. In addition, drugs such as labetalol or phentolamine provide blockade of α-adrenergic receptors, with significant SVR reduction. However, improvement of operating conditions via a reduction of SVR is seldom seen unless profound hypotension is experienced (MAP $<$50 mm Hg), and there is evidence to suggest that excessive vasodilation may exacerbate bleeding and promote increased capillary blood flow.

As stated earlier, a reduction in CO effectively decreases MAP. CO depends on several physiologic parameters, including preload, afterload, contractility, heart rate, and rhythm. Pharmacologic blockade of β-adrenergic receptors through the use of metoprolol, labetalol, and esmolol decreases heart rate and contractility. Numerous studies have shown a significant correlation between bradycardia and improved surgical conditions. In addition, studies in which β-adrenergic blockade was the primary technique in CO reduction demonstrated achievement of optimal surgical conditions at a higher MAP ($>$65 mm Hg). Short-acting β-adrenergic blockade via an esmolol infusion was found to provide superior surgical conditions compared with sodium nitroprusside, a vasodilating agent, which required a much lower MAP of 50–54 mm Hg to achieve optimal surgical conditions. This finding suggests that "deliberate hypotension," or a simple reduction in systemic blood pressure, is not the contributing factor in reduction of intraoperative bleeding, but rather a "deliberately decreased CO" via a reduction in heart rate and contractility.

## 7. Explain the risks and benefits of deliberate hypotension.

As previously stated, inducing hypotension is not without risk. The use of β-adrenergic blockers in perioperative care is controversial. Current studies on routine use of perioperative β-adrenergic blockade show an increased risk of morbidity and mortality in patients not requiring these agents perioperatively. Patients who were at high risk of cardiovascular complications and who were not receiving β-adrenergic blockers preoperatively were observed to be at higher risk for

adverse outcomes postoperatively. In patients with a low risk of cardiovascular complications, the effects of β-adrenergic blockade during the perioperative period on morbidity and mortality have yet to be studied. A significant number of patients presenting for FESS have associated reactive airways disease, and β-adrenergic blockade is contraindicated in these patients. Regardless of the use of β-adrenergic blockade or vasodilatory agents, deliberate reduction of CO is not without problems. Significant ischemia causing organ failure as a result of controlled hypotension is estimated at 0.6%. As previously stated, the benefits of a bloodless surgical field may be at odds with the risks incurred by significantly decreasing tissue perfusion and limiting oxygen delivery to vital organs. "Controlled" hypotension may be especially challenging in certain patient populations (e.g., patients with known cardiovascular disease, patients with valvular pathology such as aortic stenosis and carotid disease). Implementation of such a technique should be judiciously tailored to each patient's specific needs and limitations.

## 8. Describe the various techniques and medications used to improve the quality of the surgical field by both surgeons and anesthesiologists.

An important anesthetic goal for FESS, regardless of technique, is to minimize intraoperative bleeding. Even small amounts of blood in the surgical field can significantly compromise visibility because of the limited space of the nose and sinus. A bloodless field through deliberate hypotension is not always feasible. When successful, a bloodless surgical field improves surgical visibility, minimizes surgical time, and reduces surgical risk. Although the cause of significant intraoperative bleeding is multifactorial, a variety of effective techniques can be implemented during the perioperative period that reduce bleeding and inflammation.

### *Preoperative Medications*

There are several interventions that can reduce intraoperative bleeding before surgery. Correction of coagulopathies, induced or not, should be considered. Often a discussion with the patient's primary care physician or cardiologist is necessary, particularly if discontinuation of antiplatelet therapy and other anticoagulants places the patient at significant cardiovascular risk. Examples of such disorders are valvular disease and severe coronary artery disease. The otolaryngologist may also place the patient on a steroid regimen, which can reduce inflammation and edema and is generally advocated.

Local vasoconstriction is another common intervention used by otolaryngologists to reduce intraoperative bleeding. Vasoactive medications are injected and infiltrated into the nasal sinuses to decrease mucosal congestion, reduce blood loss, and help achieve hemostasis. Combined with local anesthetics, these medications are frequently employed to provide intraoperative and postoperative analgesia. Topical agents are also used in combination with infiltration techniques. Oxymetazoline, phenylephrine, cocaine, and epinephrine are the vasoactive agents most commonly used in FESS. These drugs are associated with significant risks secondary to systemic absorption. Reported serious adverse consequences include bradycardia, unstable tachyarrhythmias, hypertensive crisis, myocardial infarction, stroke, and cardiogenic shock. The use of these medications should be limited or avoided completely in patients with significant cardiac disease. Hypertension related to phenylephrine and epinephrine is usually short-lived and generally dissipates spontaneously. Specific treatment is not required. When hypertension from phenylephrine and epinephrine persists, β-adrenergic blockade as sole treatment can create or exacerbate unopposed α-agonist activity and greatly increase afterload on the heart. Direct vasodilators, mixed β and α antagonists, or pure α antagonists are the appropriate pharmacologic therapies in this instance.

### *Positioning*

Positioning of the patient and surgical field can have a considerable impact on the reduction of intraoperative bleeding in FESS. Placing the patient in reverse Trendelenburg position has been advocated as a technique to reduce blood loss and improve surgical conditions in FESS. Elevation of the head by at least 15 degrees creates enough venous pooling in the lower extremities to reduce venous sinus congestion and edema. However, because blood pressure measurements are commonly taken at the level of the heart, they would overestimate the blood pressure at the level of the brain and circle of Willis, which would be lower because of the effect of gravity on blood flow. This decrease in blood pressure at the level of the head is aggravated further when a deliberate hypotensive technique is employed. Lastly, because the surgical field remains above the level of the heart, this position carries a small but significant risk of venous air embolism, and such cases have been reported in FESS.

### *Airway Management*

General anesthesia with an endotracheal tube (ETT), either an oral RAE tube (named after the inventors Ring, Adair, and Elwyn) or a reinforced anode tube, is the predominant airway management option for FESS. Laryngeal mask airways (LMAs) have also been employed for this purpose. Ultimately, the choice of airway management and use of an ETT or LMA for FESS depends on several factors, such as the anesthesiologist's experience or preference for a particular device, the surgeon's preference for the procedure, the duration and complexity of surgery, and, perhaps most importantly, the patient's comorbidities and risk of aspiration. In patients with a history of significant gastroesophageal reflux disease, obesity, hiatal hernia, or prior gastric surgery, use of LMAs should be discouraged. LMAs do not protect against aspiration as well as cuffed ETTs.

### *Maintenance of Anesthesia*

In the authors' institution, the preferred maintenance technique for FESS is total intravenous anesthesia (TIVA) as opposed to potent inhaled agents. A combined remifentanil

and propofol infusion–based anesthetic provides superior visualization in the surgical field and significant decreases in intraoperative blood loss compared with volatile anesthetics and standard narcotic techniques. Both the TIVA technique and the volatile anesthetic technique were effective in achieving "deliberate" hypotension as defined by MAP <60 mm Hg; however, only TIVA with propofol and remifentanil was successful in significantly reducing blood loss. This difference was likely attributed to reduced cardiac contractility and heart rate from TIVA compared with a considerable decrease in SVR from potent inhalation agent–induced vasodilation.

Alone, remifentanil may be the agent accountable for a substantial improvement in the quality of the surgical field. Compared with other opioids such as fentanyl, alfentanil, or sufentanil; remifentanil is associated with improved visualization during FESS. When remifentanil was added to an inhaled anesthetic such as sevoflurane, similar surgical conditions were achieved compared with a propofol and remifentanil TIVA technique. This unique advantage of remifentanil is not fully understood. Similar to other opioids, remifentanil reduces sympathetic tone and increases parasympathetic tone causing a dose-dependent decrease in heart rate and CO. These properties are essential in promoting controlled hypotension for FESS and may be more effectively produced with remifentanil. A major advantage of remifentanil lies in its pharmacokinetics and its rapid elimination from plasma. This rapid elimination allows for administration of a potent opioid anesthetic with little concern for residual effects when the infusion is discontinued.

A modified nitrous oxide–opioid technique combining nitrous oxide (50%–75%) with remifentanil (0.1–0.5 μg/kg/min)/propofol (25–50 μg/kg/min) infusions can be used. This technique provides several unique advantages in FESS. Controlled hypotension and decreased CO from relative bradycardia and reduced contractility are easily achieved with excellent results via the combination of remifentanil and propofol. Because the infusions of both drugs are easily titratable, the level of hypotension and heart rate control can be adjusted rapidly. In addition, nitrous oxide has several gainful effects on the cardiovascular system. At high inhaled concentrations, it is a mild cardiac depressant, producing negative inotropy. However, its effects on vascular tone are sympathomimetic, resulting in local vasoconstriction that often counteracts its myocardial depressant properties. This combination of decreased contractility and vasoconstriction may be beneficial in a reduction of blood flow to the nasal sinuses and an improved surgical field. Owing to its *N*-methyl-d-aspartate receptor blockade, nitrous oxide has been shown to reduce postoperative hyperalgesia associated with remifentanil infusions.

This technique also offers reliable and smooth emergence via the rapid elimination of all three drugs with little or no residual effects. As stated earlier, the incidence of coughing and straining can be reduced through the use of remifentanil. Propofol has the potential to reduce PONV. Although nitrous oxide has been implicated in a slightly higher incidence of PONV, this risk is attenuated by antiemetic agents, such as ondansetron, droperidol, or dexamethasone. Commonly manipulated variables and methods for deliberate hypotension are presented in Table 45-4.

### Choice of Ventilation

Carbon dioxide, a waste gas of metabolism, has many physiologic effects. Hypercapnia generally produces tachycardia and vasodilation; this may promote bleeding and impair surgical exposure during FESS. As a result, a mild degree of hypocapnia or hyperventilation has long been advocated to induce vasoconstriction in the nasal sinuses and minimize bleeding. Despite this reasoning, hyperventilation has not been shown to provide any particularly significant benefit versus normocapnia or hypercapnia in surgical conditions or bleeding in patients under a nitrous oxide–opioid technique with propofol and remifentanil. This lack of significant benefit may be due to the effects of positive pressure ventilation on central venous pressure. Positive pressure ventilation increases central venous pressure and reduces venous return from the head and neck, and this can lead to increased venous bleeding in the surgical field. Spontaneous ventilation may be difficult to achieve with remifentanil because it strongly suppresses ventilation at infusions of >0.05 μg/kg/min. The benefit of a high-dose remifentanil infusion likely outweighs the theoretical advantage of spontaneous ventilation. Similarly, the use of positive end expiratory pressure also leads to decreased venous return and increases venous congestion, which is detrimental in FESS.

### Emergence

The goal for emergence in FESS should be as smooth as possible with minimal to no coughing or straining because this would increase venous pressure and promote bleeding. LMAs may result in smoother emergence from general anesthesia compared with ETTs; however, for reasons stated previously, the use of a LMA for FESS may be undesirable in many, if not most, cases.

**TABLE 45-4 Summary of Parameters and Variables and Their Contribution to a Bloodless Surgical Field**

| Parameter | Variable | |
|---|---|---|
| ↓ MAP | ↓ HR | ↓ SVR |
| | ++++ | + |
| ↓ HR | Remifentanil | β blockade |
| | ++++ | +++ |
| Technique | TIVA | Volatile anesthetics |
| | ++++ | + |
| Ventilation | Normocapnia | Hypocapnia |
| | ++ | ++ |
| Postoperative analgesia | Regional | Intravenous/oral |
| | ++ | ++ |

*HR,* Heart rate; *MAP,* mean arterial pressure; *SVR,* systemic vascular resistance; *TIVA,* total intravenous anesthesia; +, minimal effectiveness; ++, equivocal effectiveness; +++, moderate effectiveness; ++++, maximal effectiveness.

### 9. What techniques are available to decrease postoperative pain and minimize recovery time after functional endoscopic sinus surgery?

Postoperative pain after FESS ranges from mild to moderate. Often a multimodal approach is implemented. The use of remifentanil offers no sustained postoperative analgesia because it is rapidly metabolized. Nonselective NSAIDs, such as ketorolac, are commonly avoided in FESS because of an association between nasal polyps, aspirin sensitivity, and reactive airways disease. Additionally, inhibition of thromboxane $A_2$ by nonselective NSAIDs can impair platelet aggregation. Current evidence shows equivalence in pain relief among local anesthetics, selective cyclooxygenase (COX)-2 or COX-3 NSAIDs, and opioids when used separately in FESS. The general approach is to use nerve blocks with long-acting local anesthetics such as bupivacaine before surgery, nonopioid analgesics such as acetaminophen or selective COX-2 inhibitors intraoperatively or immediately postoperatively, and longer acting opioids such as fentanyl for rescue treatments in the postanesthesia care unit (PACU).

#### *Postoperative Regional Anesthesia for Functional Endoscopic Sinus Surgery*

The maxillary division of the trigeminal nerve (V2) provides the major sensory innervation to the midface, including the lower eyelid, upper lip, maxillary sinus, nasal cavity, and soft and hard palate. Specifically, the infraorbital nerve and sphenopalatine ganglion, branches of the maxillary nerve, are targeted for local anesthesia blockade for FESS.

The infraorbital nerve provides sensation to the cheek, upper lip, eyelid, and lateral aspect of the nose. The nerve exits the infraorbital foramen approximately 1 cm below the inferior orbital ridge along a vertical line from the medial limbus of the eye. The infraorbital notch can be easily palpated rolling one's fingertip over the inferior orbital rim. This block can be performed via intraoral or transnasal approaches. For the transnasal technique, the index finger of the nondominant hand is placed over the infraorbital foramen (Figure 45-2). A 25-gauge 1½-inch long needle is positioned through the ipsilateral nares. The needle is advanced toward the finger marking the foramen, and 2 mL of 0.5%–0.75% bupivacaine is injected after negative aspiration. This technique should be avoided in patients with pathology (e.g., neoplasms, arteriovenous malformations) involving the anterior nasal cavity or nasal vestibule.

The pterygopalatine ganglion or sphenopalatine ganglion supplies the lacrimal gland, paranasal sinuses, mucosa of the nasal cavity and pharynx, gingiva, and mucous membrane of the hard palate. The ganglion is blocked via the greater palatine foramen approach. Placing the patient supine and extending the neck, the greater palatine foramen is identified medially to the gum line of the first or second molar on the posterior portion of the hard palate. A curved blade laryngoscope is useful in providing adequate exposure and illumination after endotracheal intubation. A 25-gauge 1½-inch long needle is bent at 1.5 cm and advanced through the foramen at an angle of 45 degrees at a superior and slightly posterior trajectory. Roughly 1.5–2.0 mL of lidocaine with 1:100,000 epinephrine is injected after demonstrating negative aspiration. The use of epinephrine minimizes systemic absorption in this highly vascular region. This technique has been associated with complications such as intravascular injection, intraorbital and optic nerve injury, and transient diplopia. In a published double-blind randomized study, our group determined that patients who receive both blocks require less opioid analgesia in the PACU and are discharged home 40 minutes earlier on average compared with patients who did not receive the blocks.

Otolaryngologists are using intraoperative computed tomography image (CT) guidance with increasing frequency during FESS. Infiltration of local anesthesia during infraorbital nerve blocks can interfere with the guidance system registration by deforming facial skin depth and facial topography that is required for proper calibration and patient identification (Figure 45-3).

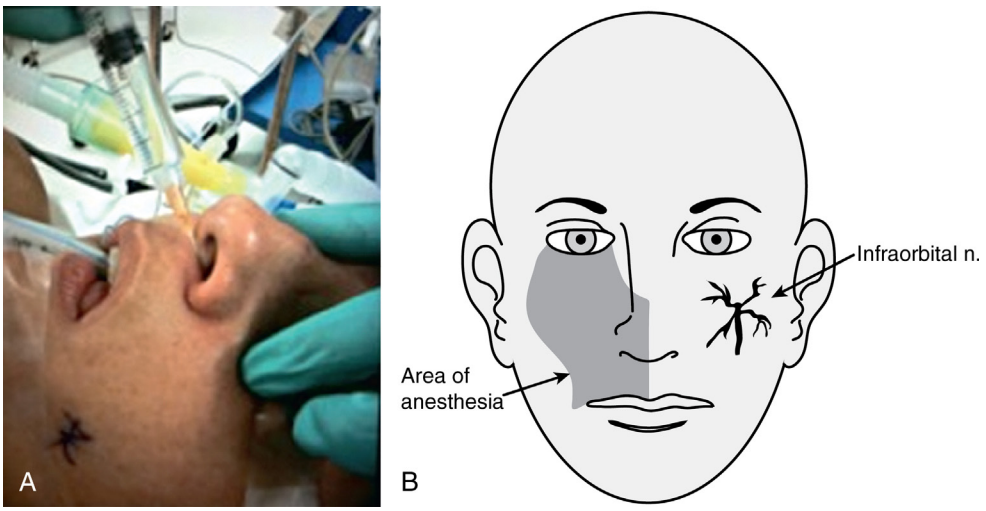


**FIGURE 45-2** ■ **A,** Transnasal approach to infraorbital nerve block. **B,** Relevant anatomy showing the distribution of anesthesia from the block.

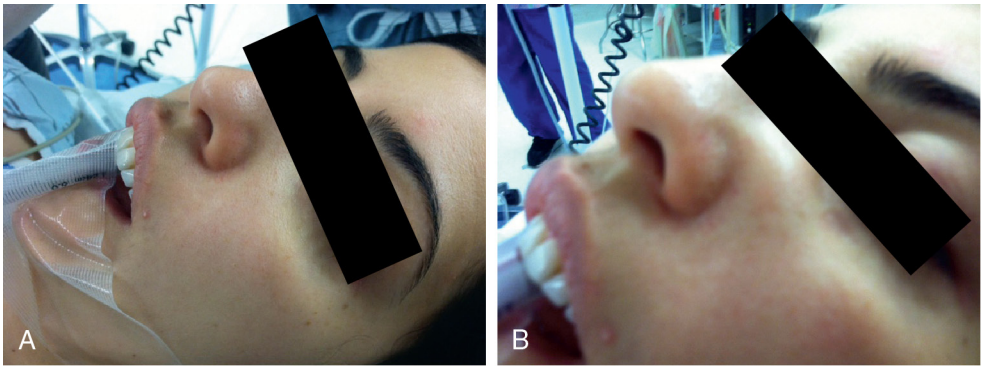


**FIGURE 45-3** ■ **A,** Topography before infraorbital nerve block placement. **B,** Subsequent derangement of facial topography from local injection.

As in all ambulatory cases, it is beneficial to limit the patient's PACU stay. It is important to discharge patients in a timely fashion with little to no anesthetic residual. However, as with many otolaryngologic procedures, there is an increased risk for postoperative airway obstruction and bleeding that can lead to airway compromise and respiratory distress. Vigilance and close observation are required postoperatively because many of these patients have nasal packing that could result in partial or complete nasal obstruction. The potential exists for nasal packing to migrate into the hypopharynx creating obstruction at that level. The risk of minor complications, such as epistaxis, is small—roughly 1%–1.6%. Major hemorrhage requiring either blood transfusion or reexploration occurs with a frequency of about 0.19%. The incidence of bronchospasm is reported to be roughly 1.8% and is similar to the incidence of epistaxis. Both conditions may be concurrent.

In addition to increasing recovery time and use of additional resources, PONV is of significant concern in FESS because retching and vomiting can precipitate or exacerbate postoperative bleeding. PONV is often multifactorial and may be attributed to anesthetic agents, opioids, upper airway inflammation, or blood in the stomach. Decompression of the stomach before extubation may be helpful in reducing the risk of PONV. The use of propofol as opposed to volatile anesthetics combined with regional nerve blocks to reduce the need for longer acting opioids may reduce the risk of PONV. In addition, PONV prophylaxis should be administered routinely, unless absolutely contraindicated (i.e., allergic reaction), via high-dose steroids such as dexamethasone (10–12 mg), ondansetron (4 mg), or droperidol (0.625–1.25 mg). Scopolamine should be reserved for extremely high-risk patients because it may delay emergence or result in postoperative delirium.

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SECTION 8

# BLOOD

CASE 46

# Transfusion Reaction

**Barry J. Segal, MD**

QUESTIONS



A 67-year-old woman with a fractured right femur presents for intramedullary nailing under spinal anesthesia. After 45 minutes, she loses 1200 mL of blood and receives 1 unit of designated donor red blood cells (RBCs). Within minutes of initiating transfusion, the patient is shivering and complains of chills, nausea, and difficulty breathing. Her heart rate increases from 84 beats per minute to 128 beats per minute, ST segments are depressed, and the blood pressure decreases from 124/72 mm Hg to 82/46 mm Hg. The urine in the urometer has turned from clear to pink.

## 1. Is this a transfusion reaction?

The immediacy of presentation as well as the scope of signs and symptoms indicates that this is an acute hemolytic transfusion reaction. This type of reaction is the most severe immediate transfusion reaction and occurs infrequently. Prior data suggested that acute reactions manifest with an incidence of 1:10,000–1:50,000 units of blood products administered. Newer data suggest a frequency of approximately 1:250,000–1:500,000.

A Canadian hemovigilance study found 11 cases of acute hemolytic transfusions out of 138,605 RBC units given in 2000. Death rates were 25% when <1000 mL was transfused and 44% when >1000 mL of incompatible ABO blood was given.

## 2. Are all transfusion reactions immediate?

Immediate transfusion reactions occur within the first 24 hours of administration of blood components. Types of immediate transfusion reactions include acute intravascular hemolytic transfusion reaction (AIHTR) and acute extravascular hemolytic transfusion reaction, allergic transfusion reactions (mild, anaphylactic, anaphylactoid), febrile nonhemolytic transfusion reaction (FNHTR), hypotensive transfusion reaction, bacteria-contaminated or septic transfusion, transfusion-related lung injury (TRALI), heat-induced hemolyzed RBCs, and transfusion-associated circulatory overload (TACO).

Delayed reactions occur after 24 hours and often 3 days to months after transfusion. Types of delayed reactions include delayed extravascular hemolytic, alloimmunization, graft-versus-host disease (GVHD), and infectious (viral, parasitic, and bacterial).

## 3. Can all blood products cause transfusion reactions?

All blood products can cause transfusion reactions. The type of transfusion reaction depends on the blood product administered. Only incompatible RBC transfusions cause intravascular or extravascular hemolytic transfusion reactions. Allergic reactions, which are probably the most common transfusion reactions (1%–3% of all transfusions), can occur with RBC, plasma, or platelet transfusions. Allergic reactions usually result from preformed antibodies to plasma proteins. IgE may mediate allergic reactions, and anaphylaxis may occur. Febrile reactions may be produced by stored leukocytes producing increased interleukin (IL)-1 (endogenous pyrogen) or anti-IgA antibodies produced by individuals who are deficient in IgA or an IgA subclass. IL-6, IL-1β, and tumor necrosis factor (TNF)-α, also endogenous pyrogens, have been found to increase in stored platelet concentrates.

## 4. What are the etiologies and presentations of transfusion reactions?

### *Immediate Transfusion Reactions*

#### *Acute Intravascular Hemolytic Transfusion Reaction*

AIHTR usually occurs intravascularly. Destruction of donor and occasionally recipient RBCs releases free hemoglobin and stroma of destroyed erythrocytes, elaborates cytokines and chemokines, activates complement, reduces

oxygen carrying capacity, and causes electrolyte imbalances. This reaction can have devastating results. Morbidity and mortality vary with the amount of blood transfused and the type and amount of antigen and antibody transfused.

The most common cause of AIHTR is ABO incompatibility. High IgM (anti-A, anti-B) antibody titers in the recipient attach to donor erythrocyte antigen. Antibody-coated donor RBCs are referred to as opsonized RBCs. Destruction of these cells and activation of complement lead to acute intravascular hemolysis.

Although ABO antibodies are most often implicated in fatal reactions, antibodies to Rh, Duffy, Kell, Lewis, and Kidd can be just as devastating. In an O-positive individual (with anti-A and anti-B antibodies), the most common antibody is anti-A. Anti-Rh is usually an IgG-mediated reaction that does not generally activate complement. The number of antigenic sites on the RBC varies, with many more ABO antigens ($2–8 \times 10^5$) per cell, in contrast to lesser antigens, such as Kell ($3–6 \times 10^3$ per cell). The higher the number of antigens present, the greater the likelihood of complement activation.

Attachment of IgM begins a cascade of events leading to complement activation; cytokine, chemokine (TNF-α, IL-1, IL-6), and kinin production; thrombin generation; tissue factor elaboration; and platelet activation. IgM-induced complement activation as well as sometimes IgG-induced complement activation, leads to anaphylotoxin production composed of complement fragments C3a, C4a, and C5a. Activation of complement components 3, 4, and 5 (particularly C3 and C5) produces cell lysis, degranulation of mast cells, histamine release, smooth muscle contraction, cytotoxic oxygen free radical production, and chemotaxis of leukocytes.

Opsonized RBCs are phagocytized, in particular by macrophages and less so by monocytes. These cells degranulate, releasing histamine, serotonin, proinflammatory cytokines and chemokines (including TNF-α and kallikrein), and activated bradykinin. This process causes hypotension and capillary leak, producing direct and reflex tachycardia, renal dysfunction, and often respiratory distress. TNF-α, which is produced during hemolysis, also leads to endothelial tissue factor release and extrinsic followed by intrinsic coagulation cascade activation, thrombin generation, and platelet activation; this contributes to disseminated intravascular coagulopathy (DIC) seen with AIHTR.

Free hemoglobin binds to endothelial nitric oxide, preventing the action of endothelial relaxing factor and leads to renovascular vasoconstriction. Norepinephrine release, owing to hypotension induced by bradykinin, serotonin, and histamine, leads to further vasoconstriction. Destroyed red cell stroma induces further vasoconstriction and clogs microtubules. IL-1, IL-1 receptor antagonist, and IL-6 activation of genes also occurs, leading to RBC autoantibody and alloantibody production, which may have a part in delayed hemolytic transfusion reaction (DHTR) and the degree to which extravascular hemolysis occurs.

### *Acute Extravascular Hemolytic Transfusion Reaction*

Acute extravascular hemolytic transfusion reaction generally involves non-ABO antigen groups. They are most commonly associated with Rh group incompatibility. Complement either is not activated or attaches only to C3b receptors, without activation to C3a or C5a receptors. There is no intravascular RBC destruction. Extravascular removal of opsonized RBCs occurs either by the spleen (C3b) or liver (IgG). The direct antibody test (DAT) becomes positive (as it does with AIHTR) from alloantibodies binding to incompatible erythrocytes. The hematocrit and haptoglobin levels decrease slowly, but hemoglobinemia or hemoglobinuria is rare. A low-grade fever may be produced by cytokine release or IL-1 production.

### *Febrile Nonhemolytic Transfusion Reaction*

FNHTR, the most common type of transfusion reaction, is related to the presence of donor leukocytes in transfused blood products (particularly RBCs and platelets). Typically, there is a 1° C (usually <2° C) increase in temperature. Febrile reactions >2° C are usually associated with transfusion of bacterial contaminated blood products.

FNHTR can occur immediately or several hours after transfusion (usually within 4 hours) and usually resolves within 48 hours. Chills, subjective feelings of cold, or rigors often accompany the febrile reaction. These symptoms may be present in the absence of increased temperature. Other conditions that produce this constellation of symptoms include AIHTR, acute extravascular hemolytic transfusion reaction, anaphylactic reactions, anaphylactoid reactions, and TRALI. Other symptoms include headache, myalgias, nausea, and nonproductive cough.

FNHTR is mediated by recipient alloantibodies against donor leukocytes. These leukocytes release cytokines, and platelets release proinflammatory cytokines (IL-1, IL-6, IL-8, and TNF-α), all of which act on the hypothalamus producing febrile reactions.

Prestorage leukoreduction of RBC and platelet units has markedly reduced the incidence of FNHTR. Before the practice of prestorage leukoreduction, temperature elevation occurred in 43%–75% of transfusions. Patients experiencing a previous febrile reaction have a 12.5% chance of having another and should be given leukocyte-depleted units.

### *Allergic Transfusion Reaction*

Allergic transfusion reactions occur in about 1% of all transfusions. Manifestations range from the most common mild reaction (e.g., urticaria, pruritus, swelling, rash) to the relatively rare anaphylactoid and anaphylactic reactions. Allergic reactions are due to release of histamine when donor plasma proteins attach to preformed IgE or IgG antibodies on mast cells in sensitized individuals. Histamine may also be infused from stored blood products. Allergic reactions are more likely to occur with fresh frozen plasma transfusions. However, a reaction can occur with RBC and platelet transfusions because there is plasma in these blood products as well.

Anaphylactic reactions consist of bronchospasm, severe hypotension, tachycardia, urticaria, and possibly laryngeal

edema. Awake patients may also complain of dyspnea, chest pain, nausea, and vomiting. This reaction occurs most commonly in IgA-deficient individuals, who are sensitized by exposure to "foreign" IgA proteins from previous transfusions or pregnancy, or individuals lacking in other plasma proteins, such as haptoglobin. Anaphylactoid reactions usually occur with a larger volume of transfusion, are less severe, and are often proportionate to the volume infused.

### Hypotensive Transfusion Reaction

A hypotensive transfusion reaction, in which the systolic or diastolic blood pressure decreases at least 30 mm Hg within the first few minutes of a blood transfusion, may be the result of contact activation (intrinsic coagulation pathway) and generation of bradykinin and other kinins. Septic transfusions, anaphylaxis, TRALI, and acute hemolytic transfusion reactions may also manifest in this manner. Awake patients may experience facial flushing, nausea, abdominal pain, shock, and respiratory distress.

Bradykinin acts on kinin receptors of blood vessel endothelium leading to hypotension and edema formation from intracellular fluid leaking. Because angiotensin-converting enzyme breaks down bradykinin, this reaction is most often seen in patients taking angiotensin-converting enzyme inhibitors. Contact activation can occur with the use of blood warmers, with the use of some leukoreduction filters, and from prostate glandular kininogen.

### Bacteria-Contaminated or Septic Transfusion

Because of improved viral contamination detection, most infectious transfusion reactions are caused by bacterial contamination of transfused blood products. Individuals may present with mild fever or frank sepsis leading to hypotension, respiratory distress, acute kidney failure, DIC, and circulatory collapse. Septic transfusions are usually associated with an increase of >2° C in temperature. Absence of hemoglobinemia (and hemoglobinuria) distinguishes this reaction from AIHTR.

Blood product contamination may occur from asymptomatic donors who later develop infection; transmission of donor skin flora into the collection system; contamination of collection bags, which then contaminate phlebotomists; and bacterial contamination of water baths used to thaw blood component units. Blood donations are declined from individuals with temperatures >37.5° C, or who present with infectious symptoms such as upper respiratory symptoms and diarrhea.

There is a higher incidence of transmitted bacterial infections from platelets that are stored at room temperature (22° C) than RBCs (stored between 1° C and 6° C). The longer the storage time (>5 days), the greater the risk of bacterial infection. Although the U.S. Food and Drug Administration limits platelet storage to 5 days, platelets are still the most common cause of transfusion-transmitted bacterial infections. Sepsis may occur from any contaminated blood component transfusion.

Some bacteria, such as *Pseudomonas*, *Enterobacter*, and *Yersinia*, can grow at the low temperatures used for RBC storage. *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus* species, and gram-negative organisms can contaminate blood components. *Salmonella* has been reported as a contaminant in platelets.

Transfused bacteria or endotoxins or both can lead to sepsis, with release of proinflammatory cytokines and interleukins (IL-1, TNF-α) as well as complement activation; this produces the clinical picture of sepsis. Interleukin and cytokine interaction with endothelial smooth muscle locally produces nitric oxide, which leads to the refractory hypotension of sepsis. Sudden development of hypotension and rigors in awake patients or hypotension and DIC symptoms in anesthetized patients suggests a bacteria-contaminated transfusion. The incidence of septic transfusions has decreased by the routine use of bacterial monitoring systems, some of which detect oxygen consumption of blood components.

### Transfusion-Related Lung Injury

The incidence of TRALI is 1:1000–1:4500 transfusions. Although uncommon, TRALI is the leading cause of transfusion morbidity and accounts for 47% of transfusion-related deaths. It can occur with a transfusion of any blood-derived product, although more commonly with platelets and plasma. There is a higher incidence with blood component transfusion donated from multiparous women (because of their exposure to fetal blood) or from individuals who received multiple transfusions in the past. Despite supportive measures and aggressive ventilatory support, there is a 5%–10% mortality rate.

TRALI is any noncardiogenic pulmonary edema occurring within 6 hours of a transfusion. It is associated with chills, hypoxemia, and fever. Bilateral pulmonary infiltrates are seen on chest x-ray, and severe pulmonary insufficiency may develop similar to adult respiratory distress syndrome. In mild cases, there is dyspnea, with spontaneous resolution of symptoms. Most patients (approximately 70%) require intubation and mechanical ventilation. The lung injury is usually transient, with return of preevent oxygenation levels within 72–96 hours, although occasionally this may take a week to resolve. Under general anesthesia, it may be difficult to differentiate TRALI from acute hemolytic reaction, hypotensive reaction, anaphylactic reaction, septic transfusion, and transfusion-associated circulatory overload.

TRALI probably occurs as a two-step process. In many cases, it develops in patients with preexisting conditions (e.g., recent surgery, malignancy, infections). These preexisting conditions cause neutrophil priming, allowing them to marginate and sequester along the pulmonary vasculature. The second step occurs when transfused blood activates these primed leukocytes and cytotoxic granules are released. Cytotoxic substances disrupt endothelium resulting in interstitial and alveolar edema. The mechanism involves transfused lipids, granulocytes, major antibodies, or platelet-derived proinflammatory mediators (CD40) reacting with sequestered recipient leukocytes. However, TRALI can also occur with fresh frozen plasma transfusions that have no cellular components.

### Transfusion-Associated Circulatory Overload

Rapid administration of blood products may result in TACO. Individuals at particular risk are patients with preexisting cardiac disease or renal insufficiency. TACO may manifest as congestive heart failure with dyspnea, oxygen desaturation, circulatory overload, jugular venous distention, increasing central vascular pressures (central venous pressure, pulmonary capillary wedge pressure), and tachycardia.

In a nonbleeding patient, transfusion rates should be limited to 2–3 mL/kg/hour and less in patients with cardiovascular compromise. TACO may easily occur with rapid transfusion devices, when active bleeding has stopped and aggressive transfusion continues.

### Other Acute Transfusion Reactions

**Hyperkalemia.** Rapid transfusion with multiple units of older RBCs can lead to intravascular hyperkalemia. This condition usually occurs when administered blood is near the end of its expiration date, and large volumes have been transfused. A review of U.S. combat patients in Iraq demonstrated that 7 units of RBCs were needed to increase potassium ($K^+$) concentrations transiently to >5.5 mEq/L. As storage time increases, there is a linear increase of $K^+$ concentration in the supernatant. RBCs have a $K^+$ concentration of 2 mEq/L, which increases to 45 mEq/L over 42 days of storage, using citrate-phosphate-dextrose (CPD) preservative. Sodium-adenine-glucose-mannitol is used in Canada and Great Britain. CPD or CPD with adenine is commonly used in the United States.

Other factors predisposing to hyperkalemia include hypovolemia, small patient size, amount of blood transfused, and prior irradiation of transfused blood. The increase in $K^+$ appears to be transient and is often normal several hours after transfusion. Techniques to limit the increase of $K^+$ include use of in-line $K^+$ scavenging filters, RBC washing (by the blood bank or more expeditiously with a cell saver), infusing through larger bore intravenous catheters, and insulin-dextrose treatment.

**Citrate Toxicity.** Massive transfusions have been associated with transient increases in citrate levels. Citrate is normally metabolized in the liver. Large volumes of RBCs, reduced liver perfusion or function, and hypothermia impair citrate metabolism leading to increased citrate levels. Citrate binds calcium and magnesium leading to hypocalcemia and hypomagnesemia, which can impair cardiac function and produce coagulopathy.

### Delayed Transfusion Reactions

### Delayed Hemolytic Transfusion Reaction

DHTR usually occurs 3–10 days after transfusion and is usually mild. It occurs more commonly extravascularly but can occur intravascularly as well. DHTR is usually due to an amnestic antigen-antibody response. The recipient, after exposure to RBC antigen (previous transfusion or pregnancy), develops antibodies whose levels decrease over time and are undetectable the next time crossmatching is performed. When the recipient is reexposed to the RBC antigen, a secondary immune response is triggered, and antibody levels increase with a more rapid and larger reaction than occurred during the first exposure, lysing donor RBCs; this usually occurs in the spleen and reticuloendothelial system, and it results in a less severe reaction and is self-limiting. This response most commonly occurs in the Rh group. The most common presentation is a low-grade temperature, increasing bilirubin, and unexplained decreasing hemoglobin. A newly positive DAT is diagnostic.

### Graft-versus-Host Disease

GVHD may occur 8–10 days after transfusion, although it is more commonly seen with bone marrow transplantation. It more commonly occurs in immunocompromised patients, in whom unopposed donor lymphocytes attack recipient tissues. It can be seen in organ transplant recipients and neonates who had a blood exchange transfusion. It can also occur in immunocompetent recipients who are transfused blood from first-degree relatives. The mechanism of GVHD is that both the donor and the recipient have similar human leukocyte antigen haplotypes. The recipient does not reject the donor lymphocytes, but the donor recognizes the recipient as having foreign cells and initiates an immune response. Irradiation is the only effective method to reduce the incidence of GVHD.

Bone marrow is frequently involved resulting in aplasia. Involvement of the liver and skin is often unrecognized. Patients frequently die from bleeding diatheses and infections within several weeks.

### Delayed Acquired Transfusion-Transmitted Infection

Delayed acquired transfusion-transmitted infections include the hepatitis viruses B and C, cytomegalovirus, and human immunodeficiency virus (HIV). Modern screening techniques employed by blood banks have significantly reduced the incidence of these transfusion-transmitted infections. At the present time, the American Association of Blood Banks reports the risk of acquiring hepatitis B virus is 1:137,000 transfusions; hepatitis C virus, 1:1,1000,000 transfusions; and HIV, 1:1,900,000 transfusions.

## 5. How are different transfusion-related reactions managed?

Immediate recognition and treatment of transfusion reactions provide for the best results. Awake patients describe myriad symptoms, including chills, fever, rigors, headache, back and flank pain, chest pain and spasms, lightheadedness, heart racing, dyspnea, itching, and a feeling of impending doom. In an anesthetized patient, a transfusion reaction may manifest as hypotension, shock, decreased oxygen saturation, bronchospasm, urticaria, coagulopathy, increased bleeding, venipuncture oozing, and hemoglobinuria.

Management of an acute transfusion reaction is directed at removing the cause and assessing airway, breathing, and circulation. The transfusion is stopped immediately, and the unit of blood is removed. Whether the intravenous tubing should also be removed has been debated. The theoretical benefit of removing the intravenous tubing is that any further blood product contained within the tubing would be prevented from reaching the patient. However, this manipulation may result in loss of intravenous access, which could be devastating in a hypotensive patient requiring emergent care.

During this time, airway patency is established, adequate oxygenation and ventilation are ensured, and hemodynamic support is provided. In an awake patient, supplemental oxygen should be provided. If oxygen desaturation or a shock state develops (as with AIHTR, allergic transfusion reaction, TRALI, or TACO), tracheal intubation and ventilation with positive end expiratory pressure should be instituted to maintain oxygenation. In the operating room with an anesthetized and already intubated patient, administered oxygen should be increased to 100%. An increased amount of positive end expiratory pressure to maintain alveolar stability and recruitment and increased minute ventilation may be required. These maneuvers may be especially helpful for TRALI and associated adult respiratory distress syndrome. Some data suggest that steroid use may be beneficial in TRALI. Diuretics are indicated for patients with TACO but not for patients with TRALI.

Pressor support may be required. Phenylephrine, norepinephrine, or epinephrine (particularly for anaphylactic or anaphylactoid reactions) is generally used. Vasopressin and occasionally methylene blue infusions may be necessary in refractory hypotension, particularly in hypotensive transfusion reactions.

A health care worker should be designated to:

- Confirm the unit's identification information against the patient's name band to rule out clerical errors.
- Send a blood sample from the patient to the blood bank along with the removed blood component unit for retyping and crossmatching (compatibility testing) as well as for a DAT.
- Send blood samples to the laboratory for complete blood count, coagulation profile, free hemoglobin levels, haptoglobin concentrations, electrolytes, blood urea nitrogen, and creatinine. An arterial blood gas should be analyzed as well. A urine sample is sent to detect the presence of hemoglobin.
- Obtain cultures from the blood component unit if bacteria contamination is suspected.

If hemoglobinemia or hemoglobinuria is present, treatment to protect renal function should be instituted. This treatment includes fluid administration to increase urine output, diuretics (e.g., furosemide, mannitol), and urine alkalinization by infusion of sodium bicarbonate (add 75 mEq of sodium bicarbonate to 1 L of 0.5 normal saline and infuse at 125 mL/hour).

Allergic reactions are treated with diphenhydramine, 25 to 50 mg, and famotidine, 20 mg intravenously. The combination of histamine $H_1$ and $H_2$ blockers is more effective than $H_1$ blocker therapy alone. Epinephrine is the mainstay therapy for anaphylactic reactions.

Broad-spectrum antibiotics administered for septic transfusions have met with equivocal results. Pressor support is often required. Febrile reactions are treated with acetaminophen or nonsteroidal antiinflammatory drugs or both and supportive care.

## 6. Can transfusion reactions be prevented?

The incidence of transfusion reactions can be markedly reduced but probably not eliminated. The most important preventive measures are proper patient and correct blood sample identification. Restriction of blood donations from multiparous women, disqualifying individuals with a history of transfusion-related reactions, eliminating designated donors, and safe blood banking techniques all contribute to safe transfusion practices.

The choice of transfused blood and blood products could decrease the incidence of adverse transfusion reactions. Leukoreduction may decrease incidences of febrile reactions, nonhemolytic transfusion reactions, and perhaps TRALI. Irradiation of blood components can decrease the incidence of GVHD reactions. Allergic reaction can be limited by transfusing saline washed cells, whereas anaphylactic reactions can be limited by transfusing washed RBCs, frozen deglycerolized RBCs, or RBCs from IgA-deficient donors.

Single donor platelet apheresis is probably safer than multiple donor units with respect to transfusion reactions and infections. The risk of TRALI, allergic reactions, and volume overload or TACO is greater with fresh frozen plasma transfusion than cryoprecipitate. However, the chance of infection is higher with cryoprecipitate because 10 donors are required rather than 4 donors, which are used in plasma.

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CASE 47

# Perioperative Coagulopathies

Edward R. Mathney, MD

QUESTIONS

1. Which patients require preoperative coagulation evaluation?
2. What laboratory tests are performed to diagnose preoperative coagulopathies?
3. What are the most common perioperative coagulopathies?
4. How are perioperative coagulopathies diagnosed?
5. How are perioperative coagulopathies treated?

A 56-year-old man with hepatitis C cirrhosis and hepatocellular carcinoma involving segments II and III presents for left hepatectomy. Preoperative laboratory tests show hemoglobin concentration, 9.8 g/dL; platelet count, 102 × $10^9$/L; prothrombin time (PT), 16 seconds (normal PT range, 11–15 seconds); international normalized ratio (INR), 1.3; and partial thromboplastin time (PTT), 49 seconds (normal PTT range, 25–39 seconds).

## 1. Which patients require preoperative coagulation evaluation?

The goal of preoperative coagulation evaluation is to optimize patient safety by identifying prothrombotic and antithrombotic tendencies that may influence the perioperative course. The more recent paradigm shift toward evidence-based approaches to preoperative evaluation and testing includes coagulation. Increased evidence has exposed the shortcomings of routine laboratory testing and point-of-care (POC) devices for monitoring coagulation in goal-directed management of intraoperative coagulopathies is becoming more common.

"Routine" preoperative coagulation studies are not useful. Platelet count, PT, and PTT are rarely abnormal in patients without a clinical indication for such tests (e.g., excessive bleeding after dental procedures). Abnormalities in these screening tests rarely affect intraoperative blood loss but may lead to further unnecessary testing and increased exposure to blood products. Instead of routine laboratory testing, all preoperative coagulation evaluations should begin with a personal and family standardized bleeding history, medication history, and physical examination, with the goal of identifying patients in need of further investigation (Table 47-1). When asked about medications, some patients neglect to mention homeopathic and natural remedies that may affect coagulation.

When adverse factors are identified, further investigation should be performed to define the specific coagulopathy. A perioperative management strategy can then be designed. An argument can be made for obtaining preoperative coagulation studies in the absence of a bleeding history if the scheduled procedure is associated with a catastrophic (e.g., intracranial surgery) or high (e.g., hepatic resection) risk of bleeding. Preoperative coagulation studies also may be indicated in situations where the patient cannot provide a history (e.g., unconscious patient) and is undergoing a high-risk procedure. However, preoperative coagulation abnormalities may not reflect the etiology of intraoperative coagulopathies.

## 2. What laboratory tests are performed to diagnose preoperative coagulopathies?

PTT was originally developed to monitor heparin effects on the intrinsic coagulation cascade (Figure 47-1). PTT is sensitive to changes in factors I, II, V, VIII, IX, X, XI, and XII; heparin; fibrinogen degradation products; acquired or congenital factor inhibitors; hypothermia; and hypofibrinogenemia. PT was developed to monitor vitamin K antagonist medications (specifically warfarin) and their effects on the extrinsic coagulation cascade. PT is sensitive to changes in factors I, II, V, VII, and X. To overcome interlaboratory variation in PT caused by different reagents, INR was introduced. Different pretest variables can affect PT and PTT results. Automated PT/PTT instruments can be affected by elevated hematocrit (>55%), which prolongs clotting time; plasma turbidity owing to lipemia (in nonfasting patients), hemolysis, or elevated bilirubin. The time between specimen collection and PTT testing (i.e., >4 hours) can lead to a falsely prolonged clotting time because of factor VIII lability.

Platelets are critical for hemostasis. Tissue injury exposes extracellular matrix proteins to which platelets adhere using von Willebrand factor (vWF) as a bridge. Platelets are then "activated," releasing fibrinogen, factor V, factor VIII, vWF, adenosine diphosphate, adenosine triphosphate, calcium, serotonin, histamine, and

TABLE 47-1 **Preoperative Evaluation**

**Personal and Family History**
- Known coagulopathy
  - Hemorrhagic
  - Thrombophilic
- Epistaxis
  - Excessive
  - Without obvious cause
- Hematoma, petechiae
  - Recurrent
  - No obvious cause
  - Unusual location (e.g., torso)
- Delayed wound healing
- Prolonged bleeding (e.g., dental extraction)
- Abnormal blood product requirement after previous surgery
- Hepatic dysfunction
- Renal dysfunction
- Gynecologic/obstetric
  - Menorrhagia
  - Recurrent spontaneous abortion
  - Fetal death in utero
- Malnutrition
- Previous transfusion
- Transfusion adverse reactions
- Stroke
- Cardiac disease
  - Coronary artery disease
  - Myocardial infarction
- Gastrointestinal bleeding
- Autoimmune or collagen vascular disease
- Amyloidosis
- Myeloproliferative disease
- Lymphoproliferative disease

**Physical Examination**
- Petechiae
- Hematomas
- Ecchymoses
- Hepatosplenomegaly
- Bleeding from mucous membranes
- Signs of autoimmune or connective tissue disease
  - Malar rash
  - Joint deformities
  - Telangiectasia
  - Acrocyanosis

**Medications**
- Antithrombotic agents
  - Vitamin K antagonists (e.g., warfarin)
  - Unfractionated heparin
  - Factor Xa inhibitors
    - Enteral
      - Rivaroxaban
      - Apixaban
      - Edoxaban
    - Parenteral
      - Low-molecular-weight heparin
      - Dalteparin
      - Enoxaparin
      - Fondaparinux
  - Direct thrombin inhibitors
    - Enteral
      - Dabigatran
    - Parenteral
      - Argatroban
      - Bivalirudin
      - Hirudin
- Antiplatelet agents
  - Aspirin
  - Nonsteroidal anti-inflammatory drugs
  - Clopidogrel
  - Prasugrel
  - Ticagrelor
  - Ticlodipine
  - Tirofiban
  - Abciximab
  - Eptifibatide
- Over-the-counter medications (homeopathic, natural, nutritional supplements)
  - Garlic
  - Ginkgo biloba
  - Ginseng
  - Ginger
  - Feverfew
  - Vitamin E
- Oral contraceptives

**Laboratory Tests**
- Complete blood count
- Prothrombin time
- Partial thromboplastin time
- Mixing studies
- Hepatic function
- Creatinine clearance
- Specific factor assays
- Lupus anticoagulant

epinephrine, all of which recruit and activate additional platelets as well as activate plasma-mediated coagulation. Exposed platelet glycoprotein (GP) IIb/IIIa receptors provide binding sites for fibrin cross-linking.

Platelet abnormalities can be either quantitative or qualitative. Quantitative platelet abnormalities are detected by platelet counts most commonly performed by automated machines but may require manual counts when platelet values are abnormally low. Hemodilution and ethylenediamine tetraacetic acid (EDTA)–induced platelet clumping are common causes of falsely low platelet counts. Generally, platelet counts $>100 \times 10^3/\mu L$ are associated with adequate hemostasis. Although there are no absolute guidelines, platelet transfusion should be considered if the platelet count is $<10 \times 10^3/\mu L$ or $<50 \times 10^3/\mu L$ in a patient with bleeding or a perioperative patient. The decision to transfuse platelets must be weighed against the risk of viral or bacterial infection, transfusion-related acute lung injury (TRALI), stroke, and death.

Despite a normal platelet count, qualitative platelet abnormalities may exist (e.g., uremia, von Willebrand disease [vWD], antiplatelet therapy). Platelet function analyzers can detect qualitative platelet abnormalities

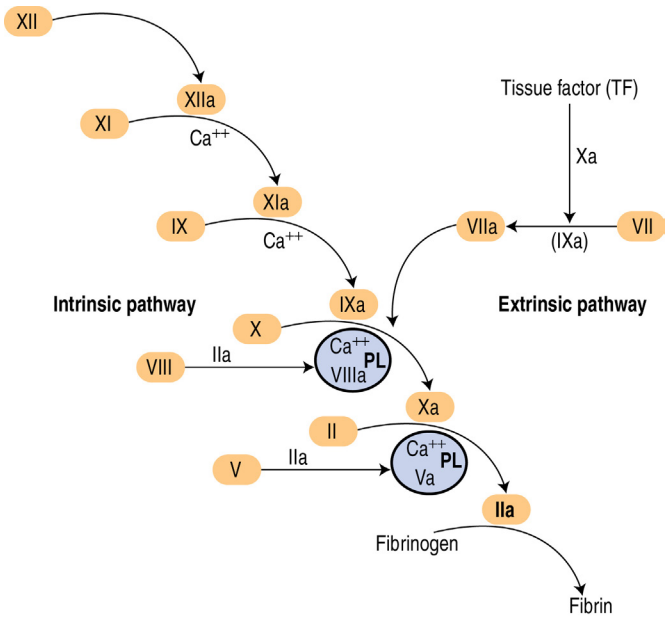


**FIGURE 47-1** ■ **Coagulation cascade.** (From Porwit A, et al. [eds]: Bone Marrow Pathology. Churchill Livingstone, Philadelphia, 2011.)

(see Question 4 for further details). The treatment of qualitative platelet abnormalities depends on its etiology. For example, uremic patients may need dialysis, and patients with vWD may need desmopressin (DDAVP). For patients who are on antiplatelet therapy that can be discontinued safely, elective surgery should be delayed to allow for the effects of the antiplatelet therapy to resolve.

Fibrinogen is a major factor in both the intrinsic and the extrinsic coagulation cascades. Thrombin acts on fibrinogen to form fibrin strands, which are then cross-linked into an insoluble fibrin clot. This mechanism of action is used by the Clauss method to measure fibrinogen concentration. Thrombin is added to the patient's plasma, and the time to coagulation is a reflection of the fibrinogen concentration. In the presence of colloid volume expanders, the fibrinogen concentration measured by the Clauss method may be artifactually high.

If preoperative coagulation studies are abnormal and sample error, medications, and systemic disease are ruled out as a cause, further testing is necessary to identify the underlying etiology. Mixing studies (i.e., mixing the patient's plasma with normal plasma) are performed to differentiate between the presence of a factor deficiency or inhibitor, either congenital or acquired. Correction of the PT/PTT by mixing would indicate a factor deficiency, whereas noncorrection would imply the presence of a factor inhibitor. Further investigation would be necessary to identify either the factor deficiency (through specific factor assays) or the specific inhibitor present (e.g., lupus anticoagulant). Consultation with a hematologist may be prudent in the setting of complex preoperative coagulopathies.

## 3. What are the most common perioperative coagulopathies?

Common perioperative coagulopathies (Table 47-2) include dilutional coagulopathy secondary to massive transfusion, platelet dysfunction, acquired or congenital factor deficiency or factor inhibitor, hyperfibrinolysis, disseminated intravascular coagulation (DIC), heparin excess, and thrombosis.

### *Dilutional Coagulopathy with Massive Transfusion*

In an adult, massive transfusion is defined as transfusion of >10 units of packed red blood cells (PRBCs) within 24 hours. Other definitions include ≥6 units of PRBCs in 12 hours or >50 units of blood products (PRBCs plus fresh frozen plasma [FFP] plus platelets) within 24 hours. In contrast to single factor deficiencies, coagulopathy seen in massive transfusion is multifactorial. Initially, levels of factor VIII and vWF are acutely increased by stress hormones, and sequestered platelets may be released from the spleen and lungs. Fibrinogen, an acute phase reactant, does not decrease below the critical threshold of 1 g/L until loss of approximately 150% of circulating blood volume. Certain factors and platelets can remain above critical levels with a loss of 200% of blood volume. As procoagulant factors decrease with hemodilution, so do natural anticoagulant factors such as antithrombin. The effect is to maintain hemostatic capabilities temporarily. Additionally, fibrinolysis is favored by hemodilution as inhibitors of tissue plasminogen activator are diluted and additional tissue plasminogen activator is released in response to stress hormones. Concurrently, hypothermia slows thrombin generation, and acidosis impairs thrombin generation.

TABLE 47-2 **Perioperative Coagulopathies**

| Coagulopathy | Etiology | Laboratory Test | Treatment |
|---|---|---|---|
| Dilutional coagulopathy | Massive hemorrhage<br>Plasma limited resuscitation | ↑ PT, ↑ PTT<br>↓ Fibrinogen<br>Thrombocytopenia | FFP<br>Cryoprecipitate or fibrinogen concentrate<br>Antifibrinolytics (ϵ-aminocaproic acid, tranexamic acid)<br>Platelets<br>*Consider* PCC, rFVIIa |
| Congenital or acquired factor deficiency | Liver disease | ↑ PT, ↑ PTT | FFP, cryoprecipitate, fibrinogen concentrate |
| | Vitamin K antagonists/malnutrition | ↑ PT, normal PTT | Vitamin K, PCC, FFP, rFVIIa |
| | Intrinsic pathway factor deficiency (e.g., hemophilia) | Normal PT, ↑ PTT | Specific plasma-derived factor concentrates, PCC, rFVIIa, FFP, cryoprecipitate, fibrinogen concentrate |
| | Factor VII deficiency | Normal PT, ↑ PTT | |
| | Common pathway factor deficiency (e.g., afibrinogenemia) | ↑ PT, ↑ PTT | |
| | Dabigatran | | Hemodialysis |
| | Rivaroxaban | | PCC |
| Congenital or acquired platelet dysfunction | Congenital (e.g., von Willebrand disease, Bernard-Soulier syndrome, Glanzmann thrombasthenia)<br>Antiplatelet medications | Decreased platelet function (possibly with normal platelet count) | Consider transfusion if platelet count $<50 \times 10^3/\mu L$ or if platelet dysfunction is suspected |
| | CPB<br>ECMO | Thrombocytopenia | |
| | Hepatic or renal disease<br>Colloid use | ↑ bleeding time | DDAVP |
| Acquired inhibitor | Autoimmune diseases<br>Malignancy<br>Postpartum<br>Medications (penicillins, sulfa drugs, phenytoin, interferon)<br>Factor concentrate exposure<br>Topical bovine thrombin exposure | Normal PT, ↑ PTT<br>In FVII inhibitor: ↑ PT, normal PTT | Depending on specific inhibitor present, the following may be administered: DDAVP, FEIBA, rFVIIa, PCC, FFP, steroids, IVIG, cyclophosphamide, plasma exchange |
| Fibrinolysis | Dilutional coagulopathy<br>Disseminated intravascular coagulation<br>Tissue ischemia<br>Prostate, brain, eye surgery<br>Hepatic disease | ↑ PT, ↑ PTT | ϵ-Aminocaproic acid and tranexamic acid<br>Maintain fibrinogen levels |
| Disseminated intravascular coagulation | Sepsis<br>Trauma<br>Burns<br>Malignancy<br>Obstetric calamities (e.g., abruption)<br>Aortic aneurysms<br>Allergic reactions<br>Immunologic reactions (e.g., transfusion reaction) | ↑ PT, ↑ PTT<br>Thrombocytopenia<br>↑ FDP | FFP<br>Cryoprecipitate, fibrinogen concentrate<br>Platelets (goal $>50 \times 10^3/\mu L$ intraoperative)<br>Antifibrinolytics (*if* fibrinolysis is predominant) |
| Heparin excess | Heparin administration<br>Inadequate heparin reversal | ↑ PTT<br>↑ ACT | Protamine |
| Thrombosis | Disseminated intravascular coagulation<br>Heparin-induced thrombocytopenia<br>Natural anticoagulant deficiency<br>Antiphospholipid syndrome<br>Factor V Leiden<br>Malignancy<br>Liver disease (↓ natural anticoagulants)<br>Immobilization | ↑ bleeding time | Thrombectomy<br>Fibrinolytic therapy<br>Anticoagulant concentrates (antithrombin, protein C)<br>Long-term anticoagulation |

*ACT,* activated clotting time; *CPB,* cardiopulmonary bypass; *DDAVP,* desmopressin; *ECMO,* extracorporeal membrane oxygenation; *FEIBA,* factor eight inhibitory bypass activity; *FFP,* fresh frozen plasma; *IVIG,* intravenous immunoglobulin; *PCC,* prothrombin complex concentrate; *PT,* prothrombin time; *PTT,* partial thromboplastin time; *rFVIIa,* recombinant factor VIIa; *FVII,* factor VII; *FDP,* fibrin degredation products.

### Platelet Dysfunction

Acquired platelet dysfunction etiologies include:

- Disease states such as hepatic or renal failure
- Antiplatelet medications
- Post cardiopulmonary bypass (CPB)
- Extracorporeal membrane oxygenators
- Heparin-induced thrombocytopenia (HIT)

Causes of congenital platelet dysfunction include vWD in 1% of the population and rarer defects in platelet aggregation, adhesion, and granule release such as Bernard-Soulier syndrome (abnormal GP Ib/factor IX/factor V receptor) and Glanzmann thrombasthenia (abnormal GP IIb/IIIa receptor).

### Congenital or Acquired Factor Deficiency

Congenital factor deficiencies can exist for almost any part of the coagulation cascade and include, but are not limited to, hemophilia A, B, and C (factors VIII, IX, and XI); factor VII deficiency; and afibrinogenemia. Acquired factor deficiency may be due to disease states or medication effects. Malnutrition or warfarin use may manifest with a deficiency of vitamin K–dependent factors. Liver disease is associated with deficiencies in factors II, V, VII, IX, X, XI, XIII, and fibrinogen. Complicating the picture of liver disease is a decrease in the production of anticoagulant factors such as protein C, protein S, and antithrombin. Coagulopathy in myeloproliferative diseases may be due to a deficiency of factor V, whereas in amyloidosis it is due to factor X deficiency.

### Acquired Factor Inhibitors

Factor inhibitors are antibodies that inhibit specific factor activity and can develop against nearly every factor involved in the coagulation cascade. Autoimmune disease (e.g., systemic lupus erythematosus, rheumatoid arthritis), malignancy, and the postpartum period all have been associated with various factor inhibitors, although factor VIII inhibitor is the most common (also known as acquired hemophilia A). Medications, such as penicillins, phenytoin, and topical bovine thrombin (previously used intraoperatively as a topical hemostatic agent), have been associated with development of acquired factor inhibitors.

### Hyperfibrinolysis

Hyperfibrinolysis may be seen in several situations commonly encountered by the anesthesiologist but is often underdiagnosed. The predominant mechanism is plasminogen activation secondary to either decreased plasminogen activator clearance or reduced levels of plasminogen inhibitors. Both dilutional coagulopathy and DIC favor fibrinolysis. Fibrinolysis may also be seen in liver disease, tissue ischemia, brain and ophthalmologic surgeries, and prostate cancer.

### Disseminated Intravascular Coagulation

DIC is characterized by systemic activation of coagulation leading to microvascular thrombosis, organ failure, consumption of clotting factors and platelets, and clinical bleeding. DIC may occur in sepsis, trauma, burns, malignancy, obstetric calamities, aortic aneurysms, and allergic and immunologic reactions. The pathophysiology always involves proinflammatory cytokine release leading to widespread tissue factor expression and thrombin generation through the extrinsic coagulation pathway. Concurrent derangement of normal anticoagulation pathways (antithrombin III, protein C, tissue factor pathway inhibitor) also favors microvascular thrombosis. Situations leading to dilutional coagulopathy may exacerbate DIC by dilution of natural anticoagulants and fibrinogen, leading to inadequate fibrin polymerization and release of thrombin and activated factor X from the site of injury into the systemic circulation, triggering microvascular thrombosis.

### Heparin Excess

Heparin excess may occur with intentional or unintentional (medication error) administration of unfractionated heparin. During CPB or vascular surgery, empiric dosing of heparin or its antagonist (i.e., protamine) without monitoring may lead to residual systemic heparin.

### Thrombotic Events

Congenital or acquired thrombotic abnormalities commonly manifest as venous thrombosis. HIT occurs in 5% of patients exposed to heparin. Thrombocytopenia occurs 5–14 days after initiating heparin therapy secondary to platelet activation and aggregation and may be the first sign of HIT. Deficiency of natural anticoagulants (antithrombin, protein C, and protein S) may also predispose patients to a thrombophilic state. In addition, immobilization, pregnancy, malignancy, and the perioperative period all are associated with an increased risk of thrombotic events.

## 4. How are perioperative coagulopathies diagnosed?

Routine coagulation tests (i.e., PT, PTT, platelet count) are of limited value in the perioperative setting for several reasons:

- Results are unavailable for at least 30–60 minutes.
- Abnormal results (e.g., prolonged PTT) are not diagnostic of the underlying mechanism of coagulopathy (e.g., factor deficiency, fibrinogen deficiency, hypothermia, and heparinization all manifest with prolonged PTT).
- They do not detect effects of hypothermia because laboratory tests are performed on plasma at 37°C.
- They do not show the mechanical properties of clot over time because PT and PTT both terminate at low thrombin levels and before fibrin is polymerized.
- Routine tests showing moderate impairment have poor predictive power.

As opposed to plasma-based coagulation laboratory tests, POC devices determine hemostatic potential of whole blood. Evolving evidence surrounding POC devices points toward their usefulness in diagnosing the pathologic mechanism of intraoperative coagulopathy,

allowing for targeting treatment to deficient components. Use of POC devices for goal-directed therapy has been shown to reduce blood product administration in cardiac, liver, trauma, and obstetric surgery. Several institutions have developed transfusion algorithms based on POC measurements with some reported success.

Thromboelastography (TEG; Haemonetics, Braintree, MA) measures viscoelasticity of whole blood from initiation of fibrin formation to maximal platelet clot strength and through fibrinolysis (Figure 47-2). A blood sample is placed in a cuvette that is rotated slowly to activate clotting. The following five values represent different mechanisms of clot formation:

- *r* value—time to initial fibrin formation
  - Increased values imply factor deficiency or inhibitor
- *K* value—time from the end of *R* time to an amplitude of 20 mm
  - Reflects clot kinetics
  - Affected by any variable that would slow clot formation (e.g., factor deficiency, heparin)
- α angle—tangent of the curve made as *K* is reached (20 mm)
  - Reflects the kinetics of fibrin production and cross-linking
  - Affected by any variable that would slow clot formation (e.g., factor deficiency, heparin)
- MA (Maximal Amplitude)
  - Indication of clot strength
  - Depends on both platelet number and function as well as adequate fibrinogen levels
- Lysis of the developed clot—measured at both 30 minutes and 60 minutes
  - Reflects degree of fibrinolysis
  - If abnormal, implies excess plasminogen activity

Figure 47-3 depicts thromboelastography results seen with different coagulation abnormalities.

Different additives can be used with thromboelastography measurements to improve diagnostic capabilities. The addition of heparinase identifies abnormal coagulation secondary to excessive heparin activity. If excessive fibrinolysis is detected, antifibrinolytics can be added to assess efficacy of treatment. c7E3 Fab (ReoPro), a monoclonal antibody that binds to platelet GP IIb/IIIa receptors, eliminates platelet activity from the thromboelastography result. The residual maximal amplitude measurement reflects fibrinogen activity only, enabling determination of platelet contribution to total clot strength. The platelet mapping assay modification allows for identification of platelet-inhibiting drugs.

Rotational thromboelastometry (ROTEM; Tem Innovations GmbH, Munich, Germany) is another viscoelastic monitor of coagulation that has more widespread use in Europe but has been approved by the U.S. Food and Drug Administration for use in the United States since 2011 (Figure 47-4). A blood sample is placed in a cuvette, and instead of the cuvette rotating (as in thromboelastography), the sensor shaft placed in the cuvette rotates. Rotational thromboelastometry provides information similar to thromboelastography on coagulation in a sample of whole blood. The following parameters are measured:

- Clotting time—time from the start of the reaction to an amplitude of 2 mm
  - Reflects defects in plasma-mediated coagulation (e.g., factor deficiency, heparin)
- Clot formation time—time from an amplitude of 2–20 mm
  - Involves fibrin polymerization and clot stabilization
  - Affected by platelet function and to some degree fibrinogen and coagulation factors
- Maximum clot firmness—maximal amplitude of the tracing
  - Reflects platelet count, platelet function, and fibrinogen concentration
- Maximum lysis—percent reduction in clot firmness
  - Identifies hyperfibrinolysis

Modifications to rotational thromboelastometry allow identification of the pathologic mechanism of intraoperative coagulopathy (Table 47-3).

Platelet POC tests have not had as much success in goal-directed management of hemostasis as viscoelastic measures of coagulation. The platelet function analyzer (PFA-100; Siemens Healthcare Diagnostics, Deerfield, IL) measures in vitro bleeding time by using a vacuum to perfuse blood through an aperture in the presence of platelet activating compounds. Further studies have shown that the platelet function analyzer requires platelet counts >100 × $10^3$/μL and a hematocrit >30%. It has a high negative predictive value and a low positive

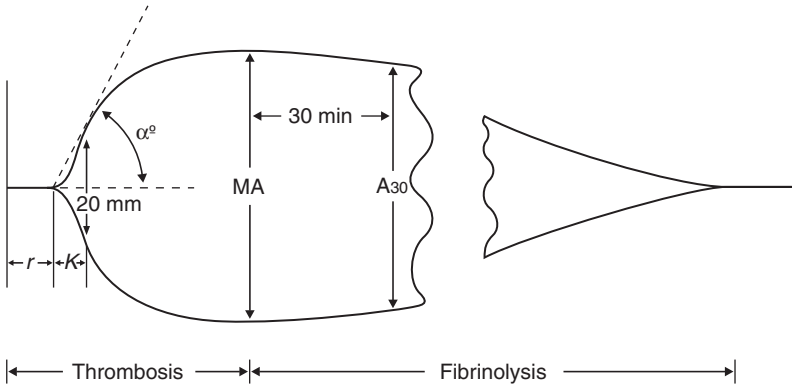


**FIGURE 47-2** ■ **Thromboelastography (see text for explanation).** (From Deakin C: Clinical Notes for the FRCA. Churchill Livingstone, Philadelphia, 2011.)

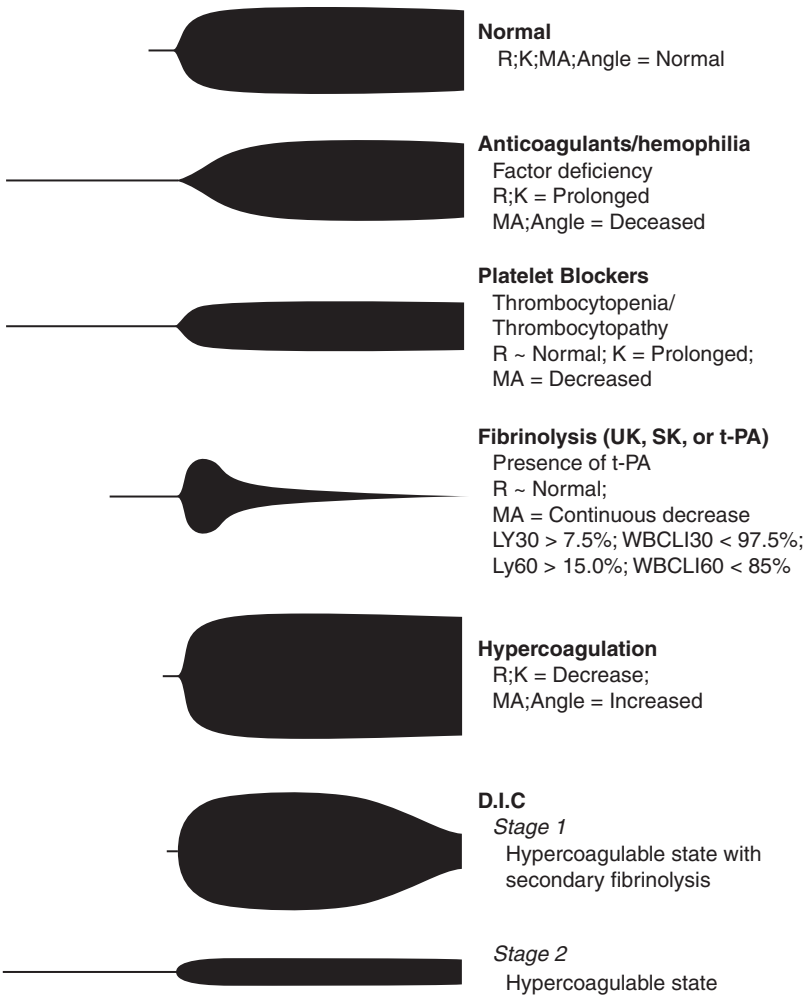


**FIGURE 47-3** ■ Normal and abnormal thromboelastography results. (From Deakin C: Clinical Notes for the FRCA. Churchill Livingstone, Philadelphia, 2011.)

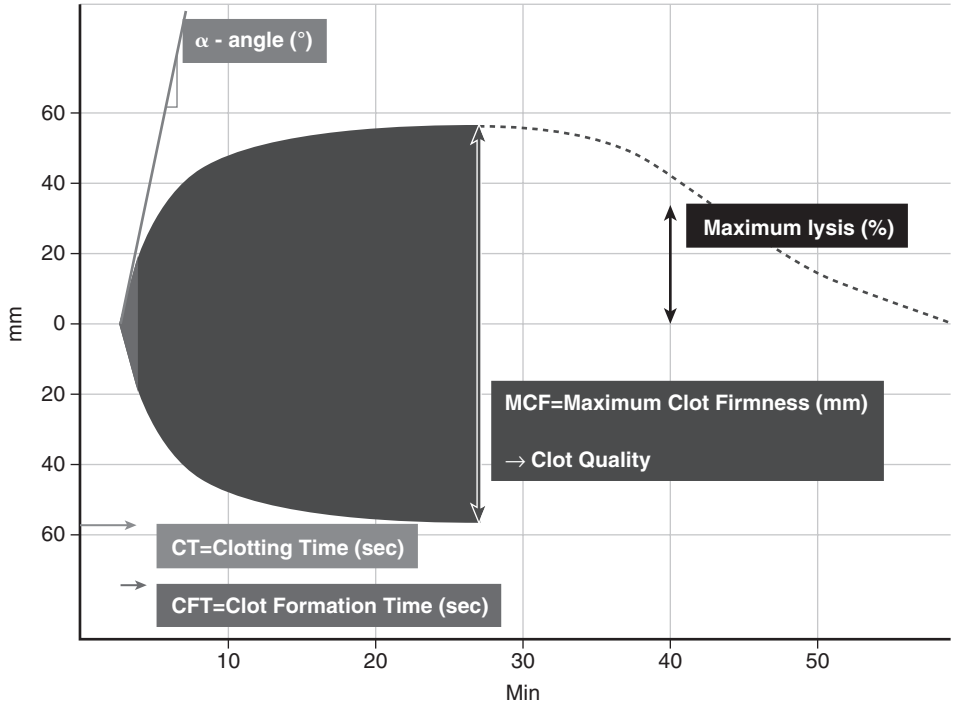


**FIGURE 47-4** ■ Rotational thromboelastometry. (From Armstrong S, Fernando R, Ashpole K, et al.: Assessment of coagulation in the obstetric population using ROTEM thromboelastometry. Int J Obstet Anesth 20:293, 2011.)

TABLE 47-3 **Modifications of Rotational Thromboelastometry**

| Test | Mechanism/Additive | Abnormality | Treatment |
|---|---|---|---|
| INTEM | Activates intrinsic pathway | Coagulation factors<br>Platelets<br>Fibrinogen<br>Heparin | Fresh frozen plasma<br>Coagulation factors<br>Fibrinogen<br>Platelets |
| HEPTEM | INTEM assay with heparinase | Confirms presence of heparin as etiology of coagulopathy | Protamine |
| EXTEM | Activates extrinsic pathway | Extrinsic coagulation factors<br>Platelets<br>Fibrinogen | Fresh frozen plasma<br>Coagulation factors<br>Fibrinogen<br>Platelets |
| FIBTEM | Eliminates platelet contribution to clot formation<br>Cytocholasin D—potent inhibitor of actin polymerization | Fibrinogen deficiency<br>Fibrinogen polymerization disorders | Fibrinogen |
| APTEM | Inhibits fibrinolysis with aprotinin | Hyperfibrinolysis<br>Identify need for fibrinogen or platelets | Antifibrinolytic therapy<br>Fibrinogen<br>Platelets |

predictive value for etiology of inadequate hemostasis, diminishing its utility in transfusion algorithms. Plateletworks (Helena Laboratories, Beaumont, TX) compares platelet counts in a control sample with counts after platelet activation and aggregation, giving a percentage of reactive platelets. Plateletworks has been shown to correlate with standard methods of laboratory platelet counts and can detect GP IIb/IIIa receptor inhibition and platelet dysfunction related to CPB.

## 5. How are perioperative coagulopathies treated?

Treatment of perioperative coagulopathies involves restoring the deficient components of coagulation and eliminating the cause. PRBCs are transfused to increase oxygen-carrying capacity but may also play a role in promoting hemostasis because red blood cell (RBC) mass leads to margination of platelets near vessel walls and sites of vascular injury. In addition, RBCs release adenosine diphosphate under shear stress, which aids in activation of platelets.

FFP contains all the components of coagulation found in patients' plasma, including factors, anticoagulants, and natural antifibrinolytics. Evolving evidence suggests that early intervention with FFP during massive transfusion and higher FFP-to-RBC transfusion ratios ($\geq$1:1) may lead to a mortality benefit. Currently, there are no guidelines to standardize the optimal FFP-to-RBC ratio. The risk of viral transmission, TRALI, and volume overload must be weighed against the benefits of plasma transfusion. In the presence of factor inhibitors (e.g., acquired hemophilia, heparin, direct thrombin inhibitor, or factor Xa inhibitor), FFP is ineffective to treat or prevent bleeding because the inhibitor acts against the factors in FFP as well. Large volumes of FFP (15–30 mL/kg) are necessary to achieve adequate factor concentrations when there is a deficiency and ongoing losses. FFP is not effective in correcting mildly elevated PT, PTT, and INR ($<$1.6). Mildly abnormal coagulation studies are unreliable predictors of perioperative blood loss. FFP is only partially effective in correcting coagulopathy associated with warfarin use and liver disease.

In the setting of massive transfusion, FFP is inadequate to increase plasma fibrinogen levels, necessitating cryoprecipitate administration. An estimated 30 mL/kg of FFP is needed to increase plasma fibrinogen by 1 g/L, whereas 15 mL (1 unit)/10 kg of cryoprecipitate increases plasma fibrinogen by 0.5 g/L. More recently, the first fibrinogen concentrate became available in the United States, but it is approved by the U.S. Food and Drug Administration only for afibrinogenemia and hypofibrinogenemia. Current evidence is shifting toward the need for higher fibrinogen levels to provide sufficient fibrin clot polymerization. All current recommendations suggest fibrinogen levels $>$1 g/L, with some European guidelines recommending $>$1.5–2 g/L, in the setting of perioperative bleeding. It has been suggested that high fibrinogen levels ($>$3 g/L) may even compensate for thrombocytopenia.

Prothrombin complex concentrate (PCC) contains factors II, IX, and X (and VII in Europe) at levels 25 times those seen in FFP. PCC eliminates disadvantages of FFP administration such as volume overload, hemodilution, infection, and the need for crossmatching. PCC is recommended to antagonize the effects of warfarin and can treat specific factor deficiencies. Evidence for use in dilutional coagulopathy and massive transfusion is equivocal. Its use must be weighed against the risk of thrombosis in the presence of diluted antithrombin. Factor eight inhibitor bypass activity (FEIBA), containing factors II, IX, X, and activated VII, is useful in patients with hemophilia A or B with inhibitors.

Recombinant activated factor VII (rFVIIa) is thought to bind to tissue factor at the site of vascular injury and amplify thrombin generation. As with PCC, evidence for rFVIIa use in hemodilution is equivocal, and it is likely

efficacious only with adequate fibrinogen levels. The theoretical risk of thrombotic complications must be weighed against the risk of ongoing hemorrhage. There are numerous reports of rFVIIa effectiveness as an off-label use during life-threatening hemorrhage that is unresponsive to conventional management.

Platelet transfusion is usually considered when the count becomes $<50 \times 10^3/\mu L$, although considering margination in vivo and release of sequestered platelets, the threshold for transfusion is unclear. If platelet dysfunction is suspected, transfusion may restore functional platelets to the circulation.

Desmopressin (DDAVP), a V-2 receptor agonist, stimulates vWF release from endothelial cells and increases available factor VIII. Outside of hemophilia A (factor VIII deficiency) and vWD, DDAVP is thought to increase platelet adhesion to vessel walls and promote a state of heightened coagulability and fibrin formation. It has been shown to decrease perioperative blood loss, but it may not reduce perioperative transfusion of PRBCs. Usefulness may be limited in critically ill patients already receiving exogenous vasopressin.

As previously stated, several situations may favor fibrinolysis, and the efficacy of antifibrinolytics (e.g., ϵ-aminocaproic acid and tranexamic acid) for reducing blood loss and PRBC transfusion requirements has been shown in trauma, cardiac, orthopedic, and hepatic surgery. Risk of thrombotic events must be weighed against the benefits of antifibrinolytic therapy when considering administration of these medications.

Successful treatment of perioperative coagulopathies depends on diagnosing the deficiency and treating with the appropriate replacement component. Continual monitoring and assessment are important because changing coagulopathies may require different management strategies.

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CASE 48

# Blood Replacement

**Mark Gettes, MD**

## QUESTIONS

1. How is oxygen transported?
2. Describe the compensatory mechanisms for blood loss.
3. What is the minimum acceptable hemoglobin concentration (transfusion trigger)?
4. List potential sources of autologous blood.
5. Explain acute isovolemic hemodilution.
6. Outline the physiologic response to acute isovolemic hemodilution.
7. How is acute isovolemic hemodilution accomplished?
8. Which patients are suitable candidates for acute isovolemic hemodilution?
9. What is intraoperative cell salvage, and how do modern cell salvage devices work?
10. Outline the characteristics of blood obtained by cell salvage.
11. Discuss the indications and benefits of intraoperative cell salvage.
12. Explain the controversies and contraindications involving intraoperative cell salvage.
13. What is preoperative autologous blood donation?
14. Who is eligible for and what are the contraindications to preoperative autologous blood donation?
15. What are the disadvantages and risks of preoperative autologous blood donation?
16. Describe postoperative blood salvage.
17. Explain the advantages and disadvantages of different autologous blood sources.

A 70-year-old, 70-kg man is scheduled for revision total hip prosthesis. He has a history of hypertension controlled on medical therapy, and type 2 diabetes mellitus. He is otherwise in good health. The starting hemoglobin (Hb) and hematocrit (Hct) are 13 g/dL and 40%, respectively. He predonated 2 units of his own blood and states that he wishes only his own blood to be used during surgery.

### 1. How is oxygen transported?

A major function of the circulation is to carry oxygen to tissues for use in metabolism. Oxygen delivery ($\dot{D}O_2$), or oxygen transport, is the product of two factors: blood flow, or cardiac output (CO), and the amount of oxygen carried in the blood, or arterial oxygen content ($CaO_2$):

$$\dot{D}O_2 = CO \times CaO_2$$

As oxygen content of blood decreases, $\dot{D}O_2$ can be maintained by a proportionate increase in CO.

Oxygen in blood exist in two forms. It is bound by Hb and dissolved in plasma. The oxygen content of 100 mL of blood is described by the following equation:

$$CaO_2 = (Hb \times 1.34 \times SaO_2) + (PaO_2 \times 0.0031)$$

where $CaO_2$ is arterial oxygen content in milliliters of oxygen per 100 mL of blood, $SaO_2$ is percent of arterial Hb saturated with oxygen, and $PaO_2$ is partial pressure of arterial oxygen.

Under normal conditions (e.g., absence of pulmonary disease, normal Hb, physiologic shunt of 2%–3%), arterial oxyhemoglobin saturation is approximately 97%, and the partial pressure of dissolved oxygen is approximately 100 mm Hg. $CaO_2$ can then be calculated as follows:

$$\begin{aligned} CaO_2 &= (15\ g/dL \times 1.34 \times 0.97) \\ &\quad + (100\ mm\ Hg \times 0.0031) \\ CaO_2 &= 19.5 + 0.31 \\ CaO_2 &= 20\ mL\ O_2/100\ mL\ blood \end{aligned}$$

This calculation demonstrates that the amount of oxygen dissolved in plasma (0.31 mL/100 mL blood) is negligible compared with the amount carried by Hb (19.5 mL/100 mL blood).

Because oxyhemoglobin binding factor (1.34) and $SaO_2$ (0.97) are constant under normal conditions, $CaO_2$ varies almost linearly with Hb concentration. Under abnormal conditions, such as obesity and term pregnancy, rapid falls in $SaO_2$ during induction of anesthesia result in immediate decreases in $CaO_2$. The compensatory tachycardia may or may not be sufficient to maintain normal $\dot{D}O_2$.

### 2. Describe the compensatory mechanisms for blood loss.

Blood loss results in diminished intravascular volume and reduced oxygen-carrying capacity secondary to loss of Hb. As intravascular volume decreases, compensatory

vasoconstriction and tachycardia occur in an attempt to preserve CO. Continuing volume loss results in decreased CO, reducing $\dot{D}O_2$ to tissues. Restoration of intravascular volume by infusion of either colloid solution in a 1:1 ratio to blood loss or crystalloid solution in a 3:1 ratio allows normalization of CO and maintenance of hemodynamic stability.

Several mechanisms are available to respond to loss of oxygen-carrying capacity. First, CO may increase with restoration of intravascular volume, maintaining or increasing $\dot{D}O_2$. Second, at the tissue level, oxygen extraction may increase. Normal mixed venous oxygen saturation is approximately 75%; this indicates that only 25% of available oxygen is being extracted. A substantial reserve of oxygen is available to the tissues, which can be used simply by increasing the amount extracted.

### 3. What is the minimum acceptable hemoglobin concentration (transfusion trigger)?

If blood loss continues during surgery, even if intravascular volume is maintained, oxygen-carrying capacity eventually falls too low to meet metabolic demands, and red cell transfusion is required. The minimum safe level of Hb, or transfusion trigger, is a question on which much attention has been focused. In the mid-twentieth century, advances in the science of transfusion medicine and the greater safety of blood banking led to routine transfusion of patients to maintain an arbitrary Hb level of >10 g/dL or Hct >30%. However, fueled largely by awareness of the role of blood transfusion in the transmission of acquired immunodeficiency syndrome (AIDS), recognition of morbidity associated with blood transfusion grew. Increasingly, attempts have been made to determine scientifically the transfusion trigger—the Hb threshold at which red cell transfusion is warranted.

From animal models and from experience with otherwise healthy Jehovah's Witnesses, it is known that survival is possible with a Hct of 5%–6% (Hb 2 g/dL) if normovolemia is maintained. Experience with other chronically anemic patients, such as patients with renal failure, showed that Hct values in the low 20s are routinely tolerated. From these data, it is apparent that previously recommended transfusion triggers of Hb 10 g/dL and a Hct of 30% are unnecessarily restrictive.

Attempts to determine the transfusion trigger have focused in particular on patients with risk factors for cardiac disease. Maximal stress on $\dot{D}O_2$ occurs in the heart, with 70% of available oxygen extracted, as opposed to 25% for the body as a whole. If $CaO_2$ decreases, the reserve for increased extraction is low, and the only available compensatory mechanism is to increase coronary blood flow. In patients with coronary artery disease, ability to increase coronary blood flow may be compromised, and the critical Hct level—the transfusion trigger—may be much higher. Similarly, patients with significant valvular heart disease or poor ventricular function as well as patients in whom $CaO_2$ is limited by pulmonary disease or who are in hypermetabolic states with large oxygen extractions may have high transfusion triggers.

Although not defining a precise transfusion trigger, several studies concur that the previous transfusion trigger of Hb 10 g/dL or Hct 30% was unnecessarily high. The TRICC (Transfusion Requirements in Critical Care) trial found no significant difference in outcomes in patients assigned to a transfusion trigger of Hb 7 g/dL as opposed to Hb 10 g/dL. Certain complications (i.e., myocardial infarction, congestive heart failure) were higher in the Hb 10 g/dL group. Similarly, a study comparing transfusion thresholds in patients with cardiac risk factors undergoing surgery for hip fracture found no significant improvements in outcomes when using a transfusion threshold of Hb 8 g/dL as opposed to Hb 10 g/dL.

The safest blood transfusion is no transfusion. However, if "no blood transfusion" is not an option, potential complications of blood transfusion can be decreased by using the patient's own blood, rather than blood from a donor.

As of this writing, the current practice guidelines of the American Society of Anesthesiologists (ASA) for perioperative blood transfusion reflect the consensus that previously recommended thresholds of Hb 10 g/dL were unnecessarily high. The precise transfusion trigger has yet to be determined. The ASA practice guidelines state that "red blood cells should usually be administered when the hemoglobin level is less than 6 g/dL and . . . are usually unnecessary when the level is more than 10 g/dL." The guidelines also support the use of preadmission blood collection, acute normovolemic hemodilution, and intraoperative red blood cell recovery in situations where autologous blood is required or preferred.

### 4. List potential sources of autologous blood.

Physician awareness of the dangers associated with homologous blood transfusions as well as increased pressure from the public to avoid transfusions has led to an increased use of autologous blood sources. These sources are the following:

- Preoperative autologous blood donation
- Acute isovolemic hemodilution (AIHD)
- Intraoperative cell salvage
- Postoperative cell salvage

Each of the above-listed autologous blood sources has a role to play in avoidance of homologous transfusion.

### 5. Explain acute isovolemic hemodilution.

AIHD is a procedure in which whole blood is removed perioperatively, while intravascular volume is maintained by simultaneous infusion of crystalloid or colloid solutions. The blood, which is withdrawn into standard blood bags containing anticoagulant, is available for transfusion to the patient either during surgery or in the postoperative period. In this way, autologous whole blood containing red cells, clotting factors, and platelets is available. The advantages of AIHD are summarized in Box 48-1.

### 6. Outline the physiologic response to acute isovolemic hemodilution.

To understand how AIHD may be safely accomplished, it is necessary to understand the physiologic response to its use. As previously discussed, $\dot{D}O_2$ is the product of CO and $CaO_2$. As whole blood is withdrawn for isovolemic hemodilution, red cells are removed from the circulation

**BOX 48-1 Advantages of Acute Isovolemic Hemodilution**

- Red blood cell loss is reduced with each milliliter of surgical hemorrhage
- Fresh whole blood is available for transfusion when required
- Tissue perfusion is improved as viscosity diminishes

and $CaO_2$ decreases. It might be expected that $\dot{D}O_2$ would decrease. However,, as the Hct decreases to 30%, $\dot{D}O_2$ increases over baseline (Box 48-2); this is because hemodilution alters the rheologic properties of blood. Blood viscosity is decreased by hemodilution, which effectively lowers systemic vascular resistance. An increase in venous return results in an increased stroke volume. CO increases proportionally more than $CaO_2$ decreases and $\dot{D}O_2$ increases. In addition, the increase in CO is accomplished without an increase in heart rate, if intravascular volume is maintained. Hemodilution to a Hct of 30% causes a 30%–50% increase in CO. $\dot{D}O_2$ does not fall to control values until a Hct of approximately 20% is reached. Additionally, during isovolemic hemodilution, local tissue oxygenation is preserved and enhanced by a more homogeneous distribution of capillary blood flow. Studies with tissue electrodes have shown that hypoxic microareas do not occur during isovolemic hemodilution.

## 7. How is acute isovolemic hemodilution accomplished?

AIHD is accomplished early in the perioperative period, usually just after induction of anesthesia. Blood is removed via a large-bore intravenous catheter and saved in standard blood bags containing anticoagulant. An arterial catheter may be used for collecting autologous blood, but we have found this to be less satisfactory. Simultaneously, crystalloid in a 3:1 ratio or colloid (albumin, hydroxyethyl starch, or dextran) in a 1:1 ratio is infused through another large-bore intravenous catheter. The amount of blood to be removed can be calculated by any of the formulas used to calculate allowable blood loss. We typically use the following formula:

$$\text{Volume to be removed in mL} = (Hct_A - Hct_B)/([Hct_A + Hct_B]/2) \times EBV$$

**BOX 48-2 Physiologic Response to Acute Isovolemic Hemodilution**

- $\dot{D}O_2$ remains constant or may increase
- $CaO_2$ decreases as red blood cells are removed
- CO increases without an increase in heart rate
  - Lowered systemic vascular resistance
  - Improved venous return
- Beneficial redistribution of capillary blood flow

where $Hct_A$ is starting hematocrit, $Hct_B$ is target hematocrit for hemodilution, and EBV is estimated blood volume.

Typically, a target Hct in the mid to upper 20s (25%–27%) is used. This value allows for substantial hemodilution but still provides some margin of safety when blood loss begins to occur during surgery. In this instance, $Hct_A$ = 40%, EBV = 70 kg × 70 mL/kg = 4900 mL, and we would choose a $Hct_B$ = 27%. The formula then yields:

$$\text{Volume to be removed in mL} = (40 - 27)/([40 + 27]/2) \times 4900$$
$$13/33.5 \times 4900 = 1900 \text{ mL}$$

Based on this formula, 3–4 units of the patient's blood could be removed for later retransfusion. As units of blood are removed, they are labeled and numbered consecutively. Blood is retransfused in reverse order of collection. The first unit removed is the least dilute and the richest in red cells, plasma factors, and platelets, and it should be the last unit retransfused. Blood removed during hemodilution may be stored in the operating room at room temperature for a maximum of 6 hours. Autologous blood remaining after surgery may be stored in a blood bank refrigerator for further use.

Invasive hemodynamic monitoring (i.e., arterial catheter, central venous catheter) is not mandatory during isovolemic hemodilution, but it facilitates serial Hct measurements and provides a guide to fluid replacement. Because CO increases in AIHD without an increase in heart rate, development of intraoperative tachycardia may indicate hypovolemia and the need for retransfusion. A urinary catheter to monitor urine output as a gauge of intravascular volume may be helpful. Also, replacing autologous blood with three times the volume of crystalloid initiates a diuresis (Box 48-3).

## 8. Which patients are suitable candidates for acute isovolemic hemodilution?

The indications and contraindications for AIHD are listed in Box 48-4. The essential criteria for AIHD are an anticipated blood loss greater than 1000 mL and a starting Hct of ≥36%. AIHD has been described for a

**BOX 48-3 Performance of Acute Isovolemic Hemodilution**

**Monitoring**

- ± Invasive monitoring
- Urinary catheter
- Serial hematocrit measurements
- Tachycardia is a warning sign of hypovolemia

**Removal**

- Two large-bore intravenous catheters
  - May substitute one intravenous catheter for an arterial catheter
- Simultaneous administration of crystalloid (3:1) or colloid (1:1)

**Retransfusion**

- Retransfuse units in reverse order of collection

**BOX 48-4 Selection of Patients for Acute Isovolemic Hemodilution**

- Indications
  - Anticipated blood loss >1000 mL
  - Starting hematocrit >36%
- Contraindications
  - Anemia
  - Coronary artery disease
  - Left ventricular dysfunction
  - Valvular heart disease
  - Renal disease
  - Pulmonary disease
  - Carotid stenosis

wide variety of cases, including major urologic surgery, orthopedics, gynecologic surgery, plastic and reconstructive surgery, neurosurgery (brain and tumor resection), and cardiothoracic surgery. Reduction in homologous blood usage has been reported to range from 18%–90%. Age per se is not a contraindication to hemodilution, and use of AIHD has been described in both elderly and pediatric patients.

Because the major compensatory mechanism for hemodilution is increased blood flow, isovolemic hemodilution is contraindicated in patients whose ability to increase either systemic or coronary blood flow might be compromised. AIHD is contraindicated in patients with anemia, carotid artery stenosis, coronary artery disease, left ventricular dysfunction, and aortic or mitral valve stenosis. Because of the fluid shifts involved, AIHD is contraindicated in patients with renal or pulmonary disease.

Significant preexisting myocardial or brain disease represents a contraindication to isovolemic hemodilution because myocardial ischemia and cerebral hypoxia are its major associated complications. Coagulopathies emanating from reduced factor levels may be exacerbated by dilutional effects.

## 9. What is intraoperative cell salvage, and how do modern cell salvage devices work?

Intraoperative cell salvage is a procedure in which blood lost during surgery is collected and made available for transfusion back to the same patient. Modern cell-saving devices function by a four-step process, as follows:

*Collection:* Blood is suctioned from the surgical field and mixed in the suction tubing with an anticoagulant containing either heparin or citrate. The suction pressures used in cell salvage systems are low (<100 mm Hg) to avoid hemolysis of collected blood. The blood is passed through a filter to remove debris and stored in a canister until a sufficient volume is present for further processing.

*Concentration:* The mixture of blood, anticoagulant, and irrigating solution collected by the suction is passed into a centrifuge bowl, where the heavier red cells are retained and the lighter elements are spun off and discarded.

*Washing:* A large volume of saline is passed through the centrifuge bowl, further removing noncellular elements and debris, leaving red cells suspended in saline.

*Reinfusion:* The red cell/saline mixture is pumped from the centrifuge into a standard plastic infusion bag, which is available for transfusion back to the patient.

Modern cell salvage devices can process and return a unit of blood every 3 minutes in the face of rapid bleeding.

## 10. Outline the characteristics of blood obtained by cell salvage.

Salvaged autologous blood differs from banked blood and other sources of autologous blood in many ways. Salvaged autologous blood is basically a suspension of red cells in saline. The Hct of salvaged blood may vary depending on the amount of blood collected from the field but is typically in the 50%–60% range. Once processed, salvaged blood contains essentially no clotting factors or platelets. If large volumes of salvaged blood are used to replace surgical blood loss, dilutional thrombocytopenia and low levels of clotting factors may result. Salvaged blood does not exhibit the storage lesion that is present in banked blood (Table 48-1). The 2,3-diphosphoglycerate level of salvaged blood is normal, and it does not exhibit the low pH, elevated potassium, and microaggregate formation found in banked blood. Chromium-labeling studies have shown that salvaged red cells have normal survival times after they are reinfused. Indices of red cell viability, such as resistance to osmotic stress, are superior in salvaged blood compared with banked blood.

## 11. Discuss the indications and benefits of intraoperative cell salvage.

Intraoperative cell salvage has been used in various surgical settings, and its ability to reduce homologous blood use is

TABLE 48-1 **Characteristics of Salvaged Autologous Blood Compared with Banked Blood**

| | Salvaged Autologous Blood | Banked Blood |
|---|---|---|
| 2,3-Diphosphoglycerate | Normal | Decreased |
| Potassium | Normal | Increased |
| pH | Normal | Decreased |
| Microaggregate formation | No | Yes |
| Resistance to osmotic stress | Normal | Decreased |

**BOX 48-5 Indications for Intraoperative Cell Salvage**

- Anticipated blood loss >1000 mL
- Jehovah's Witnesses—not all will accept it
- Homologous blood difficult to obtain
  - Rare blood type
  - Multiple antibodies
- Surgery where blood loss is confined to a discrete area
  - Vascular
  - Orthopedic
  - Trauma
  - Cardiac

well documented. Intraoperative cell salvage is indicated in cases for which blood loss is expected to be >1000 mL. Many, although not all, Jehovah's Witnesses accept cell salvage, and it may be used in cases where obtaining homologous blood is difficult because of rare blood types or multiple antibodies. Cases ideally suited for cell salvage are cases in which surgical bleeding is confined to a discrete area. Blood loss occurring slowly over a wide area is difficult to collect. Typically, because of losses from the surgical field and losses occurring during processing, approximately 50% of shed blood is returned to the patient. Recovery may be higher in some cases, such as abdominal aortic aneurysm resection, where blood loss is well localized. Use of intraoperative cell salvage has had a great impact in vascular, orthopedic, and cardiac surgeries (Box 48-5). It also has been commonly used in urologic, trauma, transplantation, and neurosurgical procedures.

Cell salvage has decreased the average homologous blood requirements. The percentage of patients who do not require any homologous blood products has sharply increased from 4% to 68% in one study involving patients undergoing vascular surgery. Another study demonstrated that 17% of the total institutional red cell requirement was obtained by intraoperative cell salvage.

## 12. Explain the controversies and contraindications involving intraoperative cell salvage.

The major controversies regarding intraoperative cell salvage involve its use in oncologic surgery and in contaminated trauma cases. In both situations, questions arise concerning the possibility of intravascular dissemination of unwanted material—tumor cells in one case and microorganisms in the other case—by the use of cell salvage.

Tumor cells may survive processing and suspension along with red cells. Consequently, viable tumor cells can be transfused back to the patient. Some experts have questioned the advisability of cell salvage during oncologic surgery. However, it has not been demonstrated that transfusion of malignant cells results in dissemination of tumor. In many forms of cancer, tumor cells may be recovered from blood without blood-borne spread. There is a particular reason for avoiding homologous transfusion in oncologic surgery. Homologous transfusions have been shown to produce an immunosuppressive effect, resulting in earlier tumor recurrence and decreased survival times in patients with some forms of cancer. Intraoperative cell salvage may be advantageous in such cases. One group of studies looked at outcome of cell salvage in patients undergoing major urologic oncologic procedures. No evidence of blood-borne dissemination or high tumor recurrence rates was found in these patients. Use of cell salvage in such cases has been recommended. It is possible to compromise by using the cell salvage suction during dissection of tumor-free areas, while employing a separate suction to collect and discard material during actual tumor dissection. Nonetheless, more clinical studies are necessary to resolve this issue fully.

In abdominal trauma, shed blood is frequently contaminated by intestinal contents. Because of red cell binding, bacteria survive processing by cell salvage equipment and can be transfused back to the patient. Whether transfusion of contaminated blood contributes to morbidity is questionable. Many experts believe that such patients are exposed to a bacterial load by the nature of their injuries. Prophylactic antibiotics significantly reduce the risk of sepsis. Consequently, there is little additional danger from bacteria in salvaged blood, and patients are spared the dangers associated with homologous blood. Some clinicians believe that salvaged contaminated blood should be used only as a lifesaving measure when no other blood is available. A definitive answer to this question awaits further clinical trials.

Cell salvage should not be used in the presence of topical hemostatic agents, povidone-iodine, polymyxin, bacitracin, or other topical antibiotics used with irrigation solutions. It is presently contraindicated if shed blood is contaminated by amniotic fluid.

Present cell salvage technology requires specially trained personnel to operate the equipment. These individuals should be free from other activities during processing. Consequently, someone other than the anesthesiologist caring for the patient should be responsible for the cell salvage process.

## 13. What is preoperative autologous blood donation?

Preoperative autologous blood donation (PABD) refers to donation of a patient's own blood before an operation. It is stored and possibly transfused intraoperatively or postoperatively. A national multicenter study in 1987 revealed that 10% of all blood transfused for elective surgery could be obtained by PABD. The driving force behind increased interest in PABD at that time was concern for transfusion transmission of viruses, particularly human immunodeficiency virus (HIV). Use of PABD peaked in 1992, when it provided 8.5% of all units of blood collected in the United States. Use of PABD has declined in recent years. In 1999, 4.7% of all units collected and 3% of all units of red blood cells transfused were provided by PABD. PABD has clearly been shown to reduce patient exposure to homologous blood.

## 14. Who is eligible for and what are the contraindications to preoperative autologous blood donation?

PABD is limited to cases in which there is a reasonable likelihood that red cell transfusion will be required during

the perioperative period. A surgical blood loss of ≥1000 mL should be anticipated. The surgical blood schedule serves as a guide to whether or not transfusion is likely. Patients should not be encouraged to donate blood for procedures in which there is little chance of significant blood loss.

Criteria for donation of autologous blood are less stringent than the criteria for volunteer donation. Autologous donors need at least a predonation Hb of 11 g/dL or Hct of 33%. Age is not a criterion for predonation. In patients weighing >50 kg, 450 mL of whole blood is donated at each visit. In patients weighing <50 kg, the volume of blood removed is proportional to weight, using the following formula:

$$\text{Volume of the blood donated in mL}/450\ \text{mL} = \text{donor weight (kg)}/50\ \text{kg}$$

PABD requires a suitable interval between the decision to undertake surgery and the date of the operation. The storage life of blood is 35 days. Consequently, there is no point in donating blood >5 weeks preoperatively. A unit of blood may be banked every 3 days, depending on the donor's Hct, but donations are usually made every 7 days. Units can be donated up to 3 days preoperatively. In the event that surgery is postponed, blood may be frozen to prevent outdating if necessary.

In rare cases where collection of large numbers of autologous units is required, blood may be frozen and stored over long periods. Patients should be started on oral iron therapy when the decision to predonate blood is made. Use of recombinant erythropoietin to increase the amount of blood available for predonation and to decrease the interval between donations has been described and may be beneficial in patients who are anemic, in patients who require large numbers of autologous units, or in situations where the presurgical intervals are short. Erythropoietin therapy as described is expensive and remains experimental as of this writing.

There are several contraindications to PABD. Because microorganisms may proliferate during blood storage, septicemia is an absolute contraindication to predonation. Lack of intravenous access may also prohibit predonation.

Patients who are positive for HIV or hepatitis B surface antigen (HBsAg) may predonate blood. Such units must be labeled and segregated to protect other patients who might erroneously receive the units as well as workers handling the units. Retransfusing this blood requires a special order from the patient's physician.

As in other aspects of transfusion medicine, patients with cardiac disease represent a gray area in terms of risk. Most centers exclude patients with unstable angina, aortic stenosis, or left main coronary artery disease but accept donors with stable coronary artery disease. Some investigators have advocated monitoring (blood pressure, electrocardiography [ECG], pulse, and oxygen saturation), simultaneous fluid administration, and physician supervision of high-risk patients making autologous donations. Future studies are needed to define precisely the risk in these patients. In contrast to homologous blood donation, a history of malignancy is not a contraindication for PABD (Box 48-6).

**BOX 48-6 Preoperative Autologous Blood Donation**

**Indications**
- Blood loss >1000 mL

**Patient Criteria**
- Hb 11 g/dL
- Hct 33%
- Age is not a criterion

**Contraindications**
- Bacteremia
- Lack of intravenous access
- Cardiac disease
  - Unstable angina
  - Aortic stenosis
  - Left main coronary artery disease

**Not Contraindications**
- HIV
- HBsAg
- History of malignancy

*HB*, Hemoglobin; *HBsAG*, hepatitis B surface antigen; *Hct*, hematocrit; *HIV*, human immunodeficiency virus.

### 15. What are the disadvantages and risks of preoperative autologous blood donation?

Some risks associated with blood transfusions (i.e., ABO incompatibility owing to clinical or administrative error, bacterial contamination) are not eliminated by PABD. For this reason, it is generally argued that the criteria for transfusing a unit of autologous blood (i.e., transfusion trigger) should be the same as for a homologous unit. Other experts believe that because the risks associated with autologous blood are decreased relative to homologous blood, the risk-to-benefit ratio is altered, and the criteria for transfusion of autologous blood should be liberalized.

Paradoxically, use of PABD can result in a lower Hct at discharge. A reduced Hct occurs because many patients who predonate blood do not have adequate time in the interval before surgery to regenerate fully the amount of blood they donated. These patients are essentially hemodiluted at the time of surgery. If they do not receive a blood transfusion (because of low intraoperative blood loss), their discharge Hct will be lower than if they had not predonated.

Similarly, in an era of cost-effectiveness analysis, the use of PABD has been challenged. In certain surgical settings (e.g., total joint replacement), the use of PABD decreases by approximately 70% the likelihood that a patient will require homologous transfusion. In other settings (e.g., hysterectomy), fewer patients require transfusion, and a higher percentage of the units collected by PABD are discarded. Factors that increase the cost-effectiveness of PABD include appropriate case selection (i.e., cases where there is a high likelihood that the units will be transfused) and providing a long enough time interval between donation and surgery to allow regenerative erythropoiesis to occur. The use of erythropoietin

**BOX 48-7 Disadvantages and Risks of Preoperative Autologous Blood Donation**

**Donor-Related**

- Vasovagal reaction
  - Loss of consciousness
  - Convulsion
- Inconvenience
  - Multiple trips
  - Repeated needle sticks
- Anemia after multiple donations

**Transfusion-Related**

- Transfusion reactions
  - Clerical/administrative errors
- Sepsis from bacterial contamination
- Congestive heart failure from volume overload

therapy in conjunction with PABD makes logical sense and is under investigation.

From the patient's standpoint, multiple trips to the hospital or blood center to donate blood are inconvenient, and repeated needle sticks are uncomfortable. Vasovagal reactions occur in 2%–5% of patients, of whom 0.3% lose consciousness and 0.03% experience convulsions. In one study, 1 in 16,783 autologous donations led to adverse events requiring hospitalization, a rate higher than that reported in normal volunteers (Box 48-7).

Blood collected for autologous use is subjected to the same tests as homologous blood. If not used, it is not "crossed over" into the general blood pool but is discarded because patients donating blood for autologous use are not considered true volunteer donors.

## 16. Describe postoperative blood salvage.

Postoperative blood salvage systems are simple, inexpensive, and highly effective in decreasing requirements for homologous blood products. The systems consist of a container attached to drains placed in a surgical wound. Blood collected in this manner is defibrinogenated and does not clot, even in the absence of anticoagulant. When enough blood has been collected, the containers are hung, and the blood passes through a filter to a conventional blood administration set. Although the returned blood is high in fibrin-degradation products, its use seems to be safe and is not associated with development of disseminated intravascular coagulation. However, machines have been introduced more recently that, similar to intraoperative salvage devices, wash the blood before returning it to the patient. Postoperative blood salvage systems have been used most commonly in cardiac and major orthopedic surgeries.

## 17. Explain the advantages and disadvantages of different autologous blood sources.

Much controversy and little consensus exist about the "best" way to use autologous blood. Although it is unclear which method is superior, each has something to offer; the relative strengths and weaknesses of each method depend on clinical circumstances (Table 48-2).

PABD has the disadvantages of expense, the same risks as homologous transfusion (i.e., administrative error, storage lesion), and requiring a substantial time interval between harvesting blood and the date of surgery. If blood is donated too close to the day of surgery, with insufficient time for the resynthesis of red cells to compensate for the amount removed, patients can be relatively anemic at the time of surgery and tend to leave the hospital with lower Hct values compared with controls. However, if blood is collected at a suitable interval before surgery, so that substantive erythropoiesis can occur, PABD can be a highly effective method of preventing exposure to homologous blood. A more recent survey of 1000 hospitals found that PABD is the most commonly practiced method of blood conservation. Its use is widely accepted by patients. In California, discussion of PABD

TABLE 48-2 **Comparison of Available Types of Autologous Blood**

| | Requires Days–Weeks Preoperatively | Acceptance by Jehovah's Witnesses | Expenses | Likely Available for Urgent or Emergent Surgery | Applicability to Oncologic Surgery | Provision of Platelets and Clotting Factors | Amount of Blood Provided |
|---|---|---|---|---|---|---|---|
| Predonated autologous | Yes | No | High | Unlikely | Yes | Yes | Limited to amount donated |
| Acute isovolemic hemodilution | No | Possibly | Low | Likely | Yes | Yes | Limited by initial hematocrit (generally 2–3 U) |
| Intraoperative cell salvage | No | Possibly | High | Unlikely | ? | No | Limited by amount salvaged |
| Postoperative cell salvage | No | Possibly | Low | Likely | ? | Defibrinogenated | Limited to postoperative collection |

is a mandatory part of informed consent for any operation in which blood transfusion is likely.

AIHD has the advantage of low cost and is a point-of-care intervention. It obviates the need for planning weeks in advance and eliminates the risk of administrative error associated with stored blood. It is of comparable efficiency and costs less than PABD or cell salvage. However, the amount of red blood cells saved by AIHD is quite small and usually clinically insignificant. For AIHD to be clinically useful, both low Hct and large surgical blood losses must be safely tolerated. Numerous authors have raised concerns about the iatrogenic introduction of risk in patients with previously unappreciated cardiac disease from moderate or profound hemodilution. Because of such concerns, the use of AIHD is probably of limited benefit to older patients. Its use is probably least controversial and of greatest benefit in pediatric or young adult patients with a low likelihood of unappreciated cardiac disease, who are not anemic, and who are having surgeries with large anticipated blood loss.

Intraoperative cell salvage is a widely used and highly effective method of reducing exposure of patients to homologous blood, and this procedure can rapidly provide autologous blood for return in cases involving large amounts of bleeding. Its use has been criticized largely on the grounds of cost-effectiveness, with the break-even point at 2 units of blood. However, expenses can be limited by initially setting up only the collection (suction) part of the apparatus. Later, after confirming that sufficient blood has been collected, the more costly remainder of the system can be installed. In this way, unnecessary costs associated with cell salvage can be decreased. Although theoretical concern exists about using cell salvage in cases of malignancy and bacteremia, clinical studies and experience have not shown an increase in either metastatic tumor spread or infection rates. Intraoperative cell salvage is an essential part of blood conservation programs.

Advances over the past decade have greatly decreased the likelihood of transmission of viral diseases such as HIV and hepatitis C via blood transfusion. Nonetheless, avoidance of blood transfusion remains a significant public concern and has been identified as one of the most important factors in a patient's decision as to where to seek medical care. The potential impact of emerging diseases such as West Nile virus, severe acute respiratory syndrome, and spongiform encephalopathies on the safety of the blood supply is of concern to both the public and the medical community. Spurred by such factors, the popularity of so-called bloodless surgery programs, designed to reduce or minimize exposure to homologous blood, has increased, and such programs are offered by approximately 100 centers in the United States.

A comprehensive program to decrease homologous blood exposure uses all of the techniques discussed in this chapter. Additional factors contributing to decreased blood loss include careful surgical techniques; maintenance of normothermia; use of regional anesthesia; and, in select patients, use of hypotensive general anesthesia. When combined with an appropriate transfusion trigger, these techniques all contribute to minimizing patient exposure to homologous blood.

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CASE 49

# The Jehovah's Witness Patient

**Cheryl K. Gooden, MD, FAAP**

## QUESTIONS

1. What is scoliosis?
2. How is scoliosis classified?
3. How is the curvature assessed in patients with scoliosis?
4. What will a Jehovah's Witness refuse and accept in terms of blood transfusions?
5. When seeking medical treatment, what document might a Jehovah's Witness present to health care providers?
6. What are the medicolegal issues concerning blood transfusion and minor children who are Jehovah's Witnesses?
7. Describe the preoperative evaluation of patients with scoliosis.
8. What are the intraoperative anesthetic considerations for posterior spinal fusion surgery?
9. What is the wake-up test?
10. What are the postoperative anesthetic concerns after scoliosis repair?

A 13-year-old girl with idiopathic scoliosis was scheduled for posterior spinal fusion with instrumentation. The patient's past medical history was otherwise unremarkable. She had no prior surgical history. The patient was a Jehovah's Witness.

### 1. What is scoliosis?

Scoliosis is characterized by one or more lateral curvatures of the spine. The lateral curvatures are associated with rotation of vertebrae and can result in deformity of the rib cage. Curves are classified as structural or nonstructural. Structural scoliosis fails to correct (improve) with side bending toward the convex side. Nonstructural scoliosis corrects with side bending toward the convex portion. The curve associated with nonstructural scoliosis is flexible.

### 2. How is scoliosis classified?

Idiopathic scoliosis is the most common form of scoliosis. There may be a genetic component, but, as the name implies, its cause is unknown. Idiopathic scoliosis can be divided into three different types: infantile, juvenile, and adolescent.

- Infantile idiopathic scoliosis is diagnosed between birth and up to 3 years of age and has a higher incidence among boys. Most of these curves resolve spontaneously without treatment. The curves of infantile idiopathic scoliosis are thought to be secondary to molding in utero.
- Juvenile idiopathic scoliosis is diagnosed between the ages of 3 and 10 years and is more evenly distributed between boys and girls.
- Adolescent idiopathic scoliosis occurs between age 10 years and skeletal maturity and is more commonly seen in girls.

There are many causes and associated conditions in which scoliosis may occur (Box 49-1).

### 3. How is the curvature assessed in patients with scoliosis?

The Cobb method (Figure 49-1) is a commonly used technique for measuring the scoliosis curvature. In the Cobb method, lines are drawn at the uppermost border of the curvature and at the lowermost border of the curvature. Perpendicular lines are drawn from the two original lines, and the angle made by the intersecting perpendicular lines is the degree of curvature.

### 4. What will a Jehovah's Witness refuse and accept in terms of blood transfusions?

The policy of the Watchtower Bible and Tract Society (WTS) with regard to blood is based on Jehovah's Witnesses (JW) elders' interpretation of biblical passages. The JW elders determined that blood transfusions violate God's law. JWs believe that blood removed from the body must be discarded. Many JWs refuse blood transfusions of whole blood and its primary components including red blood cells, white blood cells, platelets, and plasma. Fractions obtained from primary blood components are potentially acceptable to JWs (Figure 49-2).

JWs do not participate in preoperative autologous blood donation. JWs embrace the use of nonblood alternatives. Intraoperative acute normovolemic hemodilution

**BOX 49-1 Classification of Scoliosis**

- Congenital
  - Myelomeningocele
  - Hemivertebrae
- Connective tissue disorders
  - Ehlers-Danlos syndrome
  - Marfan syndrome
  - Osteogenesis imperfecta
  - Rheumatoid arthritis
- Idiopathic
  - Infantile (<3 years)
  - Juvenile (3–10 years)
  - Adolescent (>10 years)
- Neuromuscular diseases
  - Myopathic
    - Arthrogryposis
    - Muscular dystrophy
  - Neuropathic
    - Cerebral palsy
    - Riley-Day syndrome (dysautonomia)
    - Poliomyelitis
    - Spinal cord tumors
- Neurofibromatosis
- Trauma
  - Fracture
  - Post–rib resection

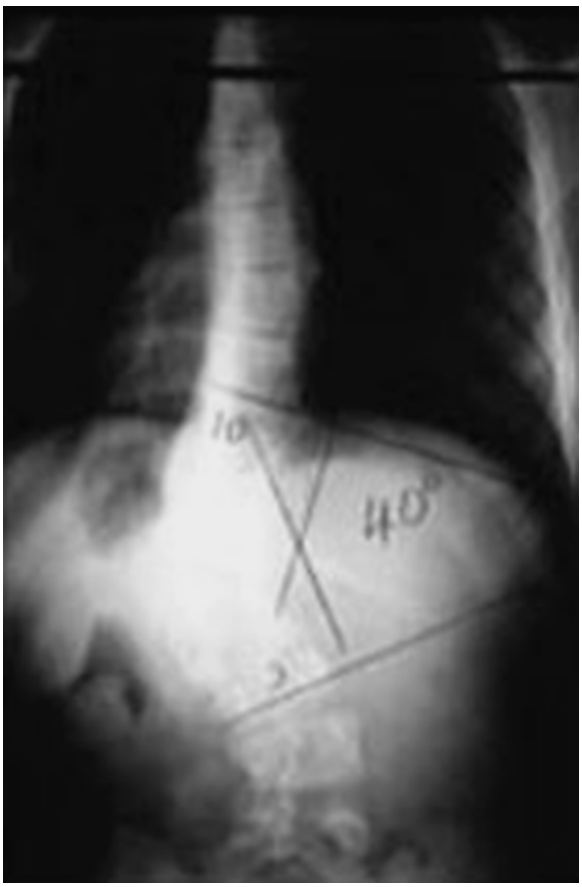


**FIGURE 49-1** ■ Cobb method. (From the Scoliosis Research Society, 2003; with permission.)

or cell salvage may be acceptable to some JWs. In such cases, many JW patients require maintenance of a continuous circuit at all times.

It is prudent to establish an unambiguous list of components and techniques that are acceptable and unacceptable to each patient before anesthesia. What is acceptable to one person may be unacceptable to another. Each JW patient must decide individually whether to accept or decline various blood fractions and procedures.

### 5. When seeking medical treatment, what document might a Jehovah's Witness present to health care providers?

More recently, JWs have provided a Durable Power of Attorney. Previously, JWs carried an advance Medical Directive/Release card that documented their refusal to accept blood under any circumstances. In many ways, the new document resembles a health care proxy form. The wording varies from state to state within the United States and abroad. Some older children and adolescents (mature minors) may present with a Durable Power of Attorney document.

### 6. What are the medicolegal issues concerning blood transfusion and minor children who are Jehovah's Witnesses?

The WTS explains that JW parents are not seeking to deny medical care to their children. They are adhering to the tenets of their religion. The WTS has resources available for health care providers through their Hospital Information Services and Hospital Liaison Committees with recommendations on alternative treatments to blood transfusion. Some of these resources are readily available on the WTS website and can be useful when the patient is seen immediately before surgery. Frequently, when they are available just before surgery, the information is not otherwise in a form that is readily reviewed in a short time.

In life-threatening emergencies involving a JW minor patient, the courts have intervened to permit blood transfusions even though it directly opposes the religious beliefs of parents. The procedure for obtaining consent to transfuse a JW minor patient involves petitioning a judge to declare the minor is a "neglected child." The court then appoints a guardian. The argument for medical necessity of blood transfusions is presented by the physician to the guardian, who can consent or decline blood transfusion. However, if an older child or adolescent (mature minor) presents a Durable Power of Attorney that states the refusal of all blood products, there is no basis for court intervention.

Court decisions have varied with respect to elective surgical procedures and blood transfusion in a JW minor. On the basis of religious beliefs held by JW parents, some of the court rulings have been in favor of their beliefs, whereas others have not been. There is no consensus at the present time when it comes to elective procedures and blood transfusion. The decision to transfuse or not to transfuse a JW minor for elective surgery continues to be determined on a case-by-case basis.

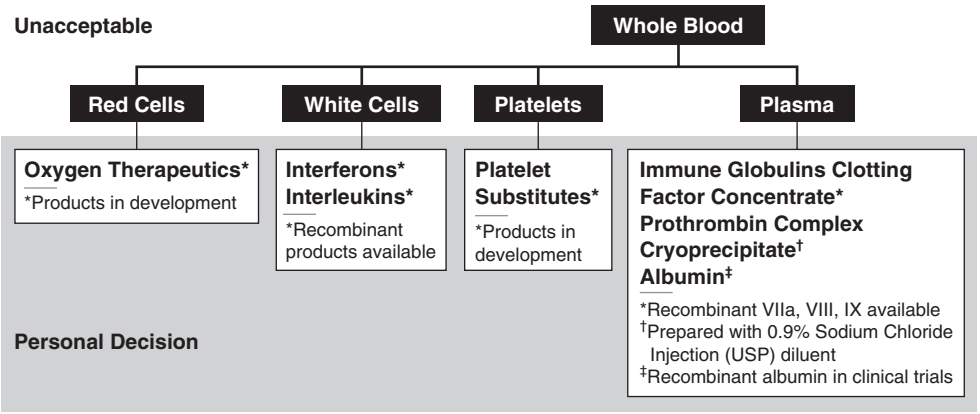


**FIGURE 49-2** ■ **Blood components acceptable to Jehovah's Witnesses.** (Reprinted with permission from Bodnaruk ZM, Wong CH, Thomas MJ. Meeting the clinical challenge of care for Jehovah's Witnesses. Transfus Med Rev 2004;18:105–16.)

## 7. Describe the preoperative evaluation of patients with scoliosis.

Preoperative evaluation begins with a history and physical examination. It should include the etiology and implications for anesthetic management. Factors for consideration involve the degree of spinal curvature, cardiopulmonary impairment, and coexisting disease. Box 49-2 lists studies that may be performed as part of the preoperative evaluation. Some or all of these tests are ordered depending on the severity of scoliosis.

Pulmonary function tests can play a major role in determining anesthetic management for patients undergoing posterior spinal fusion surgery. Restrictive lung disease is the most commonly encountered pulmonary abnormality observed with scoliosis. A vital capacity of ≤30% of predicted value forecasts the need for postoperative ventilation. Pulmonary function tests can determine if obstructive disease is responsive to bronchodilators.

**BOX 49-2 Preoperative Evaluation for Patients with Scoliosis**

- Etiology and implications of scoliosis
- Cobb angle
- Hematocrit and platelet count
- Blood type and crossmatching
- PT/PTT, INR
- Chest radiograph
- Electrocardiogram
- Pulmonary function tests (in the presence of restrictive or obstructive lung disease)
  - Spirometry (FVC, $FEV_1$, $FEV_1$/FVC)
  - Lung volumes (TLC, FRC, RV, FRC/TLC, RV/TLC)
- Arterial blood gas (in the presence of severe pulmonary disease)
- Assessment for cardiovascular impairment
- Coexisting disease

*$FEV_1$*, Forced expiratory volume in 1 second; *FRC*, functional residual capacity; *FVC*, forced vital capacity; *INR*, international normalized ratio; *PT*, prothrombin time; *PTT*, partial thromboplastin time; *RV*, residual volume; *TLC*, total lung capacity.

Cardiovascular impairment is seen in patients with scoliosis. Mitral valve prolapse is the most common cardiovascular abnormality associated with scoliosis. Severe restrictive lung disease may cause changes in pulmonary vasculature leading to pulmonary hypertension. Pulmonary hypertension can produce right ventricular failure or cor pulmonale. Clinical findings of cor pulmonale include an $S_4$ heart sound, jugular venous distention, hepatomegaly, pedal edema, and a left parasternal lift.

## 8. What are the intraoperative anesthetic considerations for posterior spinal fusion surgery?

If a wake-up test is planned, this unusual procedure must be explained to patients during the preoperative interview. In most patients, preoperative sedation is acceptable. However, some patients with scoliosis have significant respiratory dysfunction contraindicating preoperative sedation. Further impairment of an already tenuous respiratory system can cause hypoxemia, hypercarbia, and acidosis.

Either inhalation for pediatric patients or intravenous induction is acceptable. If somatosensory evoked potential and motor evoked potential monitoring are planned, isoflurane, sevoflurane, or desflurane should be maintained at <0.5 minimum alveolar concentration. The preferred anesthetic technique for cases involving evoked potential monitoring is infusion of a hypnotic agent such as propofol and an opioid such as remifentanil. Neuromuscular blocking agents are avoided if motor evoked potentials are used. (See Chapter 18 for further details.)

In addition to the standard intraoperative monitors, an arterial catheter and a urinary catheter should be placed. The arterial catheter allows for measuring arterial blood pressure on a beat-to-beat basis and facilitates blood sampling. For most of these cases, placement of a central venous catheter is not warranted and is left to the discretion of the anesthesiologist. Transesophageal echocardiography may be necessary in the presence of severe cardiopulmonary disease.

Turning and positioning the patient prone require extreme care. It is important to avoid pressure on the eyes. Retinal artery occlusion and blindness have been

reported after back surgery performed with the patient in the prone position. It is also necessary to avoid pressure necrosis of the ears, nose, and forehead. The head should be in proper alignment and positioned so that easy inspection of the face can be achieved. The chest, abdomen, and pelvic areas should rest on parallel bolsters or other devices that avoid pressure on the axillae, breasts, and genitalia. The arms should rest at the sides with the elbows flexed and the shoulders abducted no greater than 90 degrees to avoid stretching the brachial plexus.

A considerable decrease in body temperature can occur during spinal surgery if large body surface areas are exposed. Precautions should be taken to avoid intraoperative hypothermia. These include forced-air warming blankets, intravenous fluid warming systems, and adjustment of ambient temperatures.

Significant blood loss is common during this surgery. Several techniques have been designed to minimize blood loss and the need for homologous blood transfusion (Box 49-3). More specifically, intraoperative techniques are cell salvage, controlled hypotension, surgical technique, and local infiltration with an epinephrine-containing solution. The last-mentioned method helps to reduce bleeding at the site of infiltration, but the overall reduction in surgical blood loss is minimal. Acute normovolemic hemodilution and antifibrinolytic therapy are less commonly employed.

**BOX 49-3 Strategies for Avoiding Homologous Blood Transfusions**

- Preoperative erythropoietin
- Acute normovolemic hemodilution
- Pharmacologic therapy (e.g., tranexamic acid, aminocaproic acid)
- Intraoperative cell salvage with retransfusion
- Anesthetic technique (controlled hypotension)
- Surgical technique

A detailed review of techniques to minimize blood loss is beyond the scope of this chapter. Table 49-1 summarizes medications that contribute to achieving induced hypotension. Mean arterial pressure should be maintained >50 mm Hg to provide adequate spinal cord perfusion and cerebral blood flow. Generally, a mean arterial pressure of 50–60 mm Hg is ideal. In addition, arterial blood gases should be monitored during the procedure. Contraindications to the use of controlled hypotension include preexisting major end-organ dysfunction, hemoglobinopathies, polycythemia, and elevated intracranial pressure.

## 9. What is the wake-up test?

The wake-up test is aptly named. Patients are awakened intraoperatively to test motor tracts. After completion of the test, surgical anesthesia is deepened. Awareness under anesthesia is upsetting for many patients. When wake-up tests are planned, they should be discussed before induction. Many patients later report amnesia for the test. Most patients who remember the episode do not report discomfort.

The wake-up test is used to assess anterior spinal cord (motor) pathways. It does not investigate posterior spinal cord (sensory) pathways. The wake-up test is performed intraoperatively after spine instrumentation. Adequate notice should be given to the anesthesiologist by the surgeon so as to coordinate the timing of "lightening the anesthesia" to an appropriate level so that the patient can follow commands. The wake-up test can present a challenge for the anesthesiologist with regard to the balance that must be maintained between the patient performing some level of activity but without excessive movement.

TABLE 49-1 **Techniques to Achieve Controlled Hypotension**

| Category | Drug | Recommendation |
|---|---|---|
| Volatile anesthetics | Isoflurane<br>Sevoflurane<br>Desflurane | Most efficacious with combined therapy<br>Limited by use of neurophysiologic monitoring |
| Hypnotic agents | Propofol | Most popular GABA-mediated intravenous anesthetic<br>Associated with rapid recovery |
| Opioid | Remifentanil | Potent<br>Extremely short-acting |
| $\alpha_2$-Adrenergic agonists | Clonidine | Administer 1 hour before surgery<br>May work well on its own as a hypotensive agent or may need to be combined with another agent |
| | Dexmedetomidine | Relatively selective<br>Provides sedation, analgesia, and sympatholysis |
| β-Adrenergic antagonists | Labetalol | Rapid onset<br>Combined alpha and beta effects |
| | Metoprolol | Compared with labetalol, used in situations when slow onset and long duration of action are acceptable |
| Vasodilators | Sodium nitroprusside | Rapid onset, titratability, and quick offset after infusion is discontinued<br>May need to treat reflex tachycardia |
| Calcium-channel blockers | Nicardipine | Used in situations when rapid onset and intermediate duration of action are desired |

*GABA,* γ-aminobutyric acid.

The wake-up test begins by assessing the level of the patient's comprehension by asking the patient to squeeze the anesthesiologist's hand. If the response is acceptable, the patient is asked to move the feet. If the patient is unable to move the feet, spinal distraction must be decreased, and the test is repeated. Excessive distraction can compromise spinal cord blood flow leading to ischemia and may result in postoperative paraplegia. After completion of the wake-up test, anesthesia is deepened with return to general anesthesia.

The wake-up test has limitations. It evaluates the patient's motor function at only one point in time. It has no bearing on the time following the performance of the test, when spinal cord injury remains a possibility. The wake-up test is not appropriate for young children or cognitively impaired patients. Excessive patient movement may promote self-extubation, bleeding, air embolus, or disruption of the spinal instrumentation.

At the present time, neurophysiologic monitoring is used in almost all spine surgeries, and the wake-up test is rarely used. Somatosensory evoked potential and motor evoked potential monitoring offer the advantage of continuous assessment throughout surgery.

### 10. What are the postoperative anesthetic concerns after scoliosis repair?

In most patients, the goal at the end of scoliosis repair is to awaken and extubate in the operating room. In some patients, extubation may be delayed, and the factors leading to postoperative intubation can be the same as factors associated with any general anesthetic. Additionally, factors more specifically related to patients with scoliosis include possible underlying pulmonary dysfunction, persistent muscle weakness, and issues related to any coexisting diseases.

Postoperative anesthetic concerns focus on known complications after posterior spinal fusion surgery, and these include bleeding, pneumothorax, atelectasis, respiratory distress, and neurologic deficit. Another area of concern in postoperative anesthetic care is pain management. Pain in the initial postoperative period can be managed by intravenous patient-controlled analgesia with opioids. In young children or cognitively impaired patients, a continuous intravenous opioid infusion is suggested. Most patients are cared for in an intensive care unit after scoliosis repair.

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CASE 50

# Sickle Cell Disease

**Richard Y. Marn, MD**

QUESTIONS

1. Which patient populations are at risk for sickle cell trait and sickle cell disease?
2. What is the underlying genetic abnormality responsible for sickle cell disease, and how does this lead to sickling?
3. Describe the presentations of sickle cell disease.
4. What are the perioperative considerations for patients with sickle cell disease?
5. Should every patient with sickle cell disease have a hemoglobin of 10 g/dL in the perioperative period?
6. What are the postoperative concerns for patients with sickle cell disease?
7. Is regional anesthesia safer than general anesthesia for patients with sickle cell disease; should tourniquets be avoided?

A 10-year-old boy of Mediterranean descent with sickle cell disease (SCD) that was diagnosed during his first year of life presented to the operating room for laparoscopic cholecystectomy. At age 8 years, he was hospitalized for 3 days with vasoocclusive painful crisis. He currently takes no medication and had no previous surgeries.

## 1. Which patient populations are at risk for sickle cell trait and sickle cell disease?

Sickle cell trait results from asymptomatic heterozygous carriers of the abnormal hemoglobin S (HbS) gene. It occurs in 10%–30% of people in equatorial Africa as well as Mediterranean areas such as Sicily, southern Italy, northern Greece, Turkey, Saudi Arabia, southwest Asia, and central India. Malaria is endemic in these areas. It has been postulated that HbS may be protective against malaria. However, descendants of people from these areas are more likely to have sickle cell disease (SCD). About 8% of African Americans have sickle cell trait, whereas 0.3%–1.3% of African Americans have SCD.

## 2. What is the underlying genetic abnormality responsible for sickle cell disease, and how does this lead to sickling?

SCD is a heterogeneous, inherited disorder of the beta-hemoglobin chain. It is a multisystem disorder that may manifest during childhood or adulthood, with marked variability in onset and severity.

Normally, hemoglobin A (HbA), which makes up most normal adult hemoglobin (96%–98%), is composed of two alpha-globin and two beta-globin chains. However, HbS possesses one abnormal beta-globin chain because of a single valine substitution for glutamic acid at the sixth position of the beta-globin chain. The heterozygous carrier state HbAS (i.e., one abnormal and one normal beta-globin gene) is called sickle cell trait. This genetic makeup of sickle cell trait may confer protection to individuals exposed to the malaria-causing parasite *Plasmodium falciparum.*

The homozygous genotype HbSS (i.e., two abnormal beta-globin chains) results in SCD, with the potential for hemolysis and its resultant complications. The manifestations of SCD result from deoxygenation of HbS, which leads to hemoglobin instability and decreased molecular solubility. With prolonged deoxygenation, irreversible polymerization of intracellular insoluble HbSS strands (gelation) begin to form; this activates sickling, a process of cell membrane distortion and cell deformability, giving red blood cells the microscopic appearance referred to as sickle cells. The sickle shape of red blood cells makes for slower and difficult, or impossible, propagation through blood vessels. A multifactorial process of red blood cell clumping, hemolysis, reduced cell life span, sludging of vasculature, endothelial damage, vascular obstruction or occlusion, and an inflammatory response eventually leads to some of the clinical conditions discussed in Question 3. The baseline hemoglobin of patients with SCD is usually 5–9 g/dL owing to chronic hemolysis.

## 3. Describe the presentations of sickle cell disease.

- *Acute vasoocclusive (pain) crisis*, the most common presentation, manifests as skeletal bone pain from occlusion by sickled cells of the vasculature resulting in inflammatory mediator release and subsequent increased intramedullary pressure and nociceptor stimulation. Pain can occur at an early age (6 months) in the hands and feet (i.e., hand-foot syndrome) and at later ages in the long bones (e.g., ribs, spine, hips.) More than three pain episodes per year indicate severe disease and risk of early death. Aggressive management of these patients includes analgesics

(e.g., patient-controlled analgesia), hydration, warmth, rest, reassurance, antibiotics, and possibly steroids.

- *Acute chest syndrome* (ACS) is a medical emergency in which the patient presents with chest pain, hypoxemia, and respiratory distress. ACS is the leading cause of death and hospitalization in patients with SCD. Treatment consists of oxygen, continuous positive airway pressure or mechanical ventilation, antibiotics, bronchodilators, hydration, and possibly steroids. Pulmonary infarcts and pulmonary fibrosis are potential complications.
- *Hemolytic crisis* (or aplastic crisis), although rare, occurs when there is rapid red blood cell death and massive suppression of normal erythropoiesis. An infection is often implicated (e.g., parvovirus B19, Epstein-Barr virus). If treated appropriately, this crisis can be self-limited with bone marrow activity returning in 10 days.
- *Splenic sequestration crisis* typically occurs during childhood and is the result of the spleen sequestering a massive amount of red blood cells. It may be a minor or major event. Transfusion and elective splenectomy may be necessary.

Because SCD is a multisystem disease (Table 50-1), these patients can present with liver dysfunction, jaundice, cholelithiasis, stroke, cranial nerve neuropathies, sickle retinopathy, impaired growth, pregnancy complications, bone marrow infarcts, cardiomegaly, hematuria, renal infarcts, renal failure, or priapism. Autoinfarction of the spleen renders these patients functionally hyposplenic or asplenic and susceptible to infections with encapsulated bacterial organisms (e.g., *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Haemophilus influenzae*). Patients with SCD are placed on prophylactic antibiotics.

TABLE 50-1 **Clinical Manifestations of Sickle Cell Disease**

| Organ System | Manifestation |
|---|---|
| Central nervous | Acute pain<br>Stroke<br>Cranial nerve neuropathy<br>Peripheral neuropathy |
| Ophthalmologic | Sickle retinopathy |
| Pulmonary | Infarct<br>Pneumonia<br>Acute chest syndrome |
| Cardiac | Pulmonary hypertension<br>Cardiomegaly<br>Cardiomyopathy<br>Coronary syndrome |
| Hepatobiliary | Cholelithiasis<br>Liver dysfunction |
| Renal | Hematuria<br>Isosthenuria<br>Infarct<br>Papillary necrosis<br>Renal tubular acidosis<br>Renal medullary carcinoma |
| Genitourinary | Priapism |
| Immunologic | Infection<br>Splenic sequestration crisis<br>Splenic autoinfarction<br>Susceptibility to encapsulated bacterial infections |
| Musculoskeletal | Aseptic necrosis<br>Bone infarct |
| Hematologic | Hemolytic anemia<br>Jaundice |

## 4. What are the perioperative considerations for patients with sickle cell disease?

Preoperative assessment includes obtaining a history of sickle cell manifestations in the past, hospitalizations, transfusions, transfusion reactions, and a thorough review of all organ systems. A medication history should be obtained as well, focusing on analgesic usage, steroids, bronchodilators, and antibiotics. Baseline vital signs include oxygen saturation on room air, especially for patients with a history of ACS. The history and physical examination dictate whether further testing, such as pulmonary function tests, echocardiogram, arterial blood gas, renal function studies, and neurologic imaging is indicated.

In most situations, there is little clinical benefit in obtaining HbS levels, although an updated and recent assessment by the patient's hematologist should be obtained in anticipation of surgery. Communication among the hematologist, primary care physician, surgeon, and anesthesiologist is vital to establish continuity of care. A baseline hemoglobin and type and screen are warranted. Blood should be available based on the risk of surgery and baseline laboratory studies. Transfusion to correct anemia may be necessary before surgery.

Children with SCD have a much higher risk of perioperative morbidity and mortality. Intravascular sickling and sludging are potentiated in the perioperative period because there is an increased risk for pain, hypothermia, hypoxemia, acidosis, poor perfusion, dehydration, and anemia. These risk factors should be avoided and aggressively treated in the perioperative period. The perioperative goals to prevent sickling are listed in Box 50-1.

Surgical interventions are common in patients with SCD because these patients have chronic or acute system dysfunctions. Frequent surgeries in patients with SCD include cholecystectomy (elevated bilirubin levels secondary to chronic hemolysis leads to an increased incidence of cholelithiasis), splenectomy (hypersplenism, splenic sequestration of sickle cells, splenic infarction), orthopedic procedures (infections, avascular necrosis), and otolaryngologic procedures. Depending on patient factors and surgical risk, the frequency of postoperative complications in patients with SCD may be 52%.

## 5. Should every patient with sickle cell disease have a hemoglobin of 10 g/dL in the perioperative period?

Transfusion in the perioperative period is controversial. The benefits of transfusion include correcting anemia

**BOX 50-1 Perioperative Goals to Prevent Sickling**

- Oxygenation
  - Careful attention to airway management
  - Oxygen saturation by pulse oximetry ≥95%
- Tissue perfusion
  - Normovolemia
    - Avoid prolonged fasting times
    - Aggressive replacement of fluid or blood losses
    - Careful hydration in patients with cardiac or renal disease
- Acid-base regulation
- Temperature control
- Hematologic
  - Consider transfusing to increase hemoglobin to 10 g/dL (see Question 5 for details)
  - Avoid elevated hemoglobin levels that could lead to increased blood viscosity and sludging
  - Consider exchange transfusion to decrease HbS to <30% for high-risk surgeries and high-risk patients
- Infectious
  - Antibiotic therapy
- Postoperative analgesia
  - Regional anesthesia whenever possible
  - Multimodal therapy

and HbS red blood cell dilution. However, the drawbacks of transfusion include alloimmunization (10%), transfusion reactions (7%), infection, fluid overload, and economic cost.

Several observational and nonrandomized studies support the occasional use of preoperative blood transfusions, in particular, for moderate-risk to high-risk surgical procedures, to decrease the incidence of ACS postoperatively. A prospective randomized trial compared aggressive transfusion therapy (exchange transfusion to reduce HbS levels to <30%) versus conservative therapy (transfusing to Hb =10 g/dL). Although both methods resulted in the same incidence of ACS postoperatively, the more aggressive therapy exposed patients to a higher incidence of transfusion reactions. The U.S. National Institutes of Health recommends that "simple transfusion to achieve a hemoglobin of 10 g/dL should be performed before all but the lowest risk procedures." High-risk procedures include cardiothoracic surgery, neurosurgery, laparotomy, tonsillectomy, and orthopedic surgery.

For high-risk procedures and high-risk patients, exchange transfusion should be considered to decrease HbS to <30%. Coordination with the patient's health care team is essential in these cases.

### 6. What are the postoperative concerns for patients with sickle cell disease?

In addition to the aforementioned perioperative goals, early mobilization and incentive spirometry are important. In the postoperative period, ACS (10%) and vasoocclusive crisis (7%) are more likely to occur compared with other clinical manifestations of SCD. ACS, a potentially life-threatening complication, may occur within 1–3 days. Infection, stroke, and hemolytic anemia are also potential complications.

### 7. Is regional anesthesia safer than general anesthesia for patients with sickle cell disease; should tourniquets be avoided?

Patients with SCD have a higher opioid requirement, making regional anesthesia a favorable option to decrease opioid usage. Studies comparing regional with general anesthesia are conflicting, and no studies have consistently shown that either type of anesthesia reduces or increases the risk of perioperative complications. Epidural anesthesia and analgesia may result in improved oxygenation because of decreased respiratory splinting secondary to adequate pain relief and decreased opioid-induced respiratory depression. If vasoconstriction contributes to pain experienced during vasoocclusive crisis, vasodilation from regional techniques may attenuate the pain.

Tourniquet use up to 2 hours has been successfully employed. Several studies show that tourniquets are safe, provided that optimal acid-base status and oxygenation are maintained throughout the procedure.

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SECTION 9

# ORTHOPEDICS

CASE 51

# Total Hip Replacement

Yan H. Lai, MD • Meg A. Rosenblatt, MD

## QUESTIONS

1. What are the preoperative anesthetic considerations for a patient with coronary artery drug-eluting stents currently taking antiplatelet medications?
2. Is there evidence for bridging therapy to decrease the risk of stent thrombosis resulting from premature discontinuation of thienopyridine therapy?
3. What are the risks and benefits of early hip surgery in this patient; is this considered elective surgery; would you proceed with this case?
4. Summarize the current guidelines on neuraxial anesthesia for an anticoagulated patient in terms of commonly used agents, herbal agents, and new agents.
5. What anesthetic technique would you plan for this patient; what are the established benefits of regional anesthesia in terms of major postoperative outcomes?
6. Discuss the options for postoperative pain management, and explain the role of continuous lumbar plexus and femoral blockade.

An 85-year-old woman presented for left hip arthroplasty after a fall sustained 2 days previously. She has osteoarthritis with severe hip pain and had planned to have a total hip replacement in the future. She has coronary artery disease for which she required two drug-eluting stents 6 months ago. Current medications are metoprolol, 50 mg, simvastatin, 20 mg, aspirin, 325 mg, and clopidogrel, 75 mg.

### 1. What are the preoperative anesthetic considerations for a patient with coronary artery drug-eluting stents currently taking antiplatelet medications?

Elderly patients presenting for orthopedic procedures have a high prevalence of cardiopulmonary comorbidities. These patients are at considerable risk for adverse perioperative events including myocardial infarction (MI), acute stent thrombosis, and death. The evaluation and optimization of all cardiac risks are paramount to patient survival.

Percutaneous coronary intervention with balloon angioplasty and placement of stents within obstructed coronary vessels has emerged as an effective and widespread treatment for symptomatic coronary artery disease. After initial implantation, the foreign body nature of stent struts can serve as a nidus for thrombi formation. Dual antiplatelet therapy with aspirin and a thienopyridine derivative (e.g., clopidogrel) is administered to decrease the risk of stent thrombosis. After a period of time, stent struts are incorporated into coronary artery endothelium, and the risk of thrombosis is significantly reduced. Nevertheless, patients at risk for stent thrombosis requiring elective, urgent, or lifesaving surgery can present at any time.

In 2009, the American Society of Anesthesiologists (ASA) published a practice alert to address perioperative management of patients with coronary artery stents (See Chapter 2 for further details). The most critical preoperative evaluation of these patients involves the type, timing, number, and location of the stents. A cardiology consultation and echocardiography may be considered to assess myocardial perfusion and ventricular function and to plan for perioperative coronary stent management. Current recommendations from this practice alert are summarized as follows:

- Delay elective noncardiac procedures for which there is a significant bleeding risk for the following time frames:
  - Bare metal stents—minimum of 1 month (usually chosen over drug-eluting stents if urgent surgery is imminent or planned ahead of time)
  - Drug-eluting stents—12 months
- For all procedures (including urgent or emergent), continue aspirin therapy throughout perioperative period.
- Beyond this time frame, discontinue clopidogrel for 7 days or ticlopidine for 14 days before surgery and restart therapy as soon as postsurgical hemostasis is adequate.

### 2. Is there evidence for bridging therapy to decrease the risk of stent thrombosis resulting from premature discontinuation of thienopyridine therapy?

In 2007, several organizations including the American Heart Association (AHA) and American College of Cardiology (ACC) convened and authored two publications on premature discontinuation of antiplatelet therapy. The AHA/ACC guidelines emphasized the increased risk of life-threatening stent thrombosis and acute MI in the perioperative period as a result of premature

discontinuation of thienopyridine therapy. The AHA/ACC concluded that there are no clear benefits to using any anticoagulants, including warfarin or heparin, or any antithrombotics as bridging therapy to decrease the incidence of stent thrombosis.

### 3. What are the risks and benefits of early hip surgery in this patient; is this considered elective surgery; would you proceed with this case?

As with many difficult clinical decisions, informed dialogue between the patient and the perioperative care team regarding risks and benefits of surgery is essential to ensure optimal management. In this scenario, the major risks of proceeding with surgery are adverse perioperative cardiac events from premature discontinuation of clopidogrel and increased surgical hemorrhage from prolonged platelet inhibition. This clinical dilemma is a double-edged sword. According to the 2007 AHA/ACC advisory, early discontinuation of antiplatelet therapy in patients with drug-eluting stents is associated with a 25%–29% incidence of stent thrombosis. These data come from two large cohort observational studies on medical patients presenting for percutaneous coronary intervention after acute MI. The reasons for early cessation of therapy in these studies were primarily related to poor patient adherence. Although it may be unfair to extrapolate these findings for the perioperative population, clear evidence for guidance is lacking. Two frequently quoted studies in the surgical population, with only 40 patients and 47 patients in each group, established the incidence of stent thrombosis as 15%–17% (approximately 7 patients in each study). Both retrospective studies involved withholding aspirin, ticlopidine, or both agents prematurely within 2 weeks after bare metal stent placement in patients proceeding with noncardiac surgery. The antiplatelet agents were stopped at least 5 days before surgery in one study, whereas the other study continued these agents up to 2 days and even on the day of surgery. In both studies, six of the seven patients with stent thrombosis died, resulting in an 86% case-fatality rate in patients who developed stent thrombosis. Of the 20 patients who continued antiplatelet therapy throughout the perioperative period, only 1 died after surgery. The authors explain that the stressful, procoagulant, and proinflammatory nature of surgery may exacerbate stent thrombosis further in this setting. No randomized trials have studied bleeding risk in this surgical population. The increased risk of hemorrhage is inferred from studies involving patients with drug-eluting stents taking clopidogrel undergoing cardiac surgery.

Given these catastrophic cardiac and possible bleeding risks, it seems reasonable to postpone surgery. However, the decision to delay hip surgery in an elderly patient is not always straightforward. First, the 30-day and 1-year mortality rates in the elderly population with hip fractures are 5%–10% and 12%–37%, respectively. In two separate large meta-analyses, Simunovic et al. (2010) and Shiga et al. (2008) demonstrated 19%–40% risk reduction in mortality if hip surgery was performed <72 hours after fracture. These meta-analyses were based on numerous clinical trials with a cumulative number of patients up to 250,000. Risk reduction in mortality is calculated after adjusting for a myriad of perioperative confounding factors. Other benefits of early hip surgery include decreased incidences of pneumonia and pressure ulcers and improved quality of life for patients who would otherwise be bed bound. Overall, these benefits make a strong and convincing argument that early surgical intervention reduces mortality, and hip fracture surgery should not be classified as a purely elective procedure.

As mentioned, the best approach to explain the risks and benefits is to have an informed dialogue with the patient. On one hand, performing surgery after acute discontinuation of clopidogrel puts the patient at risk for the opposing problems of stent thrombosis (incidence and mortality approximately 15%) and increased risk of bleeding. As mentioned, the dearth of large prospective clinical studies makes it nearly impossible to quantify these individual risks. On the other hand, deferring surgery puts the patient at significant risk for mortality (37%), developing pneumonia and pressure ulcers while bed bound, and an overall decrease in quality of life. The urgent and complex nature of this clinical dilemma calls for a critical perioperative evaluation on an individual basis with an interdisciplinary approach that uses all pertinent medical information.

### 4. Summarize the current guidelines on neuraxial anesthesia for an anticoagulated patient in terms of commonly used agents, herbal agents, and new agents.

Table 51-1 summarizes evidenced-based guidelines published by the American Society of Regional Anesthesia and Pain Medicine (ASRA) in 2010. The authors note that "variances from recommendations contained in this document may be acceptable based on the judgment of the responsible anesthesiologist."

Several recurring themes are applicable to the general management of anticoagulated patients receiving neuraxial anesthesia, as follows:

- Review the patient's medical history to ensure that there are no concomitant anticoagulants that would increase the risk of spinal hematoma.
- During neuraxial anesthesia and analgesia in high-risk patients receiving anticoagulants (e.g., spinal, placing or removing epidural catheters, placing or removing deep blocks or catheters), intensive neurologic monitoring and vigilant nursing checks should be established (less than every 2 hours), and neuraxial solutions to minimize sensory and motor blockade should be used. (This is emphasized by the word MONITOR in Table 51-1.)
- Low-molecular-weight heparin subcutaneous dosing for perioperative thromboprophylaxis in hip replacement is as follows:
  - Twice-daily dosing: 30 mg every 12 hours, first dose within 12–24 hours after surgery
  - Once-daily dosing: 40 mg once, first dose within 9–15 hours before surgery
  - Examples of high-dose low-molecular-weight heparin:
    - Enoxaparin, 1 mg/kg every 12 hours, 1.5 mg/kg daily

TABLE 51-1 **The 2010 American Society of Regional Anesthesia and Pain Medicine Recommendations for Neuraxial Anesthesia and Concomitant Anticoagulation Therapy**

| Drug | Key ASRA Guidelines | Wait Time between Anticoagulant and Needle Insertion | Wait Time between Last Needle Puncture or Catheter Removal to Initiating Anticoagulation |
|---|---|---|---|
| Thienopyridine derivatives | Actual risk unknown due to lack of clinical trials | Clopidogrel—7 days<br>Ticlopidine—14 days<br>Prasugrel—5–7 days | Restart as soon as adequate surgical hemostasis is achieved |
| Warfarin* | Check INR if first dose given >24 hours or more than one dose given preoperatively | Initiating therapy: INR <1.5 or first dose given within 48 hours<br>Discontinuation of long-term therapy: 5 days with normal INR | No wait time necessary because warfarin takes >24 hours to reach peak effect |
| Heparin | Safe with 5000 units SQ BID >10,000 units daily or TID dosing: Proceed but MONITOR†<br>On heparin for > 4 days obtain platelet count owing to risk of heparin-induced thrombocytopenia | 2–4 hours after heparin is stopped<br>For IV or TID dosing, consider MONITOR† after needle insertion | 1–2 hours |
| LMWH (i.e., enoxaparin, dalteparin, tinzaparin) | No evidence for routine checking of anti-Xa level<br>Female, elderly, renal impairment, and concomitant anticoagulants associated with increased risks of spinal hematoma | 12 hours for prophylactic dose<br>24 hours for higher doses (e.g., bridging therapy, DVT treatment, postoperative prophylaxis) | 24 hours after bloody or difficult placement<br>BID: first dose 24 hours; remove catheters at 22 hours after surgery<br>Daily dosing: >8 hours after surgery and then second dose 24 hours afterward<br>Remove catheter >12 hours after last dose but 2 hours before next dose |
| NSAIDs | Single agent: no added risk | No contraindication | No contraindication |
| Glycoprotein IIb/IIIa antagonists | Contraindicated within 4 weeks of surgery<br>Risk with neuraxial anesthesia unknown | Abciximab—24–48 hours<br>Eptifibatide and tirofiban—4–8 hours | Unclear |
| Thrombin inhibitors: argatroban, desirudin, lepirudin, bivalirudin; dabigatran (oral)‡ | No antidote or reversal<br>Avoid neuraxial techniques | Unknown timing from published guidelines<br>Most recent ASRA expert recommendation: dabigatran—5–7 days<br>European experience: 8–10 hours | Insufficient evidence about safety<br>European experience: 2–4 hours |
| Factor Xa inhibitor: fondaparinux; Rivaroxaban (oral)§ | Unknown risk; proceed if atraumatic, first-pass needle insertion§ | Unknown<br>European experience: fondaparinux—36–42 hours | 2 hours in the trial<br>Fondaparinux in Germany: 6–12 hours |
| Fibrinolytics/ thrombolytics | Never proceed "except highly unusual circumstances" | No data; avoid needle if possible<br>Wait at least 10 days if neuraxial blockade must proceed | No data on safety and timing<br>Avoid agents after needle if possible |
| Herbal medications | Garlic, ginkgo biloba, and ginseng all increase bleeding, but clinical studies are lacking | No interference as single agent | No interference as single agent |

*ASRA,* American Society of Regional Anesthesia and Pain Medicine; *BID,* twice a day; *DVT,* deep vein thrombosis; *INR,* international normalized ratio; *IV,* intravenous; *LMWH,* low-molecular-weight heparin; *NSAIDs,* nonsteroidal antiinflammatory drugs; *SQ,* subcutaneously; *TID,* three times a day.

*See section International Normalized Ratio

†MONITOR = Intensive neurologic monitoring, vigilant nursing checks (at least every 2 hours), neuraxial solutions to minimize sensory and motor blockade.

‡See section Dabigatran

§See section Factor Xa Inhibitors

- Dalteparin, 120 units/kg every 12 hours, 200 units/kg daily
- Tinzaparin, 175 units/kg daily

There are no data to support cancellation of surgery with bloody, difficult, or traumatic needle insertion or catheter removal with any anticoagulants. However, whether to proceed or not with surgery and appropriate postoperative anticoagulation should be discussed with the surgical team.

To understand better the complex relationship between the timing of anticoagulation and neuraxial blockade, a few key issues require further clarification. It may be helpful to refer to the following sections when reviewing Table 51-1.

### *International Normalized Ratio*

Establishing guidelines for the appropriate international normalized ratio (INR) to proceed with neuraxial techniques has been controversial because of the variable clinical and pharmacologic responses to warfarin. The effects of warfarin are different at initiation of therapy (i.e., for postoperative thromboprophylaxis) than at discontinuation of long-term warfarin treatment (i.e., treatment of atrial fibrillation). It is important to appreciate the relationship between warfarin's antagonism of the four vitamin K-dependent–clotting factors and the INR.

- Factors VII, IX, X, and II (thrombin) each has a different synthetic half-life:
  - Factor VII = 6 hours
  - Factors IX, X, and II = 24–80 hours
- INR is sensitive to levels of factor VII and insensitive to factor II, which reflects acute factor turnover.
- INR of 1.5 correlates best with normal hemostatic levels of factor VII (factor activity level of 40%). Higher INR values reflect decreases in factor activity levels and higher probability of bleeding.

In the first 2 postoperative days, warfarin therapy is most likely initiated for deep vein thromboprophylaxis. When warfarin is first administered, the acute antagonism of factor VII (short half-life) causes the INR to increase rapidly despite normal activity of other clotting factors. During initiation therapy with warfarin, an INR level <1.5 is considered subtherapeutic, and removal of neuraxial catheters is reasonable. However, other risk factors should be evaluated, such as additional doses of warfarin given for subtherapeutic levels, duration of warfarin therapy, and other concomitant administered anticoagulants. Warfarin initiated for >48 hours incurs higher risks of epidural hematoma because activity of factors IX and II (not reflected by INR) may decrease to hemorrhagic levels.

When long-term warfarin therapy is discontinued in preparation for surgery or neuraxial anesthesia, the recovery of factor activity levels follows similar patterns based on their individual half-lives. The swift synthesis of normal factor VII can cause the INR to approach near-normal levels while the three other factors are still in ranges that may correspond to clinical bleeding. The full normalization of all factors is unpredictable and may take 5 days to achieve. ASRA guidelines recommend stopping warfarin for 5 days before surgery in addition to a normal INR (i.e., ideally <1.2).

### *Dabigatran*

Dabigatran (Pradaxa) is a novel oral direct thrombin antagonist that reaches peak plasma level at 2 hours after ingestion. The half-life is 8 hours after a single dose and 17 hours after multiple doses. Its effect can be monitored by the thrombin time. It should be administered with caution in patients with renal failure because 80% of the drug is cleared by the kidneys; this is of particular concern in elderly patients who have undiagnosed renal insufficiency. In clinical trials, this drug demonstrated similar efficacy and bleeding risks compared with once-daily dosing of enoxaparin. No study involving dabigatran and neuraxial anesthesia exists at the present time. According to the manufacturer, dabigatran is contraindicated in patients with indwelling epidural catheters. Nevertheless, European guidelines (from Germany and Belgium) can be used as reference in unusual circumstances.

### *Factor Xa Inhibitors*

The ASRA recommendation for factor Xa inhibitors, such as fondaparinux (Arixtra), is that neuraxial anesthesia should proceed only if conditions similar to the original clinical trials are strictly followed. In the clinical trials, neuraxial blockade was performed successfully with a single, atraumatic needle pass, and catheters were removed 2 hours before subsequent doses. Also, fondaparinux was given for postoperative thromboprophylaxis. The one-pass needle insertion criterion is difficult to satisfy or guarantee in clinical practice. The other oral factor Xa inhibitor, rivaroxaban, achieves peak plasma level in 1–4 hours and has a half-life of 12 hours. It is contraindicated in patients with liver failure and requires dosage adjustment in elderly patients and patients with renal insufficiency. Owing to a lack of evidence, ASRA recommends a "cautious approach."

## 5. What anesthetic technique would you plan for this patient; what are the established benefits of regional anesthesia in terms of major postoperative outcomes?

No clinical studies have examined the actual risk of neuraxial anesthesia in surgical patients taking clopidogrel. ASRA recommendations are based on case reports of spontaneous spinal hematomas in nonsurgical patients taking clopidogrel or ticlopidine. In the absence of significant airway or pulmonary problems, it is prudent to proceed with general anesthesia for this case. Clopidogrel should be discontinued to minimize surgical hemorrhage, and additional blood products (e.g., packed red blood cells and platelets) should be available intraoperatively.

There are numerous benefits to neuraxial anesthesia in this elderly population. The most comprehensive and contemporary review of perioperative analgesia on major postoperative outcomes is presented by Liu et al. (2007). Significant benefits regarding mortality are associated with the use of thoracic epidural analgesia in various surgical procedures. These findings are supported by large meta-analyses and clinical registries that involved >140 randomized controlled trials with >9000 patients. Other

procedure-specific meta-analyses and randomized controlled trials have failed to report conclusive or significant clinical outcomes. Nevertheless, thoracic epidural analgesia has been shown to reduce the incidence of MI and the risk of postoperative pneumonia and respiratory failure after major vascular and orthopedic procedures. Other noteworthy advantages of high-quality epidural analgesia include a decrease in postoperative ileus, a decrease in overall pain scores at rest and during activity through postoperative day 4, and increase in overall patient satisfaction.

Epidural analgesia is not the only regional technique shown to have a role in improving postoperative outcomes. A 2006 meta-analysis comparing continuous perineural analgesia with mixed systemic opioids showed that perineural techniques have superior pain control for 48–72 hours, wider applicability in ambulatory surgery, and significant reductions in both the length of hospital stay and adverse effects (e.g., nausea, pruritus, sedation) for major orthopedic procedures.

Planning the anesthetic should involve careful consideration on balancing the risk of neuraxial hemorrhage with proven advantages of regional pain management in terms of major postoperative outcomes.

### 6. Discuss the options for postoperative pain management, and explain the role of continuous lumbar plexus and femoral blockade.

If general anesthesia is chosen for this patient's intraoperative management, a multimodal postoperative analgesia regimen should be considered to optimize outcomes. Regional techniques provide adequate pain control, which decreases cardiovascular risks postoperatively. In addition, blunting severe pain allows for physical therapy necessary for optimal range of motion. The mainstay of postoperative pain management is intravenous patient-controlled analgesia with fentanyl, morphine, or hydromorphone. However, as discussed earlier, systemic opioids are inferior to regional techniques (especially epidural analgesia) in terms of desired outcomes.

Medications that can be administered for multimodal analgesia include acetaminophen, nonsteroidal antiinflammatory drugs (NSAIDs), γ-aminobutyric acid (GABA) analogues, *N*-methyl-d-aspartate (NMDA) receptor antagonists (e.g., ketamine, methadone), long-acting neuraxial opioids, and peripheral regional blockade. In 2010, the Food and Drug Administration approved the use of intravenous acetaminophen in the United States. Intravenous acetaminophen has been shown to be efficacious in reducing pain scores after major orthopedic procedures, but its use is limited by cost, clinical experience, and its contraindication in patients with liver dysfunction. In this patient taking clopidogrel, NSAIDs, neuraxial opioids, and placement of a neuraxial catheter are contraindicated. GABAergic agents and NMDA receptor antagonists are useful adjuncts and should be considered in this patient. However, controversial efficacy and adverse effects limit the widespread use of these agents in clinical practice.

Traditionally, unilateral lumbar plexus blockade involving a single injection or placement of an indwelling catheter has demonstrated comparable analgesia with epidural techniques. This technique also offers the advantage of being unilateral and often obviating the need for urinary catheter placement; performance of this block is described in Chapter 53. In the 2010 ASRA guidelines, lumbar plexus block was classified as a deep regional block and subjected to the same precautions as neuraxial anesthesia. Aggressive postoperative prophylaxis for deep vein thrombosis with enoxaparin in patients undergoing orthopedic procedures precludes the use of an indwelling catheter for postoperative pain control. In this patient, in whom antiplatelet therapy is required perioperatively, there is a minimal role for this technique.

Femoral nerve blockade has been shown to be as efficacious as lumber plexus block for postoperative pain control and has the advantage of not being considered a deep block. A disadvantage of this block is the incidence of motor weakness interfering with ambulation and physical therapy. Appropriate neurologic monitoring, patient and nursing education, and fall precautions should be established. Adjunct analgesic medications are still required with this modality.

## SUGGESTED READINGS

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CASE 52

# Brachial Plexus Anesthesia

**Lucas Bejar, MD • Meg A. Rosenblatt, MD**

## QUESTIONS

1. Describe the anatomic structure of the brachial plexus.
2. What are the terminal branches of the brachial plexus, and what do they innervate?
3. How does surgical site affect the anatomic approach to the brachial plexus; what are possible and expected effects of each of these blocks?
4. How does one perform a supraclavicular nerve block?
5. What role does ultrasound have in placement of a brachial plexus nerve block?
6. How is local anesthesia systemic toxicity diagnosed?
7. How is local anesthesia systemic toxicity treated?

A 53-year-old, 60-kg woman with a left olecranon fracture presented for open reduction and internal fixation. Her past medical history was significant for hypertension and mild exertional dyspnea. She had a negative nuclear stress test 1 month before surgery, and her estimated ejection fraction was 65%. Placement of a continuous supraclavicular brachial plexus block was performed using an ultrasound-guided technique, with an 18-gauge 50-mm Tuohy needle via an in-plane approach in a medial-to-lateral direction. A 20-gauge catheter was inserted to a distance 5 cm beyond the end of the needle, and 40 mL of 2% lidocaine was injected through the catheter. General anesthesia was induced to provide patient comfort while in the lateral decubitus position, and the airway was secured with a No. 4 laryngeal mask airway. A bolus of 20 mL of 0.375% bupivacaine was administered via the catheter 2 hours into the procedure, and the patient became hemodynamically unstable. Ventricular fibrillation was seen on the electrocardiogram (ECG).

### 1. Describe the anatomic structure of the brachial plexus.

Ventral rami of C5-T1 form the brachial plexus. The brachial plexus supplies motor and sensory innervation to the upper extremity with the exception of the trapezius muscle and cutaneous innervation to the axilla. These two areas are innervated by the ventral rami of C3 and C4 and the intercostobrachial nerve.

C5-T1 nerve roots pass posterior to the vertebral artery as they exit from the transverse processes. Shortly thereafter, the nerve roots of C5 and C6 combine to form the superior trunk of the brachial plexus. The root of C7 forms the middle trunk, and the roots of C8 and T1 form the inferior trunk. These three trunks pass between the anterior and middle scalene muscles. As the three trunks pass over the first rib, they divide into the anterior and posterior divisions of the brachial plexus, which supply ventral and dorsal innervations to the upper extremity.

After passing the first rib and continuing underneath the clavicle, these divisions merge again to form three cords, which are named relative to their position to the axillary artery: posterior (C5-T1), lateral (C5-C7), and medial (C8-T1). The posterior cord is formed from the union of the posterior divisions of all three trunks and contains innervation from all the nerve roots that compose the brachial plexus. The lateral cord is composed of the anterior divisions of the superior and middle trunks. The medial cord is a continuation of the anterior division from the inferior trunk. These cords divide into various nerve branches that innervate the upper extremity (Figure 52-1).

### 2. What are the terminal branches of the brachial plexus, and what do they innervate?

The five major terminal branches of the brachial plexus are the musculocutaneous, axillary, radial, median, and ulnar nerves. Nerves that originate from the brachial plexus and their sensory and motor innervations are listed in Table 52-1.

### 3. How does surgical site affect the anatomic approach to the brachial plexus; what are possible and expected effects of each of these blocks?

The brachial plexus comprises C5-T1 nerve roots that are surrounded by prevertebral fascia. Prevertebral fascia extends from the spine into the upper extremity. These nerves divide and exit the plexus at varying points. If a block is performed after a nerve has already exited the plexus, that nerve is spared. Anesthesia of the brachial plexus can be provided by interscalene, supraclavicular, infraclavicular, or axillary approaches. Generally, a block that is placed anatomically distal to the spinal cord provides better distal coverage of the upper extremity at the expense of proximal coverage.

The most proximal block is an interscalene nerve block. It is performed at the level of C6, between the

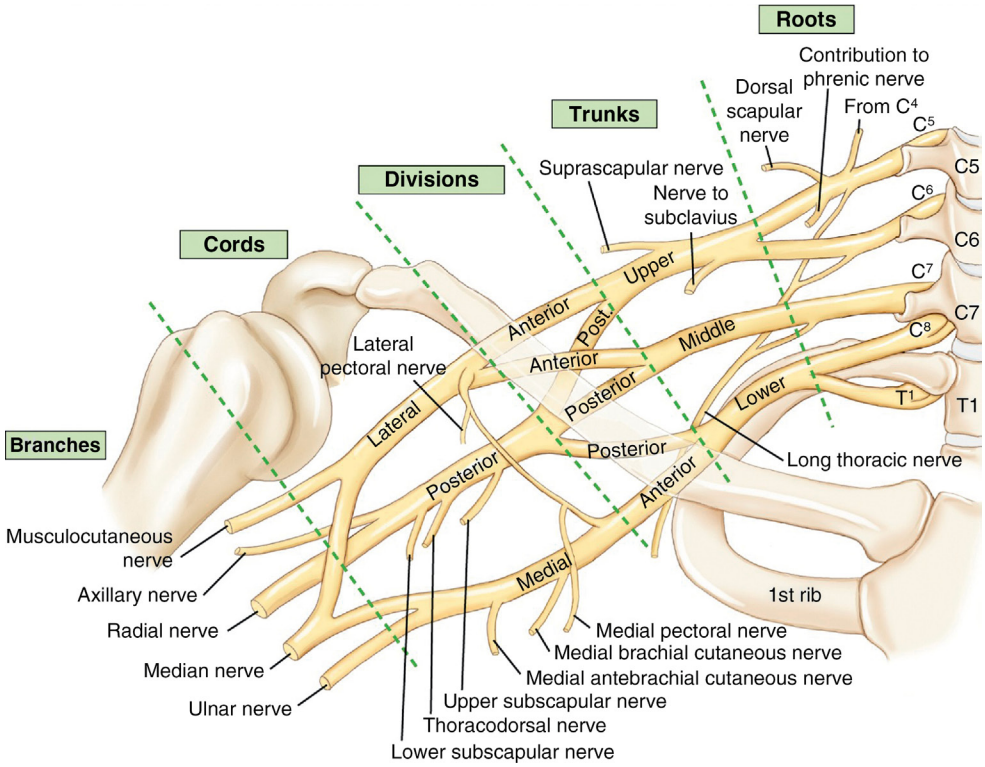


**FIGURE 52-1** ■ Anatomy of the brachial plexus. (From Neumann D: Shoulder complex. In: Kinesiology of the Musculoskeletal System: Foundations for Rehabilitation, 2nd edition, Mosby, St. Louis, 2010.)

TABLE 52-1 **Terminal Branches of the Brachial Plexus**

| Nerve | Brachial Plexus Origin | Motor Innervation | Sensory Innervation |
|---|---|---|---|
| Musculocutaneous | Branch of lateral cord (C5-C7) | Coracobrachialis<br>Biceps brachii<br>Brachialis | Lateral forearm (via lateral antebrachial cutaneous nerve) |
| Axillary | Branch of posterior cord (C5-C6) | Deltoid<br>Teres minor | Posterior upper arm<br>Deltoid |
| Radial | Posterior cord (C5-T1) | Extensors of upper arm, forearm, and hand | Posterior upper arm and forearm (via posterior antebrachial cutaneous nerve)<br>Dorsum of hand (lateral 3½ digits) |
| Median | Input from lateral and medial cords (C5-T1) | Flexors of forearm and hand*<br>Thenar eminence | Palmar surface of hand (lateral 3½ digits) |
| Ulnar | Branch of medial cord (C8-T1) | Intrinsic hand muscles†<br>Flexor carpi ulnaris<br>Flexor digitorum profundus (medial two muscles) | Medial 1½ digits and corresponding palm<br>Medial 1½ digits and corresponding dorsum of hand |

*The flexor carpi ulnaris on the medial aspect of the forearm is innervated by the ulnar nerve.
†The thenar muscles are innervated by the median nerve.

anterior and middle scalene muscles. The interscalene block is best suited for surgery of the shoulder, upper arm, and elbow and for postoperative pain relief of distal clavicle surgery. The interscalene approach often does not cover the C8 and T1 nerve roots, which are crucial for surgical anesthesia of the medial hand (ulnar distribution). Complications of an interscalene nerve block include unilateral phrenic nerve palsy. The incidence of unilateral phrenic nerve palsy reaches almost 100% when the nerve block is performed with a nerve stimulator

TABLE 52-2 **Side Effects and Coverage Areas of Brachial Plexus Blocks**

| Placement | Very Likely or Definite Side Effect | Possible Side Effect | Coverage Area |
|---|---|---|---|
| Interscalene | Ipsilateral phrenic nerve palsy*<br>Horner syndrome<br>Ptosis<br>Miosis<br>Anhidrosis<br>Nasal congestion | Vertebral artery puncture<br>Subarachnoid puncture<br>Recurrent laryngeal nerve block<br>Neuronal injury | Shoulder to elbow |
| Supraclavicular | Ipsilateral phrenic nerve palsy* | Ipsilateral pneumothorax<br>Subclavian artery puncture*<br>Horner syndrome<br>Recurrent laryngeal nerve block<br>Neuronal injury | Distal ⅔ of arm including hand |
| Infraclavicular | | Ipsilateral pneumothorax<br>Axillary artery puncture<br>Horner syndrome†<br>Ipsilateral phrenic nerve palsy†<br>Neuronal injury | Distal arm just above elbow including hand |
| Axillary | | Axillary artery puncture<br>Hematoma<br>Neuronal injury | Forearm and hand<br>Musculocutaneous nerve must be blocked separately for lateral forearm coverage |

*Can be reduced with the use of ultrasound guidance.
†Much less likely than in interscalene block.

technique, although this can be reduced under ultrasound guidance. This block also often results in a unilateral Horner syndrome (ptosis, miosis, anhidrosis) and nasal congestion of the ipsilateral nares. Other possible side effects that occur rarely include vertebral artery puncture, subarachnoid puncture, epidural block, and recurrent laryngeal nerve block (Table 52-2).

A supraclavicular nerve block is performed along the superior border of the clavicle just lateral to the subclavian artery. At this level, the nerve roots seen at the interscalene approach have combined to form the superior, middle, and inferior trunks. Bundling into trunks at this location allows for excellent coverage of the upper extremity. A supraclavicular block provides complete surgical anesthesia of the distal two thirds of the arm through to the hand, including coverage where a tourniquet is usually applied, and is considered the "spinal of the upper extremity." Complications include ipsilateral hemidiaphragm paralysis (phrenic nerve palsy), which has an incidence of 50% when the block is performed under nerve stimulator guidance. More recent studies have shown that the incidence of phrenic nerve palsy is substantially reduced when a supraclavicular nerve block is performed under ultrasound guidance, even when the same volume of local anesthetic is used. The different incidences of phrenic nerve palsy could be related to different needle paths and insertion points between the two techniques. Given the potential for hemidiaphragmatic paralysis, particularly with the nerve stimulator technique, supraclavicular approaches and interscalene techniques should be avoided in patients with poor underlying respiratory function. Other rare side effects include Horner syndrome from stellate ganglion blockade and hoarseness from recurrent laryngeal nerve blockade.

An infraclavicular nerve block is performed just superior and medial to the coracoid process, approximately 3 cm below the clavicle. At this anatomic location, the brachial plexus has become the medial, posterior, and lateral cords bundled closely around the axillary artery. This block is ideally suited for surgery of the distal arm, elbow, wrist, and hand. The supraclavicular and infraclavicular locations are similar in terms of block distribution. However, the infraclavicular block has minimal effect on respiratory function and very low incidence of Horner syndrome compared with the supraclavicular block, especially if the latter is achieved under a nerve stimulator technique.

An axillary block is the most distal block of the brachial plexus and can be performed via ultrasound-guided, nerve stimulator, and transarterial techniques. At this anatomic point, the nerves have reached their terminal branches (i.e., musculocutaneous, radial, median, and ulnar nerves). Performing a block at this level provides excellent surgical anesthesia of the hand and forearm. However, the exit of the musculocutaneous nerve from the brachial plexus is variable and often occurs proximal to this point, so consideration must be given to blocking the musculocutaneous nerve separately. Specifically, the musculocutaneous nerve can be anesthetized by injecting 5 mL of local anesthetic into the belly of the coracobrachialis muscle. If a tourniquet is required, T2 must also be anesthetized separately; this can be accomplished by performing a ring block with 5 mL of local anesthetic at the same level the axillary block was placed. Side effects of axillary nerve blocks are limited. Axillary artery puncture may occur and may be intentional depending on block technique and intravascular local anesthetic injection.

## 4. How does one perform a supraclavicular nerve block?

Supraclavicular nerve blocks can be performed via two different techniques: the plumb-bob technique with simultaneous nerve stimulator, or ultrasound guidance, with direct visualization. For nerve stimulator techniques, patients are positioned supine. ECG, pulse oximetry, and blood pressure monitors are placed, and midazolam can be administered for mild to moderate sedation and anxiolysis. The patient's head is turned to the contralateral side to which the block will be placed. The area from the lower neck lateral to the acromion process and inferior to just below the clavicle is prepared in sterile fashion. The lateralmost insertion of the sternocleidomastoid muscle on the clavicle is identified, immediately superior to the edge of the clavicle. A 22-gauge 2-inch insulated needle is inserted perpendicular to the ground while connected to a nerve stimulator delivering 1 mA of current. If flexion or extension of the digits is seen, the nerve stimulator current is turned down to 0.4–0.5 mA. If movement is still seen and negative aspiration rules out intravascular location of the needle tip, 40 mL of local anesthetic is injected in 5-mL aliquots, after ensuring negative aspiration between injections. If no muscle twitch is elicited, the needle is redirected in small steps in the cephalad direction up to a 30-degree angle, at which point the same steps can be undertaken in the caudad direction. Care must be taken to avoid subclavian artery injection.

In an ultrasound-guided technique, the patient is prepared in similar fashion. Ultrasound is used to identify the internal jugular vein and carotid artery. By continuously scanning laterally from this position and just superior to the clavicle, the next major vessel along this trajectory, the subclavian artery, can be identified. The brachial plexus can be seen just lateral to the artery. Using an in-plane approach, the 50-mm needle is inserted at a 30-degree angle from the lateral-to-medial direction. When inserting a catheter, one performs the block from a medial-to-lateral direction, threading the catheter away from the subclavian artery. In either scenario, gentle aspiration before injecting local anesthetic and at injection of every 5 mL thereafter is essential to avoid intravascular injection. Typically, 30–40 mL of local anesthetic is used.

If the block is primarily for postoperative analgesia, 0.25% bupivacaine can be used for the entire volume. However, if the block is to be used in lieu of general anesthesia and requires a quicker onset, at least half of the volume should be either 1.5% mepivacaine or 1.5%–2% lidocaine. Alkalization of mepivacaine allows for a faster onset, so 2 mL of sodium bicarbonate is added per 20 mL of mepivacaine. A block for short procedures with minimal postoperative pain could be performed solely with mepivacaine or lidocaine.

## 5. What role does ultrasound have in placement of a brachial plexus nerve block?

Classically, peripheral nerve blocks were performed using approximate anatomic landmarks, with nerve stimulators that would yield paresthesias and muscular contraction when placed in close proximity to the target nerve. With increasing access to portable ultrasound, more practitioners are using this modality in lieu of nerve stimulators. Potential benefits of ultrasound for peripheral nerve blocks include decreased time to block performance and decreased overall complication rate, particularly in relation to vascular puncture.

Various studies have been performed to compare nerve stimulator and ultrasound-guided techniques for brachial plexus nerve blocks. Most of these studies found that ultrasound guidance leads to faster onset of sensory block and increased block success. Many studies also showed decreased block performance time, decreased incidence of vascular puncture, and decreased number of needle passes. However, some studies did not clarify whether ultrasound scanning before performing the block was included in this performance time, leaving some controversy surrounding this claim. The increased vascular puncture rate and increased number of needle passes in the nerve stimulator groups did not increase the rate of complications or affect patient satisfaction.

In terms of complications, evidence suggests that hemidiaphragmatic paresis can be avoided when performing a supraclavicular block with ultrasound guidance as opposed to nerve stimulator technique even when identical local anesthetic injections are made. Similarly, studies suggest that using smaller volumes of local anesthetic can decrease hemidiaphragmatic paresis associated with interscalene nerve block. Smaller local anesthetic volumes are possible when ultrasound-guided techniques are used. One complication that is not avoided by an ultrasound-guided technique is nerve injury. Multiple studies have demonstrated no difference in the rate of nerve injury whether a block is performed by nerve stimulator technique or ultrasound-guided technique.

Finally, multiple studies have demonstrated that residents perform ultrasound-guided blocks faster and with greater success compared with nerve stimulator techniques. Increasing availability and decreasing cost of portable ultrasound machines have resulted in increased interest for this technique and have contributed to a resurgence in the use of regional anesthesia.

## 6. How is local anesthesia systemic toxicity diagnosed?

Local anesthesia systemic toxicity (LAST) is a syndrome resulting from intravascular accumulation of local anesthetic. This accumulation occurs via direct intravascular injection of local anesthetics or from the absorption of large deposits of local anesthetic as administered during a nerve block. In a review of 93 cases of LAST from 1979–2009, patients with preexisting cardiac and neurologic disease seem to be at higher risk of developing cardiac and neurologic symptoms.

Initial signs of systemic toxicity in an awake patient include central nervous system (CNS) complaints of tinnitus, metallic taste, circumoral numbness, and psychomotor agitation. These symptoms can progress quickly to loss of consciousness, seizure, and respiratory arrest. The aforementioned review showed that 89% of cases included CNS involvement as presenting symptoms, although neurologic and cardiac signs and symptoms can be concurrent, particularly with intravascular injection.

Primary cardiovascular symptoms include bradycardia, decreased myocardial contractility, distributive shock, and ventricular arrhythmias. Approximately half of cases that initially displayed CNS involvement went on to include cardiac symptoms. Typically, if cardiac toxicity occurs, it is preceded by CNS toxicity. However, inadvertent intravascular administration of local anesthetic may speed the progression of symptoms, and the patient may display concurrent cardiac and CNS toxicity. In addition, general anesthesia or heavy sedation may mask CNS symptoms that could warn of impending hemodynamic depression.

The onset of LAST occurs within 50 seconds in approximately half of cases, and a further 25% of episodes occurred within 5 minutes. These cases are likely secondary to inadvertent intravascular injection. LAST can develop over a longer time course as well; 25% of cases in the aforementioned review began after 5 minutes and occurred up to 60 minutes after injection. For this reason, patients must be monitored closely for at least 1 hour after placement of a nerve block.

Although all local anesthetics can cause CNS toxicity when administered at high enough doses, bupivacaine and other lipid-soluble agents have a greater cardiac-to-CNS toxicity ratio than other local anesthetics and are more likely to cause cardiac events. These events are also typically more resistant to treatment. Bupivacaine specifically was shown to block inactivated sodium channels tenaciously during the action potential in cardiac myocytes, preventing cellular repolarization; this has been linked to an increased incidence of atrioventricular nodal conduction depression and decreased myocardial contractility compared with the toxicity seen with other local anesthetic agents.

## 7. How is local anesthesia systemic toxicity treated?

The treatment of LAST (Box 52-1) should be focused on airway management, cessation of seizure activity, and cardiovascular support. Seizure activity is treated with intravenous benzodiazepine or barbiturate as a first-line agent to increase the seizure threshold. Induction of general anesthesia with propofol is an acceptable alternative, although concurrent cardiac depression could be problematic. Airway management is of utmost importance in the prevention of hypoxia and hypercarbia that could exacerbate cardiovascular toxicity. There should be a low threshold for endotracheal intubation in this situation, especially with concurrent signs of cardiac toxicity.

Cardiac toxicity may be severe, and cardiac arrest is common. Maintenance of cardiac perfusion pressure in an effort to wash out local anesthetic is essential. However, animal studies demonstrated that large doses of epinephrine are associated with poor outcome, and current recommendations include the use of smaller than normal epinephrine dosing with initial boluses of 10–100 μg. In addition, vasopressin has been linked to poor outcomes and is not recommended. Ventricular arrhythmias should be treated with amiodarone.

The cornerstone therapy for cardiac toxicity is 20% lipid emulsion, which is believed to act as a lipid sink and cause redistribution of local anesthetic away from the cardiac sodium channels and into the lipid bilayer. Initial treatment consists of a bolus dose of 1.5 mL/kg of a 20% lipid emulsion, followed by an infusion of 0.25 mL/kg per minute. A further bolus and increase in infusion to 0.5 mL/kg per minute can be used if the initial treatment does not achieve hemodynamic stability. The concentration of lipid in propofol is *not* sufficient to treat LAST.

**BOX 52-1 Pharmacologic Treatment of Local Anesthetic Systemic Toxicity (LAST)**

- Get help
- Initial focus
  - Airway management: ventilate with 100% oxygen
  - Seizure suppression: benzodiazepines are preferred; *avoid* propofol in patients with signs of cardiovascular instability
  - Alert the nearest facility with *cardiopulmonary bypass* capability
- Management of cardiac arrhythmias
  - Basic and advanced cardiac life support requires adjustment of medications and perhaps prolonged effort
  - *Avoid* vasopressin, calcium-channel blockers, β-adrenergic blockers, or local anesthetic
  - *Reduce* individual epinephrine doses to <1 μg/kg
- Lipid emulsion (20%) therapy (values in parentheses are for a 70-kg patient)
  - Bolus 1.5 mL/kg (lean body mass) intravenously over 1 minute (approximately 100 mL)
  - Continuous infusion 0.25 mL/kg per minute (approximately 18 mL per minute; adjust by roller clamp)
  - Repeat bolus once or twice for persistent cardiovascular collapse
  - Double infusion rate to 0.5 mL/kg per minute if blood pressure remains low
  - Continue infusion for at least 10 minutes after attaining circulatory stability
  - Recommended upper limit: approximately 10 mL/kg lipid emulsion over the first 30 minutes
- Post LAST events at www.lipidrescue.org and report use of lipid to www.lipidregistry.org

Adapted with permission from Neal JM, Mulroy MF, Weinberg GL: American Society of Regional Anesthesia and Pain Medicine checklist for managing local anesthetic systemic toxicity: 2012 version. Reg Anesth Pain Med 37:16, 2012.

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CASE 53

# Lower Extremity Anesthesia

Rachel E. Outterson, MD • Meg A. Rosenblatt, MD

## QUESTIONS

1. Describe the sensory innervation of the lower extremity.
2. Which nerves are affected during anterior cruciate ligament surgery?
3. What are the anesthetic options for anterior cruciate ligament surgery?
4. What is the benefit of placing a femoral nerve catheter?
5. How are femoral nerve blocks performed, and how are femoral catheters placed?
6. Which local anesthetic would you choose for a femoral nerve block; what solution would you use for continuous infusion via the femoral nerve catheter?
7. What are the differences between a femoral nerve, 3-in-1, fascia iliaca, and lumbar plexus blocks?
8. How would you manage severe posterior knee pain occurring postoperatively?
9. What are the regional anesthetic options for open reduction internal fixation (ORIF) of a fifth metatarsal fracture?

A 29-year-old man presented for arthroscopic-assisted repair of a torn right knee anterior cruciate ligament (ACL). The patient was discharged home after adequate analgesia was achieved with both a femoral nerve catheter and a sciatic block. He returned to the emergency department the following evening after falling when he got up to use the bathroom. An x-ray showed a fracture of the left fifth metatarsal. An open reduction and internal fixation (ORIF) of the fifth metatarsal is planned.

### 1. Describe the sensory innervation of the lower extremity.

Innervation of the lower extremity is derived from nerves of the lumbar and sacral plexuses, sometimes collectively referred to as the lumbosacral plexuses (Figure 53-1). The lumbar plexus, which lies between the psoas major and quadratus lumborum fascias, is derived from the ventral rami of L1 to L4, with some contribution from T12, and branches into the iliohypogastric, ilioinguinal, genitofemoral, lateral femoral cutaneous (also known as the lateral cutaneous nerve of the thigh), obturator, and femoral nerves. The saphenous nerve is the largest terminal branch of the femoral nerve. Sensory innervation of the lumbar plexus is shown in Table 53-1.

The sacral plexus is derived from the ventral rami of L4 to S4 and gives off the superior and inferior gluteal nerves, the posterior cutaneous nerve of the thigh, the pudendal nerve, and the sciatic nerve. The sciatic nerve is composed of two nerves, tibial and common fibular (formerly known as peroneal), bound together by a common sheath. The terminal branches of the tibial nerve include the medial and lateral plantar nerves. The terminal branches of the common fibular nerve include the deep and superficial fibular nerves. The union of branches from the common fibular and tibial nerves forms the sural nerve. Sensory innervation of the sacral plexus is shown in Table 53-2.

### 2. Which nerves are affected during anterior cruciate ligament surgery?

Postoperative pain after ACL repair originates from skin incisions, tibial periosteum at the bone tunnel site, inflammation and swelling within the knee joint, and the tendon harvest site (if an autograft is used). The nerves involved are the following:

- Femoral nerve: skin incisions adjacent to the patellar tendon
- Tibial nerve: tibial periosteum
- Branches of femoral, obturator, sciatic nerves: internal knee joint
- Autograft harvest:
  - Femoral nerve: patellar tendon
  - Obturator nerve: gracilis tendon
  - Tibial nerve: semitendinosus tendon

### 3. What are the anesthetic options for anterior cruciate ligament surgery?

ACL surgery may be successfully performed under general anesthesia, neuraxial anesthesia, or peripheral nerve block. Although general anesthesia provides excellent operating conditions during surgery, it does not provide postoperative analgesia. Postoperative pain relief can be accomplished with either intravenous analgesic agents

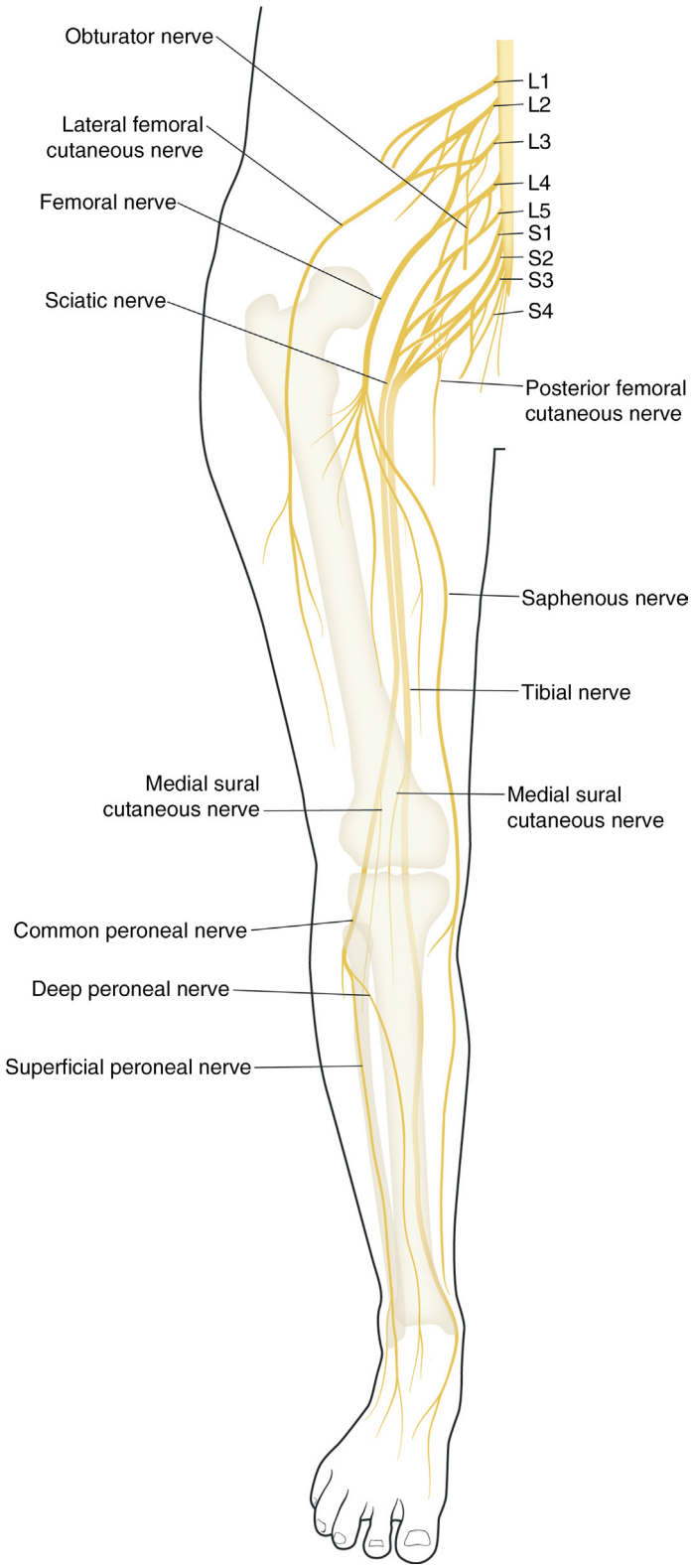


**FIGURE 53-1** ■ Extension of nerves from the lumbosacral plexus. Sciatic nerve (divides in midthigh—tibial division and peroneal division), femoral nerve, and obturator nerve. (From Miller MD, Chhabra AB, Hurwitz SR, et al., editors. Orthopaedic surgical approaches. Philadelphia: Saunders; 2008. p. 434.)

or femoral or lumbar plexus blocks or catheters placed perioperatively.

Spinal or epidural neuraxial anesthesia provides adequate analgesia for the procedure but limited postoperative pain relief. Although placement of an epidural catheter provides the potential for an extended period of postoperative analgesia, it is inappropriate for ambulatory procedures. For optimal postoperative pain control, a single-shot spinal technique should be combined with a femoral nerve catheter. The femoral nerve

TABLE 53-1 **Sensory Distribution of Lumbar Plexus**

| Nerve | Roots | Sensory Distribution |
|---|---|---|
| Iliohypogastric | L1 | Superolateral buttock and thigh |
| Ilioinguinal | L1 | Proximal anteromedial thigh |
| Genitofemoral | L1-L2 | Inguinal region and proximal anteromedial thigh |
| Lateral femoral cutaneous | L2-L3 | Lateral thigh from greater trochanter to proximal knee |
| Obturator | L2-L4 | Medial thigh |
| Femoral<br>Saphenous | L2-L4 | Anterior thigh, distal medial thigh<br>Medial leg and foot |

TABLE 53-2 **Sensory Distribution of Sacral Plexus**

| Nerve | Roots | Sensory Distribution |
|---|---|---|
| Superior gluteal | L4-S1 | None |
| Inferior gluteal | L5-S2 | None |
| Pudendal | S2-S4 | Perineum |
| Posterior femoral cutaneous | S1-S3 | Posterior thigh and popliteal fossa |
| Tibial | L4-S3 | Lateral ankle and foot, posterior calf, heel and plantar surface of the foot (via medial and lateral plantar nerves) |
| Medial plantar | | Plantar surface, medial to a line splitting the fourth toe |
| Lateral plantar | | Plantar surface, lateral to a line splitting the fourth toe |
| Common fibular | L4-S3 | |
| Superficial fibular | | Distal third of anterior leg and dorsum of foot |
| Deep fibular | | Web space between first and second toes |
| Sural | S1-S2 | Posterolateral leg and foot |

catheter provides extended postoperative analgesia without motor weakness in the nonoperative leg.

Peripheral nerve blocks alone can provide anesthesia, with or without the addition of sedation. They can also provide postoperative pain relief, either by continuous local anesthetic infusion via a catheter or by administration of a long-acting local anesthetic in the original block. Depending on the surgical plan, options include sciatic nerve block combined with either a lumbar plexus or fascia iliaca block.

## 4. What is the benefit of placing a femoral nerve catheter?

Continuous peripheral nerve blocks have been shown to decrease pain, sleep disturbances, opioid use, and opioid-related side effects. They also improve overall patient satisfaction after moderately painful orthopedic surgeries in both the upper and the lower extremity. Femoral nerve catheters after ACL repair specifically have been shown to provide superior analgesia compared with intraarticular or patellar tendon wound infusions, intravenous agents alone, or placebo. In studies involving total knee replacement, femoral nerve catheters have been found to reduce pain with movement, which can aid in achieving recovery milestones expected during physical therapy.

## 5. How are femoral nerve blocks performed, and how are femoral catheters placed?

For all blocks described in this case, the following steps are standard. Physiologic monitors are placed and sedation is administered, if appropriate. After the clinician dons a mask, washes hands, and puts on sterile gloves, a sterile preparation of the skin is performed with chlorhexidine. Subcutaneous infiltration with local anesthetic is achieved before inserting the block needle. When appropriate needle placement is confirmed and after negative aspiration for blood is confirmed, local anesthetic is injected in small aliquots. Aspiration for blood should be repeated between each aliquot injection.

Multiple techniques have been described for performing femoral nerve blocks, all of which are placed in the supine position. Differences in the techniques are as follows:

- *Paresthesia technique:* The femoral arterial pulse is palpated and marked 1–2 cm caudad to an imaginary line corresponding to the inguinal ligament. Approximately 1 cm lateral to this mark, a needle is inserted at a 90-degree angle to the skin and advanced until paresthesias are evoked in the femoral nerve distribution (see Table 53-1). After appropriate

needle placement is determined, 20 mL of local anesthetic is injected.

- *Nerve stimulator technique:* A stimulating needle is advanced in an identical fashion to the paresthesia technique or at the level of the femoral crease but always lateral to the femoral arterial pulse. The stimulating needle is initially set to deliver 1 mA of current at a frequency of 2 Hz and then reduced to 0.2–0.4 mA once quadriceps stimulation is achieved, as evidenced by a "patellar snap" (visible or palpable contraction of the quadriceps muscle), usually at a depth of 2–3 cm. If the quadriceps response is retained as current is reduced, placement is appropriate, and local anesthetic is injected. A sartorius muscle twitch (transverse contraction across the thigh) is not considered an adequate response. If a sartorius muscle twitch is elicited, the stimulating needle is redirected laterally until a true quadriceps response is appreciated.
- *Ultrasound-guided technique:* The ultrasound probe is placed in the femoral crease producing an axial view. In this view, the femoral vein, artery, and nerve can be identified medial to lateral. The nerve may be approached with either an in-plane or out-of-plane view. In the in-plane view, the block needle is advanced from lateral to medial with the goal of placing the tip just lateral to the femoral nerve. When appropriate positioning is achieved, 10–20 mL of local anesthetic is injected under direct visualization. In the out-of-plane view, the block needle is placed adjacent to the ultrasound probe, directly over the femoral nerve, and advanced until its tip is visualized at the desired injection site (just lateral to the nerve); under direct visualization, local anesthetic is injected.

The paresthesia technique is rarely used because both nerve stimulator–guided and ultrasound-guided techniques are more successful. Nerve stimulator and ultrasound-guided techniques are equally efficacious. An advantage of the ultrasound-guided technique is the ability to observe local anesthetic spread and make adjustments midway through performance of the technique, if necessary. The ultrasound-guided technique may also provide protection against intravascular injection of local anesthetic.

A continuous nerve block catheter can be placed using any of the above-described techniques. To facilitate passage of the catheter, a larger bore hollow needle is inserted at an acute angle to the skin. After injection of local anesthetic, a catheter is threaded through the needle into the space created by the local anesthetic bolus. After threading the catheter 5–10 cm past the needle tip, the needle is carefully withdrawn over the catheter, which is secured with a sterile dressing. An alternative method is to inject saline instead of local anesthetic to "open the space" so that the catheter can be easily threaded. Local anesthetic is injected through the catheter to ensure that anesthesia and analgesia occur, minimizing "secondary block failure."

There are two types of catheters, stimulating or nonstimulating. The advantage of the stimulating catheter is that its position can be confirmed by eliciting the appropriate muscle responses. Although some practitioners prefer stimulating catheters, they are more costly and take longer to insert compared with nonstimulating catheters, and block success is not improved.

### 6. Which local anesthetic would you choose for a femoral nerve block; what solution would you use for continuous infusion via the femoral nerve catheter?

The desired block density and duration of postoperative analgesia dictate the choice of local anesthetic. For the initial bolus injection of local anesthetic, a long-acting local anesthetic such as bupivacaine or ropivacaine may be appropriate to establish lasting analgesia. A shorter-acting local anesthetic, such as lidocaine or mepivacaine, can also be appropriate and would be preferred by some because these agents have less cardiotoxicity. If the nerve block is the sole anesthetic, a higher concentration, such as 0.5% bupivacaine or 0.75%–1% ropivacaine, is required to achieve surgical anesthesia. If used as an adjunct to general or spinal anesthesia, a lower concentration, such as 0.25% bupivacaine or 0.5% ropivacaine, is adequate.

For a continuous postoperative infusion via catheter, a long-acting local anesthetic is preferred because it provides continued analgesia even after the catheter is removed. Typically, 0.1% –0.2% bupivacaine or 0.1%–0.3% ropivacaine is infused at 5–10 mL per hour.

### 7. What are the differences between a femoral nerve, 3-in-1, fascia iliaca, and lumbar plexus blocks?

As previously described, femoral nerve blocks are performed with the intent of anesthetizing a single nerve. Three-in-one blocks are performed with the intent of spreading local anesthetic around three major nerves of the lumbar plexus, the femoral, obturator, and lateral femoral cutaneous nerves, as they pass in a common plane beneath the fascia iliaca. Performance of a three-in-one block is nearly identical to performance of a femoral block, but a larger volume of local anesthetic, 25–30 mL, is needed. Pressure is applied 2–4 cm below the injection site during injection to promote proximal flow toward the plexus. Even with perfect technique, the block often does not adequately anesthetize all three nerves. The femoral and lateral femoral cutaneous nerves are reliably blocked; however, obturator nerve block is not guaranteed, with reported success rates ranging from 4%–78%.

The fascia iliaca block is performed lateral to the site where a femoral or three-in-one block is performed. Needle entry is 1 cm below the inguinal ligament, two thirds the distance from the pubic tubercle to the anterior superior iliac spine. Using either the "two pop" technique or ultrasound guidance, the needle is advanced first through the fascia lata and then the fascia iliaca. Local anesthetic is injected in the plane below the fascia iliaca. The technique for fascia iliaca block relies on the anatomic proximity of the lateral femoral cutaneous and femoral nerves below the fascia iliaca. The obturator nerve may be blocked with this technique, but as with the three-in-one block, it is not reliably anesthetized.

The lumbar plexus block is the only block that reliably anesthetizes the femoral, lateral femoral cutaneous, and

obturator nerves. It also blocks the genitofemoral, ilioinguinal, and iliohypogastric nerves. It is a deeper, more difficult block to perform and carries a higher risk of local anesthetic systemic toxicity. The block is performed with the patient in the lateral position with the operative side up. Approaching posteriorly, the needle is inserted 3–4 cm lateral to the midline, at the level of the iliac crest. A nerve stimulator may be used to elicit first paravertebral muscle twitches and then quadriceps muscle twitches. When the quadriceps muscle twitches are maintained as the current is decreased to 0.5–1 mA, the needle is in the appropriate position, and 25–30 mL of local anesthetic is injected. For ultrasound-guided blocks, a curved 2- to 5-MHz ultrasound probe is used to approximate the depth of the plexus by localizing the psoas muscle. The lumbar plexus lies within the posterior one third of the psoas muscle bulk (Table 53-3).

For all of these nerve blocks, the choice of local anesthetic would be determined by desired block density and duration of analgesia.

## 8. How would you manage severe posterior knee pain occurring postoperatively?

The posterior knee joint is innervated by branches of the sciatic nerve that are not covered by a femoral nerve catheter. Replacing or administering a bolus of local anesthetic in a patient with a femoral catheter would not treat this pain. Available options include intravenous opioids and sciatic nerve block. Either single-shot or continuous sciatic block provides pain relief without further sedation and retains the advantages conferred by the femoral nerve catheter.

Sciatic nerve block is performed via either a posterior or an anterior approach. The posterior approach is accomplished in the semiprone Sims position with the operative side up and the knee and hip flexed. Either a nerve stimulation or ultrasound-guided technique may be used. With the nerve stimulation technique, a line is drawn between the greater trochanter and posterior superior iliac spine. The needle is inserted perpendicular to the skin 4 cm inferior to the midpoint of this line. The needle is advanced with a current of 1.5 mA. Stimulation should generate gluteal twitches and with further advancement, usually 5–8 cm, twitches of the hamstring muscles, calf, or foot to indicate sciatic nerve stimulation. If these twitches are preserved when the current is decreased to 0.2–0.5 mA, 15–20 mL of local anesthetic is injected.

With the ultrasound-guided technique, the nerve is visualized deep to the gluteus maximus muscle and superficial and lateral to the ischial bone. For better anatomic identification, color Doppler may be used to locate the pudendal vessels adjacent to the ischial spine and the inferior gluteal artery adjacent to the sciatic nerve. The sciatic nerve is imaged in the transverse or short-axis view. The block needle is advanced using either an in-plane or out-of-plane technique through the gluteus maximus to the level of the sciatic nerve. At this point, nerve stimulation may be used to verify correct needle placement further. Ideally, local anesthetic spread should be visualized circumferential to the nerve.

The anterior approach to the sciatic nerve block is more difficult and usually reserved for patients who cannot tolerate the posterior approach position. This option blocks the sciatic nerve further distally as it passes the lesser trochanter. The articular branches to the hip and the posterior cutaneous nerve are not included. Although this approach would be adequate for surgery or pain at the level of the knee or below, it would not adequately anesthetize the thigh for tourniquet placement.

Needle insertion for the anterior approach to the sciatic nerve is 4–5 cm distal to the femoral arterial pulse on a line drawn perpendicular to the femoral crease. A stimulating needle is inserted perpendicular to the skin and advanced until twitches of the calf, foot, or toes are achieved, usually at a depth of 10–12 cm. If these twitches are maintained with the current reduced to 0.2–0.5 mA, 20 mL of local anesthetic may be injected.

## 9. What are the regional anesthetic options for open reduction internal fixation (ORIF) of a fifth metatarsal fracture?

This patient's fall illustrates an important point regarding patient safety after femoral nerve block. Patients with

TABLE 53-3 **Comparison of Femoral, Three-in-One, Fascia Iliaca, and Lumbar Plexus Blocks**

| Nerve Block | Site of Block Needle Insertion | Nerves Blocked | Amount of Local Anesthetic |
|---|---|---|---|
| Femoral | At or just below femoral crease, lateral to femoral artery | Femoral | 10–20 mL |
| Three-in-one | At or just below femoral crease, lateral to femoral artery, with pressure applied inferior to injection site | Femoral<br>Lateral femoral cutaneous<br>± Obturator | 25–30 mL |
| Fascia iliaca | 1 cm below inguinal ligament, ⅔ the distance from pubic tubercle to anterior superior iliac spine | Femoral<br>Lateral femoral cutaneous<br>± Obturator | 30–40 mL |
| Lumbar plexus | 3–4 cm lateral to spinous process at level of iliac crest | Femoral<br>Lateral femoral cutaneous<br>Obturator<br>Genitofemoral<br>Ilioinguinal<br>Iliohypogastric | 25–30 mL |

femoral nerve catheters or even single-shot blocks must be warned that they are at risk for falls because of weakened quadriceps muscles or unintentional injury to the anesthetized leg. Patients should be instructed to wear a knee immobilizer and to use crutches when ambulating.

There are several regional anesthetic options for ORIF of the fifth metatarsal. The following nerves must be blocked to ensure adequate anesthesia for this procedure:

- Sural (lateral aspect of the foot)
- Superficial fibular (dorsal aspect of the foot)
- Plantar branches of the tibial nerve (plantar surface of the foot)

A spinal block and combined spinal-epidural anesthetic are options. However, these techniques block a much greater area than necessary for the surgery and carry the usual risk of hypotension and delay in mobilization after surgery.

A popliteal block would be an appropriate choice for this procedure. This technique anesthetizes the sciatic nerve at the level of the popliteal fossa, where the common fibular and tibial nerves separate, anesthetizing both nerves and all their branches, including the sural, superficial fibular, and plantar nerves. The popliteal block may be performed using nerve stimulation or ultrasound-guided techniques.

A popliteal block is usually performed in the prone position unless patient-related issues (e.g., pain or patient condition) preclude use of this position, in which case the block may be performed in the lateral position. Using nerve stimulation, the biceps femoris tendon (laterally), the semitendinosus tendon (medially), and the popliteal crease are identified. The needle is inserted halfway between the two tendons, 7 cm proximal to the popliteal crease. The nerve stimulator is initially set to deliver a current of 1.5 mA. There should be no local muscle twitches above the knee if needle placement is correct. Stimulation of the sciatic nerve is confirmed by movement of the foot that persists when the stimulating current is reduced to 0.2–0.5 mA; this usually occurs at a depth of 3–5 cm. At this point, 30–40 mL of local anesthetic is injected.

Using the ultrasound-guided technique, an ultrasound probe is placed laterally across the popliteal crease, producing an axial view of the popliteal fossa. First, the popliteal artery is identified. Just superficial and lateral to it (sometimes referred to as "high and outside") is the tibial nerve. More superficial to that is the common fibular nerve. At this site, the nerves are usually separate, requiring scanning proximally to identify the point of bifurcation, often 7–10 cm proximal to the popliteal crease. If the point of bifurcation is prohibitively high, the tibial and common fibular nerves may be blocked separately. The block needle is inserted using either an in-plane or out-of-plane technique. When the needle tip is positioned adjacent to the desired nerve, 30–40 mL of local anesthetic is injected. Repositioning of the needle may be required midway through the procedure to ensure circumferential spread of the local anesthetic.

An ankle block may also be performed for this procedure. An ankle block is composed of five separate nerve blocks, two of them deep (posterior tibial and deep fibular nerves) and three of them superficial (saphenous, sural, and superficial fibular nerves). Although all five nerve blocks of the ankle block are described here, not all are necessary for reduction of the fifth metatarsal. Block of the deep fibular and saphenous nerves is unnecessary for this particular procedure. For each nerve blocked, approximately 6 mL of local anesthetic is injected. This block is usually performed without ultrasound guidance or nerve stimulator guidance; its efficacy relies entirely on accurate identification of landmarks (Table 53-4).

TABLE 53-4 **Individual Nerve Blocks Composing the Ankle Block**

| Nerve Block | Area Anesthetized | Needle Insertion | Details of Block Performance |
|---|---|---|---|
| Deep fibular | Web space between first and second toes | At level of ankle, between extensor hallucis longus and extensor digitorum longus tendons, just lateral to dorsalis pedis arterial pulse | Needle is advanced until contact with bone, then withdrawn 1–2 mm. "Fan" technique may be used to inject slightly medial and lateral to insertion point. |
| Posterior tibial | Heel and plantar surface of foot | Posterior to medial malleolus, deep to superficial fascia | Needle is advanced until contact with bone, then withdrawn 1–2 mm. "Fan" technique may be used to inject slightly medial and lateral to insertion point. |
| Saphenous | Medial foot | Middle of medial malleolus | Local anesthetic is administered in two separate injections forming a subcutaneous ring from the point of entry to Achilles tendon posteriorly and tibial ridge anteriorly. |
| Superficial fibular | Dorsal foot | Tibial ridge | Local anesthetic is injected in a subcutaneous ring from the point of entry to lateral malleolus. |
| Sural | Lateral foot | Just superior to lateral malleolus | Local anesthetic is injected in a subcutaneous ring from the point of entry to Achilles tendon posteriorly. |

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### Web Resources

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SECTION 10

# OBSTETRICS

CASE 54

# Labor and Delivery

Yaakov Beilin, MD

## QUESTIONS

1. What options are available to the mother for labor analgesia?
2. What are the advantages and disadvantages of various neuraxial anesthetic techniques for labor and delivery?
3. What is a "walking epidural"?
4. Describe neuraxial anesthetic techniques that can be employed for cesarean delivery.
5. Outline treatment for postdural puncture headache.
6. What are the advantages and disadvantages of general anesthesia for cesarean delivery?
7. Describe the elements of placental drug transfer.
8. What techniques can be used for pain relief after cesarean delivery?
9. What is the differential diagnosis of postpartum hemorrhage?
10. Explain the risk factors, presentation, and treatment of uterine atony.
11. Describe the presentation and treatment of retained placenta.

A 27-year-old woman presented to the delivery suite in labor after an uncomplicated pregnancy. A lumbar epidural catheter was placed at the L4-L5 interspace to facilitate analgesia. After an adequate trial of labor, the obstetrician elected to perform a cesarean delivery for cephalopelvic disproportion. A T4 level of anesthesia was achieved via the epidural catheter, and the cesarean delivery was initiated. Immediately after delivery of the infant, maternal hemorrhage ensued.

### 1. What options are available to the mother for labor analgesia?

Many techniques have been used to reduce the perception of pain during labor. In addition to systemic medications, inhalation agents, neuraxial anesthesia, hypnosis, psychoprophylaxis, acupuncture, and transcutaneous electrical nerve stimulation have been used.

Systemic opioids can be used to attenuate labor pains; however, they do not completely eliminate the pain. The opioids meperidine, morphine, fentanyl, and the agonist-antagonist butorphanol have been used. Opioids can be administered as an intravenous bolus or with intravenous patient-controlled analgesia. The choice of opioid varies by institution and local experience. Remifentanil can also be used with intravenous patient-controlled analgesia. The advantage of remifentanil is that its onset and duration of action are shorter than those of other opioids. However, it is also very potent, and close maternal respiratory monitoring, preferably with pulse oximetry, is required.

Inhalation analgesia during labor is another option. The goal is to achieve analgesia without depressing airway reflexes. Typically, the mother, using a hand-held device, self-administers nitrous oxide at the beginning of each contraction. Although this technique provides moderately good analgesia, it is not commonly used because of the risk of maternal aspiration with deep levels of anesthesia.

Epidural and combined spinal-epidural (CSE) neuraxial anesthesia techniques have become popular modalities for labor analgesia because of their safety and efficacy profile.

### 2. What are the advantages and disadvantages of various neuraxial anesthetic techniques for labor and delivery?

Rational use of neuraxial anesthesia necessitates an understanding of the pain pathways involved during labor. Labor is traditionally divided into three distinct stages (Table 54-1):

- First stage begins with the onset of regular contractions and ends with complete cervical dilation.
- Second stage begins when the cervix is completely dilated and ends with delivery of the fetus.
- Third stage begins after delivery of the fetus and concludes with delivery of the placenta.

The first stage of labor is associated with uterine and cervical pain mediated by spinal segments T10-L1 (Figure 54-1). Local anesthetics administered to the epidural, spinal, or caudal spaces readily anesthetize these pain pathways. In addition, subarachnoid opioids and paracervical blocks can be used for pain relief during the first stage of labor. Caudal anesthesia is rarely used because of the risk of inadvertent fetal scalp penetration and the associated high fetal levels of local anesthetic.

The second stage of labor is associated with perineal and vaginal distention mediated by spinal segments S2-S4. Epidural, spinal, and caudal anesthetics are also effective during the second stage of labor. In addition, pudendal nerve blocks can be used for second-stage analgesia.

TABLE 54-1 **Stages of Labor**

| Stage | Begins | Ends | Innervation | Anesthesia |
|---|---|---|---|---|
| First | Regular contractions | Complete cervical dilation | T10-L1 | E, S, C<br>Subarachnoid opioids<br>Paracervical block |
| Second | Complete cervical dilation | Delivery of fetus | S2-S4 | E, S, C<br>Pudendal block |
| Third | Delivery of fetus | Delivery of placenta | | |

Caudal analgesia is rarely used.
*E,* epidural; *S,* spinal; *C,* caudal.

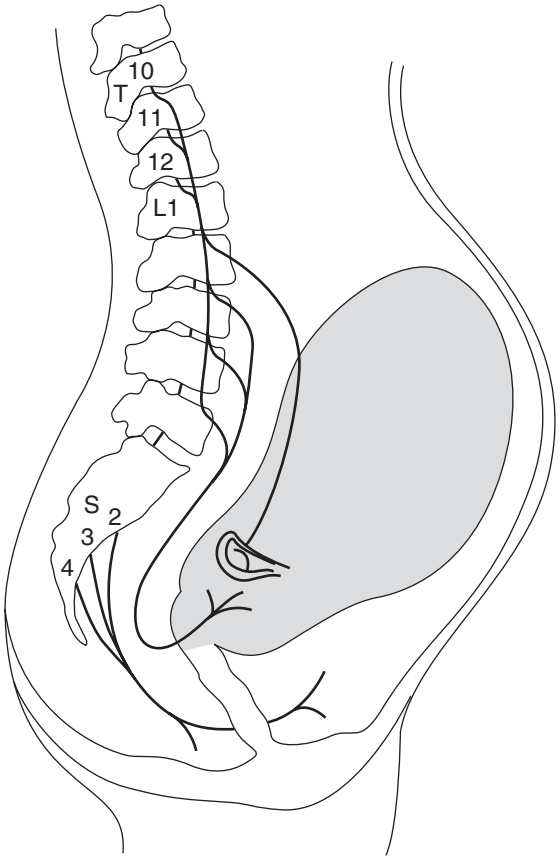


**FIGURE 54-1** ■ Schematic drawing of parturition pain pathways. First-stage labor pain is due to uterine contraction and cervical dilation. Afferent pain fibers from the uterus and cervix accompany sympathetic fibers and enter the spinal cord from T10-L1. Second-stage labor pain originates from the vagina and perineum. Afferent pain fibers from the vagina and perineum course with the pudendal nerves, S2-S4. (From Stoelting RK, Miller RD. Basics of anesthesia, 3rd ed. New York: Churchill Livingstone; 1994. p. 364, with permission.)

Epidural analgesia is the most popular technique for the relief of labor pain. The popularity of epidural analgesia is due to its efficacy. Women can obtain almost complete relief from the pain of labor. From the anesthesiologist's perspective, because a catheter is threaded into the epidural space, it is also a versatile technique. During the earlier stages of labor, dilute solutions of local anesthetic can be used to achieve analgesia. As labor progresses, a more concentrated solution of local anesthetic may be necessary or an adjunct, such as an opioid, may be needed. Additionally, the epidural catheter can be used to maintain a low dermatomal level of anesthesia for labor (T10-L1) and, when needed, the dermatomal level can be raised to T4 for cesarean section.

Patient-controlled epidural analgesia (PCEA) is a technique that allows the patient to self-administer medication, controlling her own analgesia. Compared with continuous infusion or intermittent bolus techniques, PCEA is associated with lower total dose of local anesthetic, less motor blockade, fewer interventions by anesthesiologists, and greater patient satisfaction. We routinely use PCEA for all our patients.

A commonly used PCEA regimen is bupivacaine 0.0625% and fentanyl 2 μg/mL with the following PCEA settings: basal rate of 10 mL per hour, bolus dose of 5 mL, 10-minute lockout, and maximum of four bolus injections per hour. Theoretical risks of PCEA, such as high dermatomal levels or overdose, have been described in patients undergoing general surgery. Overdose occurs because of catheter migration into the subarachnoid space or from excessive administration by the patient or a family member. To date, these complications have not been reported in the parturient during labor.

Many disadvantages associated with labor epidural analgesia have prompted the search for alternative techniques. One disadvantage is the time it takes to provide analgesia to the patient. The time from epidural catheter placement until the patient is comfortable varies but depending on the local anesthetic used can be 15–30 minutes. Other disadvantages of labor epidural analgesia include maternal hypotension, inadequate analgesia (15%–20% of cases), and motor blockade, even with the very dilute local anesthetic solutions.

Subarachnoid opioids offer rapid, intense analgesia with minimal changes in blood pressure or motor function. Most patients can ambulate with this technique. The opioid is usually administered as part of a CSE technique where a spinal and an epidural are performed at the same time. After locating the epidural space in the usual manner, a long small-gauge spinal needle is inserted through the epidural needle into the subarachnoid space. An opioid (usually fentanyl 25 mcg or sufentanil 5 mcg), either alone or in combination with a local anesthetic, is administered through the spinal needle. The spinal needle is removed, and an epidural catheter is inserted for future use. Analgesia begins within 3–5 minutes and lasts 1–1.5 hours (Table 54-2).

TABLE 54-2 **Advantages and Disadvantages of Spinal versus Epidural Anesthesia**

| | Spinal | Epidural |
|---|---|---|
| **Advantages** | Reliable and rapid onset | Better control of spread<br>Mitigates precipitous decrease in blood pressure<br>Unlimited duration |
| **Disadvantages** | Potential for hypotension<br>Inability to control spread<br>Limited duration<br>Postdural puncture headache | Prolonged time to achieve adequate surgical anesthesia<br>Local anesthetic toxicity |

There are several advantages to the CSE technique. The primary advantage is the rapid (3–5 minutes) onset of analgesia. There is also less motor blockade, and there may be less hypotension because the spinal component is primarily with an opioid. Most concerns associated with CSE are only theoretical. There is no increased risk of subarachnoid catheter migration of the epidural catheter. Metallic particles are not produced as a result of passing one needle through another. The incidence of postdural puncture headache (PDPH) is not increased by the intentional dural puncture. Fetal bradycardia in association with a hypertonic uterus may occur immediately or shortly after administration of the spinal medication. There does not appear to be any difference in the incidence of fetal heart rate decelerations or emergent cesarean delivery after labor epidural or spinal anesthesia. One proposed theory for increased uterine tone after CSE is related to the rapid decrease in maternal catecholamines associated with the rapid onset of pain relief. The decrease in circulating β-adrenergic agonists results in a predominance of α-adrenergic activity, which causes uterine contractions. If this should occur, treatment is with subcutaneous terbutaline or intravenous nitroglycerin.

## 3. What is a "walking epidural"?

The term "walking epidural" has become popular, especially in the lay community. This term refers to any epidural or spinal technique that allows the parturient to ambulate during labor. Some initial retrospective data suggested that ambulating or the upright position is associated with a shorter first stage of labor, less pain in early labor, and decreased analgesia requirements. However, prospective and randomized studies have not been able to document any medical benefit of ambulating, in terms of either duration of labor or mode of delivery.

Even if the patient does not want to ambulate, using a technique that produces minimal motor blockade improves maternal satisfaction. Minimal motor block may also improve obstetric outcome in terms of mode of delivery. The incidence of operative vaginal delivery may be lower when dilute local anesthetics are used. Both epidural analgesia using dilute local anesthetic and opioid solutions and a CSE technique can achieve this goal. However, several precautions should be taken before allowing a parturient to walk after receiving epidural or CSE analgesia. First, it should be determined whether she is a candidate for intermittent fetal heart rate monitoring. Blood pressure and fetal heart rate should be monitored for 30–60 minutes after induction of analgesia and reassessed at least every 30 minutes thereafter. Because even small doses of subarachnoid and epidural local anesthetics can produce motor deficits, motor function should be assessed. This assessment is accomplished by asking the parturient to perform a modified deep knee bend or step up and down on a stool. She must have an escort at all times.

## 4. Describe neuraxial anesthetic techniques that can be employed for cesarean delivery.

Neuraxial anesthetic techniques include spinal, epidural, and CSE anesthesia. During neuraxial anesthesia, the mother remains awake during the delivery, significantly decreasing the risk of maternal aspiration associated with general anesthesia. Neuraxial anesthesia also minimizes the potential for depression of the neonate from maternal drug administration. Because neuraxial anesthesia is safer than general anesthesia for both the mother and the fetus, it should be used for all elective cesarean deliveries unless there are specific contraindications.

Few absolute contraindications exist to neuraxial anesthesia. Absolute contraindications include infection at the injection site, severe hypovolemia, increased intracranial pressure, patient refusal, and coagulation abnormalities. Relative contraindications include neurologic disease such as multiple sclerosis, history of back surgery or back pain, and systemic infection (Box 54-1).

Spinal anesthesia provides reliable and rapid anesthesia. In certain urgent situations, spinal anesthesia can be used in place of general anesthesia. Disadvantages of spinal anesthesia include a potential for hypotension, inability to control the spread of anesthesia, limited duration, and possibility of PDPH.

Continuous epidural anesthesia allows for multiple repeat doses of local anesthetic, which offers better control over anesthetic spread, mitigates against precipitous decreases in blood pressure, and allows almost unlimited duration of anesthesia. Epidural anesthesia can be used for both labor and cesarean delivery. Compared with spinal anesthesia, the major disadvantages of epidural anesthesia are the time required to place a needle or catheter and the potential for local anesthetic toxicity.

The CSE technique can also be used for cesarean delivery. It has the advantages of a spinal: The anesthetic is reliable with quick onset. It has the advantages of an epidural: The resultant block can be prolonged with repeated doses (Box 54-2).

**BOX 54-1 Advantages and Contraindications to Neuraxial Anesthesia for Cesarean Delivery**

**Advantages**

- Decreased risk of maternal aspiration
- Minimizes neonatal depression from maternal drug administration

**Absolute Contraindications**

- Infection at site
- Severe hypovolemia
- Increased intracranial pressure
- Patient refusal
- Coagulation abnormalities

**Relative Contraindications**

- Neurologic disease (e.g., multiple sclerosis)
- History of back surgery
- History of back pain
- Systemic infection

**BOX 54-2 Suggested Technique for Performing Neuraxial Anesthesia for Cesarean Delivery**

1. Check anesthesia machine. Prepare resuscitative equipment and drugs including endotracheal tubes of different sizes, laryngoscopes, airways, suction, induction agent (propofol, etomidate, or ketamine), succinylcholine, ephedrine, and phenylephrine.
2. Transport to the operating room with left uterine displacement.
3. Administer a nonparticulate antacid by mouth.
4. Place standard American Society of Anesthesiologists monitors including blood pressure cuff, electrocardiogram, and pulse oximeter. Administer oxygen via nasal cannula or facemask.
5. *Epidural:* After placing an epidural catheter, administer 3 mL of 2% lidocaine as a test dose. Wait 5 minutes, observing for signs of either intravascular or subarachnoid injection. After confirming catheter position, inject 2% lidocaine with epinephrine 1:200,000, 3% chloroprocaine, or 0.5% bupivacaine in aliquots of 5 mL, no more frequently than every 5 minutes until a T4 level of anesthesia is achieved. After delivery of the infant, administer preservative-free morphine sulfate 3–4 mg for postoperative analgesia.
6. *Spinal:* Use a small-gauge pencil-point spinal needle. Administer 1.5 mL of 0.75% hyperbaric bupivacaine with preservative-free morphine sulfate 0.1–0.25 mg for postoperative analgesia
7. Monitor vital signs every 1–2 minutes for the first 15 minutes and then every 5 minutes thereafter, if stable.
8. If hypotension occurs, administer 250–500 mL boluses of crystalloid and ephedrine in 5-mg or phenylephrine in 50-μg increments, until blood pressure returns to normal.

### 5. Outline treatment for postdural puncture headache.

PDPH can occur any time the dura is punctured. Persistent cerebrospinal fluid leak decreases the amount of liquid available to cushion the brain. In the absence of an adequate fluid buffer, the brain shifts within the calvaria, placing tension on pain-sensitive blood vessels. Risk factors for PDPH include increasing size of needle, type of needle (risk is lower with pencil-point needles), bevel positioned perpendicular to dural fibers (for non–pencil-point needles), female gender, pregnancy, and increasing number of attempts.

PDPHs are classically located over the occipital or frontal regions. They are frequently accompanied by neck tension, tinnitus, diplopia, photophobia, nausea, and vomiting. An important diagnostic feature of a PDPH is exacerbation with postural changes—worse in the sitting or erect position and better in the supine position.

Treatment is divided into noninvasive and invasive measures. Noninvasive therapy includes analgesics, hydration, and caffeine. Invasive therapy involves placing an epidural blood patch; this is accomplished by sterilely injecting 20 mL of autologous blood into the epidural space. The overall success rate is 70%–75%. A second blood patch is occasionally needed. Prophylactic blood patching, injecting blood through an existing epidural catheter after labor and before its removal, has been considered, but more recent data suggest it is not beneficial.

### 6. What are the advantages and disadvantages of general anesthesia for cesarean delivery?

The major advantages of general anesthesia over neuraxial anesthesia are the shorter preoperative preparatory time and the absence of a sympathectomy. The disadvantages of general anesthesia include the need to intubate the trachea, possibility of maternal aspiration, and neonatal depression. In addition, general anesthesia precludes immediate maternal bonding.

Tracheal intubation can be more difficult in the parturient than in the general population. Airway difficulty is the leading cause of maternal morbidity and mortality. Care must be taken both at the initiation of general anesthesia and when the mother awakens because airway catastrophes can occur at that point as well.

Aspiration pneumonia is an important cause of morbidity and mortality in the parturient undergoing general anesthesia, and general anesthesia should be reserved for emergent situations. Before induction of general anesthesia, a careful evaluation of the airway should be performed, and a nonparticulate antacid should be administered. Antacids increase gastric pH resulting in a decreased incidence and severity of pneumonitis should aspiration occur. Defasciculating doses of nondepolarizing muscle relaxants are avoided before induction because they may produce weakness predisposing to aspiration and may delay the onset time of succinylcholine.

After preoxygenation, induction of anesthesia can proceed with essentially any of the available induction agents and application of cricoid pressure. Propofol is often chosen

for patients who are hemodynamically stable, whereas ketamine or etomidate is frequently selected when there is hemodynamic instability or severe bronchospasm.

Muscle relaxation for endotracheal intubation is achieved with succinylcholine because it provides the most rapid onset among relaxants currently available. Duration of action of succinylcholine may be prolonged because of decreased levels of pseudocholinesterase compared with the nonpregnant state. The extended duration of action generally does not exceed 15 minutes and is clinically insignificant. Muscle relaxants do not cross the placenta because they are highly ionized and have a large molecular weight.

Anesthesia is maintained with 50% nitrous oxide in oxygen and any of the potent inhaled agents. Nitrous oxide does cross the placenta, but it does not cause significant fetal depression owing to fetal tissue uptake if the induction to delivery time is <20 minutes. Sub-minimum alveolar concentrations of potent inhaled anesthetic agents administered before delivery protect from maternal recall without causing fetal depression or uterine relaxation. After delivery of the fetus, nitrous oxide concentrations are increased, and opioids are administered to supplement the anesthetic.

Extubation of the trachea follows classic full stomach precautions. Residual muscle relaxation is antagonized with an anticholinesterase and vagolytic agents, and the patient must be fully awake (Box 54-3).

**BOX 54-3 Suggested Method of Performing General Anesthesia for Cesarean Delivery**

1. Check anesthesia machine. Prepare resuscitative equipment and drugs including endotracheal tubes of different sizes, laryngoscopes, airways, suction, induction agent (propofol, etomidate, or ketamine), succinylcholine, ephedrine, and phenylephrine.
2. Transport to the operating room with left uterine displacement.
3. Administer a nonparticulate antacid by mouth.
4. Place standard American Society of Anesthesiologists monitors including blood pressure cuff, electrocardiogram, pulse oximeter, and end-tidal carbon dioxide.
5. After denitrogenation with 100% oxygen for 3–5 minutes, induce anesthesia with propofol 1–2 mg/kg, etomidate 0.2–0.3 mg/kg, or ketamine 1–2 mg/kg followed by succinylcholine 100 mg, and apply cricoid pressure. Do *not* use a defasciculating dose of a nondepolarizing agent.
6. Maintain anesthesia with 50% nitrous oxide in oxygen and sub-minimum alveolar concentrations of potent inhaled anesthetics until the infant is delivered.
7. After delivery of the infant, administer fentanyl 100 μg and increase nitrous oxide concentration to 70%. Keep concentration of halogenated agents <0.5 minimum alveolar concentration to avoid uterine relaxation.
8. At completion of procedure, administer neostigmine 0.07 mg/kg and glycopyrrolate 0.01 mg/kg to antagonize residual neuromuscular blockade.
9. Extubate trachea when the patient is fully awake.

## 7. Describe the elements of placental drug transfer.

Placental drug transfer occurs by diffusion. Fick equation describes the factors governing transfer of drugs across the placenta.

$$Qd = Kd \bullet A \bullet [Pd(m) - Pd(f)]/b$$

where:

Qd = quantity of drug transferred per unit time
Kd = diffusion constant for the drug
A = surface area of the placenta
Pd(m) = mean drug concentration of maternal blood in the intervillous space
Pd(f) = mean drug concentration of fetal blood in the intervillous space
b = thickness of the placenta.

Factors over which the anesthesiologist has control are limited to the specific drug administered and the amount used. Other factors, such as the surface area and thickness of the placenta, are not under the control of the anesthesiologist. To minimize the amount of drug reaching the placenta, the quantity of maternally administered drug needs to be reduced.

Diffusion constants, which vary from one drug to another, are determined by four main properties: molecular weight, lipid solubility, protein binding, and electrical charge. Placental transfer of drug is facilitated by a molecular weight of <500, high lipid solubility, minimal maternal protein binding, and a low degree of ionization. Fentanyl, a nonionized, highly lipid-soluble molecule with a low molecular weight, easily crosses the placenta. In contrast, succinylcholine, a highly ionized molecule, does not readily cross the placenta.

## 8. What techniques can be used for pain relief after cesarean delivery?

Intravenous, intramuscular, and neuraxial opioids can be administered for pain relief after cesarean delivery. Women who receive epidural morphine sulfate complain of less pain than women who receive intravenous or intramuscular morphine sulfate. Morphine sulfate in either the subarachnoid or the epidural space provides analgesia for up to 24 hours. The dose of epidural morphine is 3–4 mg, and the dose of subarachnoid morphine is 0.1–0.25 mg.

## 9. What is the differential diagnosis of postpartum hemorrhage?

The most common cause of postpartum hemorrhage is uterine atony, which occurs in 2%–5% of all deliveries. Other causes of postpartum hemorrhage include retained placenta, placenta accreta, cervical and vaginal lacerations, inverted uterus, and conditions associated with coagulopathy such as amniotic fluid embolism and preeclampsia. Treatment of postpartum hemorrhage depends on the etiology. Coagulopathies often respond to treating the underlying cause (Box 54-4).

**BOX 54-4 Differential Diagnosis of Postpartum Bleeding**

- Uterine atony
- Retained products of conception
- Placenta accreta, increta, percreta
- Cervical and vaginal lacerations
- Inverted uterus
- Coagulopathy
- Preeclampsia
- Amniotic fluid embolus

## 10. Explain the risk factors, presentation, and treatment of uterine atony.

Any condition associated with overdistention of the uterus, such as multiple births, polyhydramnios, or a large fetus, is a risk factor for uterine atony. Other risk factors include multiparity, retained placenta, prolonged labor, previous tocolysis, β agonists, prolonged general anesthesia with potent inhaled anesthetic agents, ruptured uterus, and chorioamnionitis.

Uterine atony manifests as continued painless vaginal bleeding after delivery. The noncontracting uterus appears boggy and large. Obstetric management is aimed at increasing myometrial tone. Massaging the uterus through the abdominal wall or directly via the vagina is initially attempted to induce contractions. If massaging does not work, oxytocin, ergot derivatives, and prostaglandin $F_{2\alpha}$ should be administered.

Anesthetic management is initially aimed at maternal resuscitation. Intravascular volume is restored with crystalloid, colloid, or blood. Massive blood loss may lead to shock. Coagulation factor replacement may be required. Vaginal examination and suturing in attempts to stop the bleeding require anesthesia; however, conduction techniques should be used with caution in the face of hypovolemia. Intravenous sedation with small amounts of fentanyl, ketamine, or midazolam may suffice. If sedation is inadequate, a rapid-sequence induction of general anesthesia with endotracheal intubation is required to reduce the risk of maternal aspiration.

Continued hemorrhage may require hypogastric artery ligation or hysterectomy, which usually necessitates general anesthesia. Anesthetic management for these procedures is the same as for placenta previa (see Chapter 56). Pelvic artery embolization, usually performed in the radiology suite, can sometimes reduce the bleeding and prevent the need for a hysterectomy. Although general anesthesia is not required, maternal fluid resuscitation must continue during embolization. Frequent monitoring of vital signs is necessary, and resuscitative equipment must be available.

Successful intraoperative cell salvage (cell saver) has been reported in obstetrics. The major concern with its use is the potential for amniotic fluid embolism. Recommendations for cell salvage include discarding all surgical field fluids before collecting blood with the cell saver. Use of this technique should be reserved for situations in which there is no other blood available or the patient refuses autologous blood transfusion (e.g., Jehovah's witness).

## 11. Describe the presentation and treatment of retained placenta.

Retained placenta occurs with an incidence of about 1 in 300 deliveries and is characterized by painless vaginal bleeding after delivery. Treatment goals focus on manually removing the placenta, which prevents uterine contractions. Dilation and curettage may be required to evacuate the uterus.

Abnormal implantation in the uterus, such as placenta accreta, placenta increta, or placenta percreta, may make removal of the placenta impossible. Hysterectomy, hypogastric artery ligation, or arterial embolization may be lifesaving procedures.

For the anesthesiologist, maternal resuscitation is the first priority. Intravenous sedation usually suffices for evacuation of the uterus. Hysterectomy or hypogastric artery ligation generally requires general anesthesia. Management of general anesthesia is this situation is similar to general anesthesia management described earlier.

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CASE 55

# PREECLAMPSIA

Yaakov Beilin, MD

## QUESTIONS

1. Classify the hypertensive disorders of pregnancy.
2. What are the incidence and risk factors of preeclampsia?
3. Explain the etiology of preeclampsia.
4. Describe the pathophysiology of preeclampsia.
5. What is the obstetric management of preeclampsia?
6. How is preeclampsia prevented from degenerating into eclampsia?
7. How is preeclampsia-related hypertension managed?
8. What are the potential consequences of epidural analgesia in a patient with preeclampsia?
9. What are the anesthetic options for cesarean delivery for a patient with preeclampsia?
10. Outline the anticipated postpartum problems associated with preeclampsia.

A 15-year-old nulliparous patient presented to the labor and delivery suite in week 35 of her pregnancy. Her chief complaint was headache. Her blood pressure was 145/95 mm Hg, and she appeared edematous.

### 1. Classify the hypertensive disorders of pregnancy.

The hypertensive disorders of pregnancy are classified into four groups: chronic hypertension, preeclampsia-eclampsia, chronic hypertension with superimposed preeclampsia, and gestational hypertension (Box 55-1).

Hypertension is defined as:

- Systolic blood pressure: >140 mm Hg or 30 mm Hg above baseline
- Diastolic blood pressure: >90 mm Hg or 15 mm Hg above baseline

Blood pressures should be measured at rest with left uterine displacement and should be reproducible at least 6 hours later.

Chronic hypertension is diagnosed when the blood pressure is elevated before week 20 of pregnancy. Because blood pressure normally decreases during pregnancy, any parturient with a diastolic blood pressure >80 mm Hg is suspected to have chronic hypertension.

**BOX 55-1 Classification of Hypertensive Disorders in Pregnancy**

- Chronic hypertension
  - Manifests before week 20 of gestation
- Preeclampsia-eclampsia
  - Manifests after week 20 of gestation
  - Associated with proteinuria
- Chronic hypertension with superimposed preeclampsia
- Gestational hypertension
  - Manifests after week 20 of gestation without associated symptoms

Preeclampsia-eclampsia is a hypertensive disorder unique to pregnancy. Preeclampsia is hypertension associated with proteinuria. Edema no longer has to be present to make the diagnosis. Except in association with hydatidiform mole, preeclamptic hypertension does not manifest before 20 weeks of gestation. Proteinuria is defined as the excretion of >0.3 g of protein in a 24-hour urine collection or 1+ on dipstick analysis. Preeclampsia is classified as either mild or severe depending on the degree of hypertension, extent of proteinuria, or patient complaints. Preeclampsia degenerates into eclampsia when generalized seizures occur (Table 55-1).

Gestational hypertension is defined as hypertension occurring after 20 weeks of pregnancy in the absence of other signs of preeclampsia. Gestational hypertension is frequently essential hypertension that is unmasked by pregnancy.

### 2. What are the incidence and risk factors of preeclampsia?

Preeclampsia occurs in approximately 5%–10% of pregnancies, and eclampsia occurs in 0.2%–0.7% of pregnancies. A primigravida, at both extremes of age, with poor prenatal care is at highest risk for preeclampsia. Other risk factors include the use of barrier contraception, obesity, chronic renal failure, and hypertension. Women with antiphospholipid syndrome are also at risk. Preeclampsia is associated with rapid uterine enlargement such as occurs with hydatidiform mole, diabetes mellitus, and multiple gestations. There is a 33% probability of preeclampsia recurring with subsequent pregnancies.

### 3. Explain the etiology of preeclampsia.

Although the etiology of preeclampsia is unknown, uteroplacental ischemia appears to be a common factor. Beer (1978) suggested that uteroplacental ischemia may result

TABLE 55-1 **Signs and Symptoms of Preeclampsia**

| | Mild Preeclampsia | Severe Preeclampsia |
|---|---|---|
| Hypertension | | |
| Systolic pressure | >140 mm Hg<br>>30 mm Hg above baseline | >160 mm Hg |
| Diastolic pressure | >90 mm Hg<br>>15 mm Hg above baseline | >110 mm Hg |
| Proteinuria | 1–2 + by dipstick<br>>1 g/24 hours | 3–4 + by dipstick<br>>5 g/24 hours |
| Patient symptoms | | Headache<br>Visual disturbances<br>Epigastric pain<br>Cyanosis |

from altered immunity such as graft-versus-host reaction. It is also possible that placental prostaglandin imbalance between thromboxane and prostacyclin leads to preeclampsia. In a normal pregnancy, prostacyclin and thromboxane are produced in equal amounts by the placenta. In a pregnancy complicated by preeclampsia, there is a relative increase in thromboxane production. Thromboxane causes increased vasoconstriction, platelet aggregation, and uterine activity and a simultaneous decrease in uteroplacental blood flow. These effects are observed in preeclampsia.

Uteroplacental ischemia leads to the production of substances similar to renin and thromboplastin. Renin causes release of angiotensin and aldosterone, which result in hypertension and edema. Thromboplastin can initiate coagulopathies such as disseminated intravascular coagulation (DIC).

## 4. Describe the pathophysiology of preeclampsia.

The hallmark of preeclampsia is vasospasm that occurs secondary to increased circulating levels of renin, aldosterone, angiotensin, and catecholamines. Aldosterone also causes sodium and water retention, which leads to generalized edema. Because almost every organ system is affected in a parturient with preeclampsia, it is best to take a systematic approach when discussing the changes seen in preeclampsia (Box 55-2).

**BOX 55-2 Pathophysiologic Changes in Preeclampsia**

**Central Nervous System**
- Cerebral edema and vasospasm
  - Headache
  - Hyperreflexia
  - Blurry vision
  - Blindness
  - Seizures
  - Coma
- Cerebral hemorrhage

**Pulmonary System**
- Upper airway and laryngeal edema
  - Difficult tracheal intubation
- Predisposition to upper respiratory infections
- Pulmonary capillary leak
  - Increased A-a gradient

**Cardiovascular System**
- Vasoconstriction
  - Hypertension
  - Impaired tissue perfusion
  - Cellular hypoxia
  - Increased cardiac work
- Fluid translocation
  - Generalized edema
  - Hypovolemia
  - Hemoconcentration
- Increased blood viscosity
- Left ventricular hypertrophy and dysfunction

**Renal System**
- Decreased renal blood flow
- Decreased glomerular filtration rate
- Decreased creatinine clearance
- Proteinuria
- Increased uric acid levels correlate with severity of disease

**Hepatic System**
- Periportal hemorrhage
- Subcapsular hematomas
- Abnormal liver function tests

**Hematologic System**
- Decreased platelet count
- Qualitative platelet abnormality
- Abnormal coagulation profile
- Disseminated intravascular coagulation
- HELLP*syndrome

**Uteroplacental System**
- Decrease in intervillous blood flow
- Premature labor
- Small placenta
- Uterine hyperactivity
- Uterine sensitivity to oxytocin
- Placental abruption

*Hemolysis, elevated liver function tests, and low platelet count.

### Central Nervous System

The central nervous system effects of preeclampsia include cerebral edema and cerebral vasospasm. Intracranial pressure increases in some cases, but cerebral blood flow and oxygen consumption remain normal. Clinical findings related to central nervous system changes include headache, hyperreflexia, blurred vision, vertigo, blindness, seizures, and coma. Cerebral hemorrhage is the leading cause of death in patients with preeclampsia.

### Pulmonary System

Tracheal intubation may be difficult secondary to laryngeal and upper airway edema. Increased secretions and airway congestion predispose the mother to upper airway infections. Pulmonary capillary leak into the interstitium accounts for intrapulmonary shunting and a deteriorating alveolar-arterial (A-a) oxygen gradient.

### Cardiovascular System

Generalized vasoconstriction produces hypertension, impaired tissue perfusion, and cellular hypoxia. Translocated fluid from the vascular compartment to the interstitium leads to generalized edema, hypovolemia, and hemoconcentration. An inverse relationship exists between the intravascular volume and the degree of hypertension. Hemoconcentration leads to increased blood viscosity, which exacerbates tissue hypoxia further. Although hematocrit is typically elevated, a relative anemia usually exists, and blood loss is poorly tolerated. Vasospasm leads to an increase in systemic vascular resistance, which increases cardiac work. The already hyperdynamic cardiovascular system becomes stressed further, and cardiac output increases. Over time, left ventricular hypertrophy occurs leading to left ventricular dysfunction.

### Renal System

Renal blood flow is reduced leading to a decrease in the glomerular filtration rate and creatinine clearance. Almost all renal function tests are impaired. An increasing uric acid level correlates with the severity of disease. Damaged glomeruli allow for renal loss of proteins.

### Hepatic System

Vasospasm leads to hepatic periportal hemorrhages and hepatocellular damage. Swelling of the liver capsule from subcapsular hematomas may produce abdominal pain. Hepatic rupture has been reported in severe cases. Elevated liver enzymes occur with deteriorating hepatic function.

### Hematologic System

Coagulation abnormalities also occur. The most common finding is thrombocytopenia, which can occur with or without other coagulopathies. A syndrome of hemolysis, elevated liver function tests, and low platelet count (HELLP) has been described. A qualitative platelet abnormality also frequently is present even without a quantitative problem. Prothrombin time, thrombin time, and partial thromboplastin time can also be elevated. Fibrinogen levels can decrease, and frank DIC can occur.

### Uteroplacental System

Intervillous blood flow is decreased twofold to threefold and is a major contributing factor of fetal morbidity and mortality. The incidence of premature labor is increased because of placental hypoperfusion. Because of decreased uteroplacental blood flow, the placenta is often small and shows signs of premature aging. The uterus is also hyperactive and markedly sensitive to oxytocin. A parturient with preeclampsia is at an increased risk for placental abruption.

## 5. What is the obstetric management of preeclampsia?

Obstetric management of a patient with preeclampsia is aimed at controlling the disease and preventing progression to eclampsia. The patient should be on complete bed rest with left uterine displacement. Serial determinations of blood pressure, weight gain, renal and coagulation function, and central nervous system irritability should be done. Oral fluid and sodium intake should not be restricted. The routine use of diuretics to control edema is no longer recommended. Fetal well-being should be monitored via a nonstress test, oxytocin challenge, or biophysical profile. Delivery of the fetus and placenta is considered the definitive treatment of preeclampsia and should be done for either fetal or maternal reasons. Fetal indications include evidence of fetal distress or cessation of fetal maturation. Maternal indications include worsening preeclampsia.

## 6. How is preeclampsia prevented from degenerating into eclampsia?

Magnesium sulfate ($MgSO_4$), a central nervous system depressant and anticonvulsant, is the first-line drug for the prevention of eclampsia. One of the many sites of action of $MgSO_4$ is at the myoneural junction. The decrease in hyperreflexia seen with the administration of $MgSO_4$ is due to the inhibition of acetylcholine release at the neuromuscular junction, decreased sensitivity of the motor end plate to acetylcholine, and decreased excitability of the muscle membrane. $MgSO_4$ is also a mild vasodilator and decreases uterine hyperactivity, which results in an increase in uterine blood flow. It also causes vasodilation at the renal and liver beds improving their function (Box 55-3).

**BOX 55-3 Magnesium Sulfate Properties**

- Central nervous system depressant
- Anticonvulsant
- Myoneural junction
  - Inhibits release of acetylcholine
  - Decreases acetylcholine sensitivity of motor end plate
  - Decreases excitability of muscle membrane
- Mild vasodilator
- Decreases uterine hyperactivity
- Crosses placenta
- Toxicity treated with calcium administration

The range of therapeutic levels of magnesium is 4–8 mEq/L. Above this level, magnesium has both maternal and neonatal side effects. Magnesium can lead to electrocardiogram (ECG) changes and ultimately cardiac and respiratory arrest. However, these severe side effects do not occur until after the loss of deep tendon reflexes (Table 55-2). Cardiac and respiratory side effects may be avoided by monitoring serum magnesium levels and deep tendon reflexes. Because of its actions at the neuromuscular junction, magnesium increases the sensitivity of the mother to both depolarizing and nondepolarizing muscle relaxants.

Because magnesium crosses the placenta, the neonate can also exhibit signs of magnesium toxicity. Signs of magnesium toxicity in the newborn include respiratory depression, apnea, and decreased muscle tone. Magnesium toxicity in the newborn and the mother can be reversed with the administration of calcium.

$MgSO_4$ is administered intravenously with a loading dose of 2–4 g over 15 minutes followed by an infusion of 1–3 g per hour. $MgSO_4$ is primarily excreted by the kidneys. Renal function must be carefully monitored, and the magnesium dose is decreased accordingly when renal insufficiency is present.

## 7. How is preeclampsia-related hypertension managed?

Control of hypertension in a parturient with preeclampsia is imperative because acute elevations of blood pressure can lead to cerebral hemorrhage, the leading cause of mortality. The patient's blood pressure should be neither acutely decreased nor decreased to levels considered normal for other parturients because a low blood pressure could compromise uteroplacental blood flow. Although $MgSO_4$ causes vasodilation, it does not treat hypertension adequately, and an alternative antihypertensive drug is usually needed. Also, as in any patient with hypertension, responses to both antihypertensive and pressor agents are exaggerated. Reduced doses of these agents should be used initially and the response noted before increasing the dose.

The most frequently used antihypertensive agent is hydralazine, which not only decreases blood pressure but also increases renal and uteroplacental blood flow. The tachycardia that occurs with the use of hydralazine can be treated with a β blocker. Hydralazine is not the agent of choice in the acute situation because it takes 10–20 minutes before an effect is seen.

Nitroprusside, a potent arterial vasodilator, is often used when immediate control of blood pressure is required. It is administered by infusion making it easy to titrate to effect. However, nitroprusside crosses the placenta, and cyanide toxicity has been described in the neonate after prolonged infusion in the mother. Trimethaphan, a ganglionic blocker, has also been used with good success in the emergent situation.

Nitroglycerin, a venous dilator, is useful when tight control of blood pressure is required for prolonged periods. Nitroglycerin is not as potent as nitroprusside, but it is easy to titrate and has minimal effect on the fetus.

Propranolol, diazoxide, and methyldopa are generally not used in patients with preeclampsia because of their adverse side effects (Table 55-3).

TABLE 55-2 **Effects of Magnesium at Different Plasma Levels**

| Magnesium Plasma Levels (mEq/L) | Systemic Effects |
|---|---|
| 1.5–2 | Normal plasma levels |
| 4–8 | Therapeutic range |
| 5–10 | ECG changes—prolonged P–R interval, widened QRS |
| 10 | Decreased deep tendon reflexes<br>Respiratory depression |
| 15 | Respiratory arrest<br>Sinoatrial and atrioventricular conduction defects |
| 25 | Cardiac arrest |

## 8. What are the potential consequences of epidural analgesia in a patient with preeclampsia?

Epidural anesthesia can be beneficial for a patient with preeclampsia. Decreasing or eliminating the sensation of pain reduces hyperventilation, decreases catecholamine release, decreases anxiety, and increases uteroplacental blood flow. A neuraxial anesthetic also obviates the need for a general anesthetic in case of cesarean delivery with its inherent risk of aspiration. However, before inserting the epidural catheter, the blood pressure must be controlled, the intravascular volume must be repleted, and the coagulation profile must be normal.

The diastolic blood pressure should be <110 mm Hg before beginning a neuraxial anesthetic. Frequent blood pressure measurements are needed during the anesthetic. An arterial line may be necessary if the blood pressure is labile.

A parturient with hypertensive disease may be fluid-depleted. Urine output is monitored to guide fluid administration. If urine output is diminished, a fluid challenge of 500–1000 mL of an isotonic crystalloid should be given depending on the clinical scenario. If urine output does not increase, central venous pressure monitoring or transthoracic echocardiography should be considered.

Platelet consumption is a component of preeclampsia that can lead to coagulation factor consumption and DIC. A platelet count and coagulation profile must be checked before administering the anesthetic. Generally, the platelet count decreases before other indices of coagulation are prolonged. It is acceptable to check the platelet count first and, if it is <100,000 $mm^{-3}$, then to check the prothrombin time, partial thromboplastin time, and fibrinogen. Because preeclampsia is a dynamic

TABLE 55-3 **Antihypertensive Treatment in Toxemia of Pregnancy**

| Drug | Mechanism of Action | Advantage | Disadvantages |
|---|---|---|---|
| Hydralazine | Vasodilator | Onset of action approximately 10-20 minutes<br>Increased renal blood flow<br>Duration of action approximately 2 hours | Tachycardia |
| Propranolol | β Blocker | Augments antihypertensive action of hydralazine | Fetal bradycardia<br>Fetal hypoglycemia |
| Sodium nitroprusside | Direct smooth muscle relaxation | Onset of action 1 minute<br>Duration of action 1–10 minutes | Fetal cyanide toxicity<br>Increased maternal intracranial pressure |
| Nitroglycerin | Direct smooth muscle relaxation | Onset of action 1–2 minutes<br>Duration of action 10 minutes<br>Improves uterine blood flow | Increased maternal intracranial pressure |
| Methyldopa | $\alpha_2$ Agonist | Good maintenance drug owing to prolonged duration of action | Neonatal tremors |
| Labetalol | α and β Antagonist | As effective as methyldopa for maintenance | Not recommended with bronchoconstrictive disease |
| Diuretics | Sodium and water excretion | Generally not recommended | Hypotension |
| Nifedipine | Calcium-channel blocker | Uterine relaxation<br>Increased renal blood flow | Hypotension in combination with magnesium |
| Clonidine | $\alpha_2$ Agonist | Insufficient data | Fetal hypoxia<br>Increased uterine tone<br>Decreased uterine blood flow in animals<br>Generally not recommended |

process, the coagulation parameters should be checked close to the time of administering the block.

### 9. What are the anesthetic options for cesarean delivery for a patient with preeclampsia?

After the blood pressure is controlled and the fluid status and coagulation parameters are normalized, cesarean delivery can be safely performed under epidural, spinal, or general anesthesia. The benefit of neuraxial anesthesia is avoidance of airway manipulation in a patient at risk for pulmonary aspiration. Also, a parturient with preeclampsia is exquisitely sensitive to blood pressure increases during laryngoscopy. Blood pressure is generally well maintained during both spinal and epidural anesthesia; this author routinely uses spinal anesthesia.

General anesthesia is often required for an emergency cesarean delivery. Even in the presence of fetal distress, time should be taken to control the blood pressure adequately before induction because laryngoscopy may cause a significant increase in blood pressure, which can lead to cerebral hemorrhage. After preoxygenation, a rapid-sequence induction with cricoid pressure is performed. If the patient is receiving $MgSO_4$, succinylcholine and nondepolarizing muscle relaxants may have a prolonged duration of action. However, the dose of succinylcholine should not be reduced because a fast onset of paralysis is needed. A neuromuscular monitor should be used to guide subsequent doses of muscle relaxants. An array of laryngoscopes, endotracheal tubes, laryngeal mask airways, and videolaryngoscopes should be available to deal with a potentially difficult airway.

### 10. Outline the anticipated postpartum problems associated with preeclampsia.

Although delivery of the fetus and placenta are considered the definitive treatment for preeclampsia, it can take hours to days for the symptoms to resolve completely. The patient is still at risk for convulsions. The blood pressure should be monitored and the $MgSO_4$ infusion should be continued for at least 24 hours after delivery.

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CASE 56

# Abruptio Placentae and Placenta Previa

Howard H. Bernstein, MD • Yaakov Beilin, MD

## QUESTIONS

1. What are the major causes of third-trimester bleeding?
2. What is abruptio placentae, and what are the risk factors for this condition?
3. What are the manifesting signs and symptoms of abruptio placentae, and how is the diagnosis made?
4. Describe the obstetric management of abruptio placentae.
5. Describe the effects of pregnancy on coagulation.
6. What is disseminated intravascular coagulopathy, and how is it managed?
7. How is fetal distress diagnosed?
8. The patient is given a trial of labor, and the obstetrician requests a consultation for labor analgesia. What are your concerns, and how would you proceed?
9. The obstetrician notes 3 hours into labor a significant increase in vaginal bleeding and a decrease in maternal blood pressure to 80/40 mm Hg with a pulse of 120 beats per minute. Fetal tachycardia with late decelerations and absent variability are noted on the fetal heart rate monitor. Assuming the patient has not yet received an epidural for regional analgesia, how would you anesthetize this patient for an emergency cesarean delivery?
10. What is placenta previa?
11. Describe the clinical presentation of placenta previa, and explain how the diagnosis is made.
12. Discuss the obstetric management of placenta previa.
13. How would you anesthetize a patient with placenta previa for cesarean delivery?
14. How would you manage massive obstetric hemorrhage?

A 25-year-old woman at 37 weeks gestation presents to the labor floor complaining of abdominal pain accompanied by vaginal bleeding. Her blood pressure on admission is 110/60 mm Hg with a pulse of 90 beats per minute. She is contracting every 5 minutes and her cervix is 3 cm dilated. Fetal heart rate (FHR) monitoring demonstrates a category I tracing.

### 1. What are the major causes of third-trimester bleeding?

A "bloody show" is the most common cause of bleeding during the third trimester. This bleeding occurs during labor and is due to effacement and dilation of the cervix. Placental problems are responsible for most pathologic bleeding in the third trimester, and placental abruption and placenta previa are the most common placental problems. Cervical bleeding secondary to polyps and carcinoma is much less common. Vasa previa, umbilical cord vessels traveling within the placental membranes and covering the cervical os, is a rare cause of third-trimester bleeding. Other rare causes of third-trimester bleeding are maternal coagulopathy, owing to preeclampsia, and intrauterine fetal demise (Box 56-1).

### 2. What is abruptio placentae, and what are the risk factors for this condition?

Abruptio placentae refers to premature separation of the placenta (i.e., before delivery of the fetus). It occurs in about 1 in 100 to 1 in 150 deliveries and carries a perinatal mortality rate of approximately 20%. The incidence of abruption increases with age and is more common in African American women. Abruption is associated with chronic or pregnancy-induced hypertension, multiparity, cigarette smoking, and cocaine abuse. In women who have experienced a prior abruption, the risk of recurrence is 10 times higher than that of the general population.

### 3. What are the manifesting signs and symptoms of abruptio placentae, and how is the diagnosis made?

Classically, abruptio placentae is described as painful bleeding. The patient may experience a sudden "tearing" pain in the abdomen, followed by the onset of vaginal bleeding and labor pains. A tumultuous labor pattern follows, with frequent contractions and an increase in base tone of the uterus. The patient may state that it feels as though the contraction never ends. The amount of vaginal bleeding is variable and

**BOX 56-1 Differential Diagnosis of Third-Trimester Bleeding**

- Bloody show
- Abruptio placentae
- Placenta previa
- Vasa previa
- Uterine rupture
- Cervical pathology
  - Polyps
  - Carcinoma
  - Varicosities
- Maternal coagulopathy
  - Preeclampsia
  - Intrauterine demise
  - Other causes of coagulopathy

does not always correlate with the degree of placental separation. If the abruption is central, little vaginal bleeding may be noted because most of the bleeding is retroplacental. An increase in uterine fundal height may occur because up to 2 L of blood may collect behind the placenta. Blood extravasation into the myometrium causes the purple-colored Couvelaire uterus. Severe hemorrhage may lead to maternal hypovolemic shock, fetal distress, or fetal demise. Disseminated intravascular coagulopathy (DIC) may also occur in the face of severe abruption. Pritchard and Brekke (1967) were the first to demonstrate that the retroplacental clot could not account for the degree of systemic hypofibrinogenemia seen in abruptio placentae. Gilabert et al. (1985) explained how open venous sinuses beneath the detached placenta could allow thromboplastic material to enter the maternal circulation and initiate DIC.

Diagnosis of abruption is initially made by clinical evaluation. Ultrasound evaluation of the placenta may identify a retroplacental clot and separation of the placenta from the uterine wall. After delivery, examination of the placenta may reveal an adherent clot; however, the placenta may appear normal.

## 4. Describe the obstetric management of abruptio placentae.

The diagnosis of placental abruption usually results in a decision to deliver the fetus. If the infant is preterm, delivery may lead to neonatal complications or death. In this scenario, if the abruption is deemed to be small, without evidence of continued bleeding, and the mother remains stable (i.e., normal vital signs, stable hematocrit and clotting), conservative management with observation may be warranted. Any evidence of extension of the abruption usually leads to immediate delivery.

After a decision to deliver the fetus, preterm or term, is made, the mode of delivery, vaginal or cesarean delivery, is determined. Cesarean delivery is not always needed. If the abruption is small and there is no evidence of maternal compromise, a trial of labor, either spontaneous or induced, may be allowed. However, if there is evidence of either maternal or fetal compromise, a cesarean delivery is warranted. Management includes vigorous maternal resuscitation with fluids, blood, and blood products to treat a coagulopathy. Management is discussed in more detail in the following sections.

## 5. Describe the effects of pregnancy on coagulation.

Pregnancy is commonly referred to as a hypercoagulable state and is associated with an increased incidence of thrombotic disease. Pregnancy is characterized by increased levels of clotting factors, especially fibrinogen. There is an enhanced fibrinogen catabolism by thrombin, marked by increased levels of fibrinopeptide A. Platelet count may decrease or remain normal in pregnancy. Rolbin et al. (1988) demonstrated no statistically significant change in platelet count during pregnancy; however, 104 of 2000 patients had platelet counts $<150 \times 10^9$/L. Fay et al. (1983) reported a decrease in platelet count secondary to increased platelet consumption during the last 8 weeks of gestation. Additionally, there is a dramatic short-term increase in coagulability immediately after delivery as manifested by an increase in factor V and factor VIII activity, a decrease in fibrinogen levels, and a decrease in partial thromboplastin time (PTT) (Box 56-2).

## 6. What is disseminated intravascular coagulopathy, and how is it managed?

DIC is characterized by activation of systemic coagulation leading to consumption of clotting factors and activation of secondary fibrinolysis. This condition results in hypofibrinogenemia, thrombocytopenia, and production of fibrin degradation products. The clinical presentation is marked by hemorrhage, poor clot formation, and bleeding

**BOX 56-2 Coagulation Changes in Pregnancy**

- Increased
  - Fibrinogen
  - Factor V
  - Factor VII
  - Factor VIII
  - Factor IX
  - Factor X
  - Factor XII
  - Fibrin split products
  - von Willebrand factor
- No change
  - Factor XI
  - Antithrombin III
  - Anti–factor Xa
  - Platelet count
- Decreased
  - Factor XIII
  - Platelet count
  - PT
  - PTT

*PT*, Prothrombin time; *PTT*, partial thromboplastin time.

from all puncture sites, such as intravenous insertion sites. Abnormal laboratory values include elevation in prothrombin time (PT), PTT, low platelet count, and fibrinogen level (Box 56-3).

Successful treatment of DIC requires removal of the source (i.e., delivery of the fetus and placenta). In addition to delivery, treatment of the coagulopathy with fresh frozen plasma (FFP), cryoprecipitate for fibrinogen replacement, and platelets is necessary until the process begins to reverse.

**BOX 56-3 Diagnosis of Disseminated Intravascular Coagulopathy**

Clinical suspicion
- Nonclotting blood
- Inability to control hemorrhage

Laboratory
- Prolonged PT/PTT
- Low fibrinogen levels
- Low platelet count
- Presence of fibrin degradation products

*PT*, Prothrombin time; *PTT*, partial thromboplastin time.

## 7. How is fetal distress diagnosed?

In the 1960s, continuous electronic FHR monitoring was developed to assess fetal well-being during labor. FHR monitoring can be performed directly by placing an electrode on the fetal scalp or indirectly by placing an ultrasound probe on the maternal abdomen. Characteristics of FHR patterns are divided into baseline and periodic features (Box 56-4).

**BOX 56-4 Fetal Heart Rate Monitoring**

Baseline: Beat-to-beat variability
- Heart rate: 110–160 beats per minute
- R-R interval: 3–5 beats per minute

Long-term periodic accelerations
- 10–15 beats per minute for 10–15 sec
- Occurs ≥3 times per 20 minutes

Baseline features include heart rate and variability. The FHR is determined by a balance between the sympathetic and parasympathetic innervation of the fetal heart. Normal FHR is 110–160 beats per minute. Variability of the FHR is very important in determining fetal well-being. Variability is described as moderate, 6–25 beats per minute; minimal, 1–5 beats per minute; and absent. Moderate variability is normal.

Periodic accelerations, lasting 15 seconds with an increase of at least 15 beats per minute, may also be noted (Figure 56-1). FHR tracings demonstrating moderate variability without decelerations, as described subsequently, are referred to as a category I tracing and imply normal neonatal acid-base status. A category I tracing is associated with delivery of a healthy and vigorous neonate with an Apgar score ≥7 at 5 minutes.

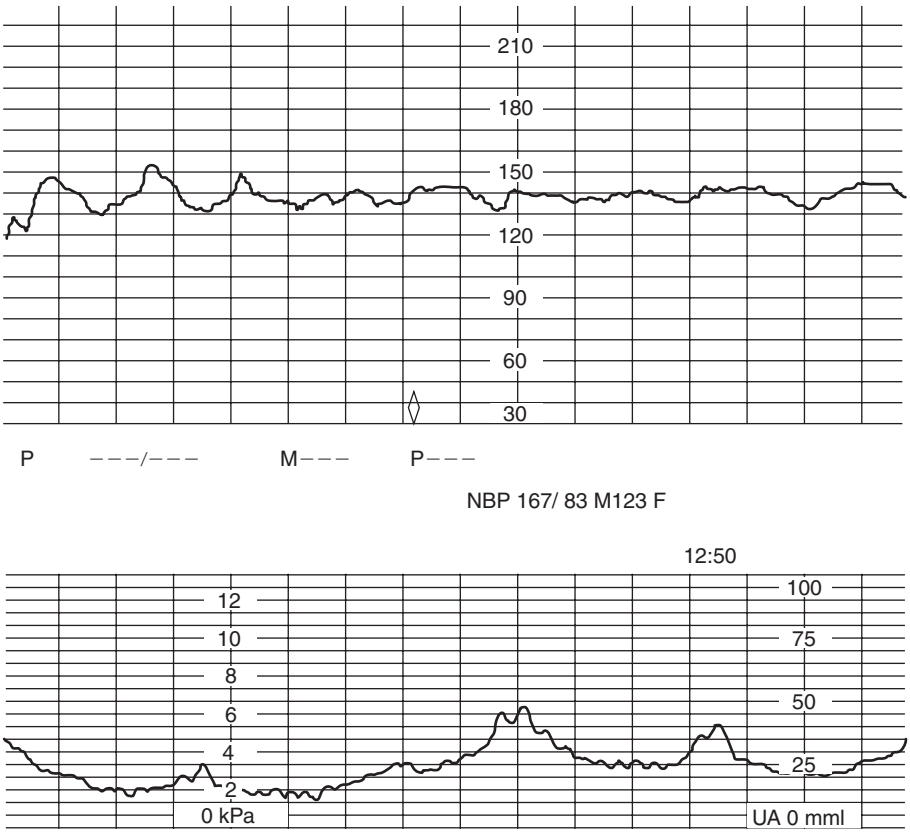


**FIGURE 56-1** ■ Fetal heart rate tracing demonstrating good variability.

The absence of variability may indicate fetal hypoxia (Figure 56-2).

The presence of moderate variability is the most sensitive indicator of fetal well-being. However, minimal or absent FHR variability is not always due to fetal hypoxia. Non–rapid eye movement fetal sleep cycles, lasting about 20 minutes, are the most common cause of poor variability. Congenital fetal heart disease, such as heart block, and fetal anencephaly are associated with poor FHR variability. Iatrogenic causes include maternal administration of opioids, local anesthetics, and atropine.

Periodic decelerations, early, late, and variable, have been described. Periodic decelerations are classified according to the rate of descent and the location of the nadir of the deceleration relative to the peak of the contraction (Table 56-1).

TABLE 56-1 **Fetal Heart Rate Decelerations**

| Type | Relation to Contraction | Significance |
|---|---|---|
| Early | Onset | Fetal head compression |
| Late | After onset | Fetal hypoxemia secondary to uteroplacental insufficiency |
| Variable | Variable | Vagal-mediated secondary to umbilical cord compression |

### *Early Decelerations*

Early decelerations reach nadir in ≥30 seconds, and the nadir coincides with the peak of the contraction. An early deceleration appears as a mirror image of the contraction. Early decelerations are thought to occur secondary to fetal head compression. They are accompanied by good variability and are not associated with fetal hypoxia or acidosis.

### *Late Decelerations*

Late decelerations reach nadir in ≥30 seconds, and the nadir occurs after the peak of the contraction. Late decelerations are always associated with fetal hypoxemia (Figure 56-3). In the presence of uteroplacental insufficiency, there is a significant decrease in fetal partial pressure

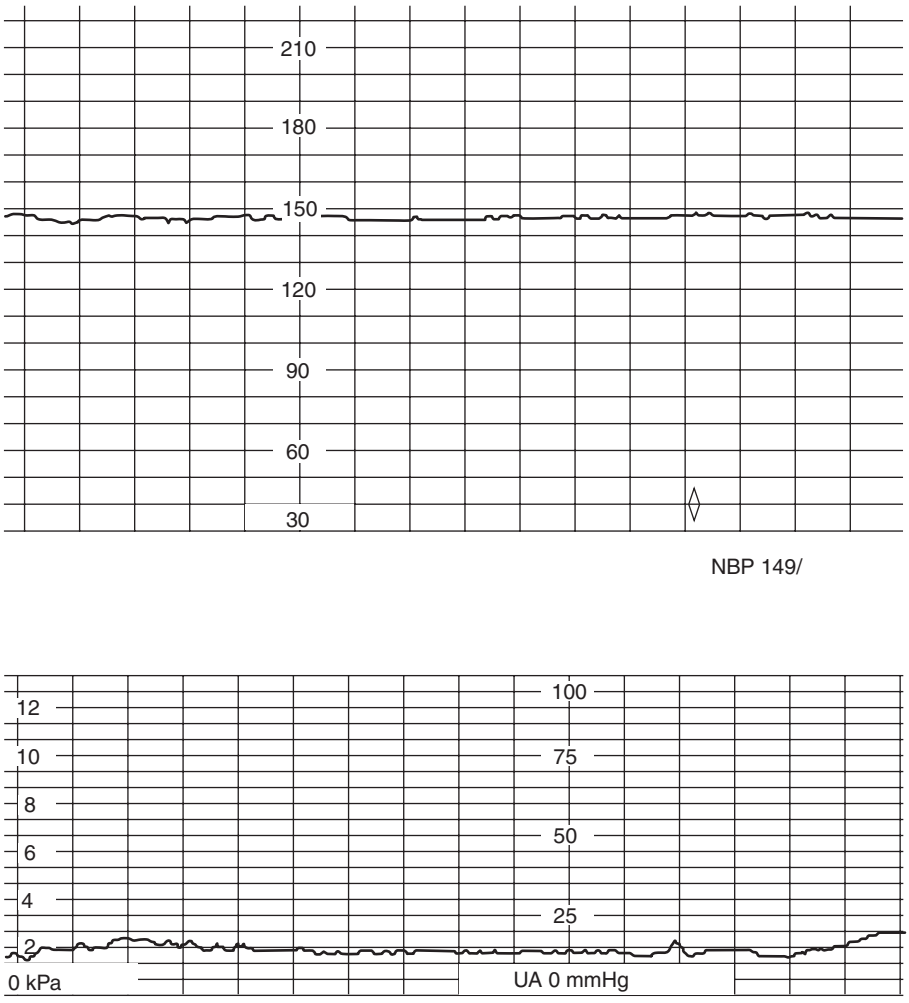


**FIGURE 56-2** ■ Fetal heart rate tracing demonstrating poor variability.

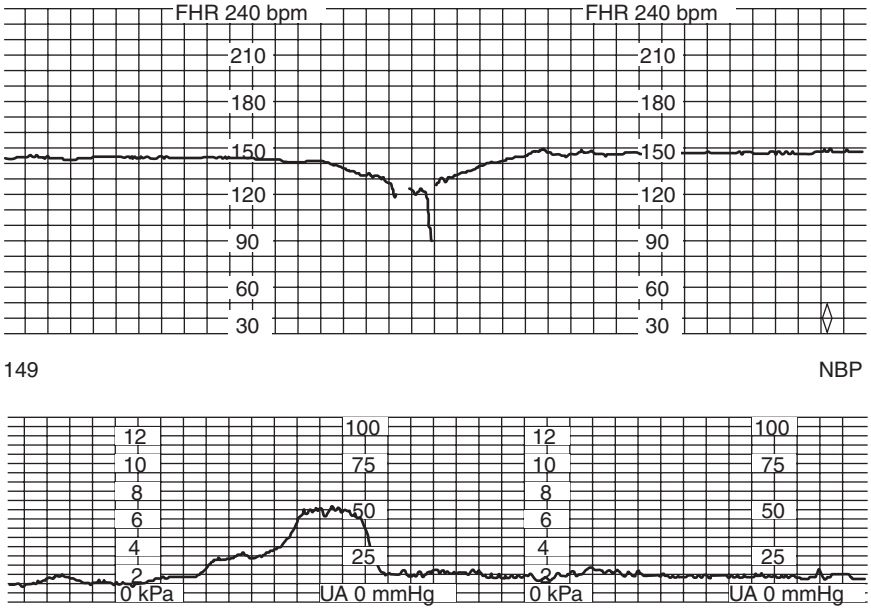


**FIGURE 56-3** ■ Fetal heart rate tracing demonstrating a late deceleration.

of oxygen ($pO_2$) resulting in vagal-mediated slowing of the FHR. In interpreting the significance of a late deceleration, FHR variability must be assessed. In the presence of moderate variability, significant neonatal cerebral hypoxia has not yet occurred, and a good neonatal outcome can be expected. If late decelerations occur with minimal or absent FHR variability, the tracing is more ominous.

### *Variable Decelerations*

Variable decelerations reach nadir in <30 seconds. The nadir of a variable deceleration is not related to the peak of the contraction. Variable decelerations are unrelated to the time of onset of the uterine contraction (Figure 56-4). Variable decelerations are due to vagal-mediated reflexes stimulated by umbilical cord compression. Variable decelerations are considered severe if they last >30 seconds with a nadir FHR of ≤60 beats per minute. Mild to moderate variable decelerations are rarely associated with fetal hypoxia. However, severe and recurrent decelerations may lead to the development of fetal hypoxia and acidosis. In that case, the FHR tracing also demonstrates loss of variability.

In addition to FHR monitoring, fetal scalp stimulation, by digital examination, or fetal acoustic stimulation may be used to assess fetal well-being. The presence of FHR acceleration after scalp stimulation is associated with a fetal pH >7.20. Intrapartum fetal pulse oximetry is a new technology that may offer advantages over traditional monitoring techniques, but it is currently not widely used.

When a nonreassuring FHR tracing is identified, in utero fetal resuscitation should commence. Correctable causes include maternal hypotension, hyperstimulation of the uterus by oxytocin (Pitocin), and umbilical cord compression. Fetal well-being may be enhanced by administering oxygen to the mother, improving left uterine displacement, and increasing maternal blood pressure with either fluids or vasopressors.

**8. The patient is given a trial of labor, and the obstetrician requests a consultation for labor analgesia. What are your concerns, and how would you proceed?**

Painful vaginal bleeding is consistent with placental abruption. Before a regional anesthetic is initiated, the patient's intravascular volume, blood count, and coagulation status require careful evaluation. Initial laboratory evaluation should include hemoglobin, hematocrit, platelet count, PT and PTT, fibrinogen level, and fibrin split products to evaluate the degree of hemorrhage and to rule out DIC. Volume repletion should proceed with crystalloid, colloid, or packed red blood cells, as indicated. If significant hemorrhage has not occurred and there is no laboratory evidence of DIC, epidural analgesia may be instituted.

**9. The obstetrician notes 3 hours into labor a significant increase in vaginal bleeding and a decrease in maternal blood pressure to 80/40 mm Hg with a pulse of 120 beats per minute; fetal tachycardia with late decelerations and absent variability are noted on the fetal heart rate monitor. Assuming the patient has not yet received an epidural for regional analgesia, how would you anesthetize this patient for an emergency cesarean delivery?**

To decide on an anesthetic plan, both maternal and fetal conditions must be evaluated. In this case, both

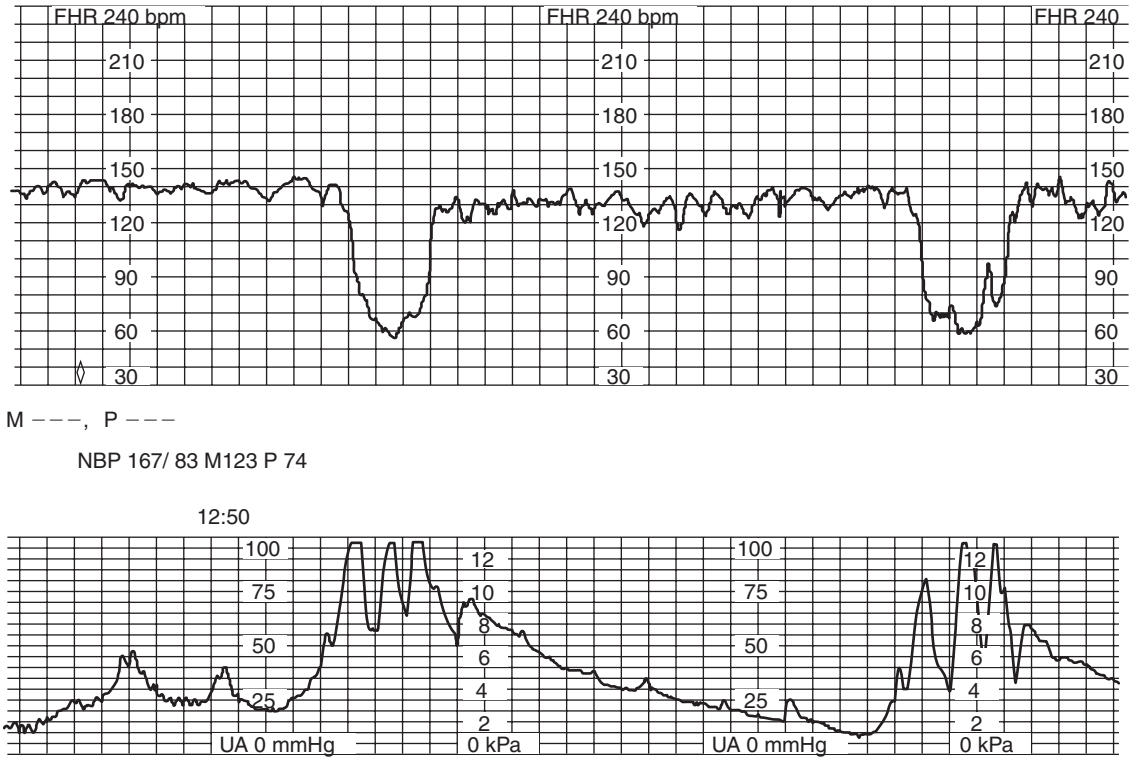


**FIGURE 56-4** ■ Fetal heart rate tracing demonstrating variable decelerations.

maternal and fetal conditions have deteriorated since admission and are consistent with worsening abruption, complicated by significant blood loss and fetal compromise. The amount of vaginal bleeding may underestimate the true blood loss because a significant volume of blood may be concealed behind the placenta. Hemoglobin concentration should be determined to guide blood transfusion therapy. Maternal coagulopathy, such as DIC, secondary to placental abruption must also be ruled out. If maternal or fetal instability exists, cesarean delivery may be performed before laboratory assessments are obtained.

Spinal anesthesia can be rapidly established to provide surgical anesthesia for an emergency cesarean delivery. However, maternal coagulopathy and hypovolemia secondary to hemorrhage are contraindications to regional anesthesia. For these reasons, regional anesthesia should be avoided, and the cesarean delivery should be performed under general anesthesia.

Before induction of general anesthesia, adequate intravenous access must be established. Blood should be drawn and sent for typing and crossmatching, hematocrit level, platelet count, PT and PTT, fibrinogen level, and fibrin degradation products. Fluid resuscitation should also begin immediately. A rapid-sequence induction with cricoid pressure is recommended. In the hypovolemic patient, etomidate 0.1–0.3 mg/kg or ketamine 0.5-1 mg/kg intravenously should be considered as induction agents. Propofol should be avoided because it is associated with more hypotension than ketamine or etomidate after induction. Succinylcholine is recommended for tracheal intubation (Box 56-5).

**BOX 56-5 Cesarean Delivery for Abruptio Placentae**

- Laboratory testing
  - Type and crossmatch
  - Hematocrit
  - Platelet count
  - PT/PTT
  - Fibrinogen level
  - Fibrin degradation products
- Adequate intravenous access
- Fluid resuscitation
  - Crystalloids
  - Colloids
  - Blood products as indicated
- Anesthetic choice
  - Regional anesthesia contraindicated in the presence of coagulopathy or hypovolemia
  - General anesthesia preferable
- Induction agents
  - Etomidate 0.1–0.3 mg/kg IV
  - Ketamine 0.5-1 mg/kg IV
- Rapid-sequence induction

*IV*, Intravenously; *PT*, prothrombin time; *PTT*, partial thromboplastin time.

## 10. What is placenta previa?

Placenta previa is a condition in which a low-lying placenta covers the internal cervical os; it occurs in about 1 in 200 deliveries. Predisposing factors include multiparity, advanced maternal age, and prior cesarean delivery.

The previa may be marginal, partial, or complete. With a complete placenta previa, the placenta covers the entire cervical os, preventing vaginal delivery of the fetus. Incomplete coverage of the cervical os is referred to as a partial placenta previa. A marginal previa is a partial placenta previa with minimal placental coverage of the cervix. A low-lying placenta is one that implants in the lower uterine segment but does not cover the internal cervical os.

### 11. Describe the clinical presentation of placenta previa, and explain how the diagnosis is made.

Bleeding from a placenta previa is not associated with abdominal pain and may be sudden in onset. The amount of bleeding may range from very mild and intermittent to profuse and life-threatening.

Diagnosis is usually made by ultrasound evaluation of the position of the placenta relative to the internal cervical os. If the diagnosis cannot be made by ultrasound, a vaginal examination is performed in the operating room (Table 56-2). The patient is brought to the operating room and prepared for emergency induction of general anesthesia and cesarean delivery in the event of profuse hemorrhage after vaginal examination. This is referred to as a "double setup."

### 12. Discuss the obstetric management of placenta previa.

Management of placenta previa depends on the amount of blood lost, the presence or absence of further bleeding, the type of previa, and the gestational age of the fetus. If bleeding has stopped and both the mother and the fetus are stable, a conservative approach is elected. Bed rest with fetal monitoring is prescribed to allow further maturation of the fetus. Additional bleeding episodes or signs of fetal distress indicate the need for an immediate cesarean delivery.

### 13. How would you anesthetize a patient with placenta previa for cesarean delivery?

As with a placental abruption, both the fetal and the maternal conditions must be evaluated. Most women with placenta previa have an uneventful prenatal course. Because the placenta covers the cervical os, cesarean delivery is needed. In the absence of maternal hemorrhage, a regional anesthetic, spinal or epidural, may be performed in the usual fashion. Adequate intravenous access should be obtained before placement of the spinal anesthetic and the patient should have crossmatched blood available in case unexpected hemorrhage occurs. The anesthesia team must be prepared to convert to general anesthesia in the event significant hemorrhage and maternal hemodynamic instability develop.

In the presence of significant hemorrhage, regional anesthesia is contraindicated, and a general anesthetic should be performed. Adequate intravenous access should be obtained before induction, and appropriate monitoring (e.g., intraarterial catheter) should be placed. Induction of anesthesia would follow the same guidelines as for a placental abruption.

TABLE 56-2 **Placenta Previa versus Abruptio Placentae**

| | Placenta Previa | Abruptio Placentae |
|---|---|---|
| Pain | Painless bleeding | Painful bleeding |
| Blood | Bright red | Port wine |
| Clotting | Yes | No |
| Blood loss | Obvious | Concealed behind the placenta |
| DIC | Rare | Possibility |
| Diagnosis | Confirmed by ultrasound | Clinical and ultrasound |

*DIC,* Disseminated intravascular coagulation.

### 14. How would you manage massive obstetric hemorrhage?

Management of massive obstetric hemorrhage is based on principles established to manage hemorrhage secondary to trauma. To date, there are no controlled trials of the management of obstetric hemorrhage.

As soon as abnormal bleeding is diagnosed, additional large-bore (i.e., ≥16-gauge) intravenous catheters should be placed. In addition, it is frequently useful to place an arterial catheter for both ease of sampling blood and beat-to-beat blood pressure monitoring. It is easier to place venous and arterial catheters before the onset of hemorrhagic shock. These lines can always be removed if the emergency is more easily handled than expected.

The management of massive hemorrhage requires a multidisciplinary approach. Blood bank personnel should be informed that an obstetric massive hemorrhage is occurring so that appropriate personnel can be assigned to prepare blood and blood products. In addition, early surgical consultation should be obtained to assist the obstetricians. At many institutions, the surgeon would be a gynecologic oncologist, but if one is unavailable, a general surgeon should be called. If a coagulopathy develops, a hematologist may also be consulted.

Based on data from the trauma literature, massive transfusion protocols have been developed. It has been found that transfusion of equal numbers of equivalent units of blood, FFP, and platelets results in a greater survival rate. Massive transfusion protocol should be initiated when any of the following has occurred:

- Estimated blood loss of one blood volume
- Development of sustained hypotension or acidemia (pH ≤7.1 or base deficit >−6)
- Development of coagulopathy or thrombocytopenia or both

Packed red blood cells (PRBCs) and FFP are transfused in a ratio of 1:1. Single-donor apheresis platelets should be administered when 4–6 units of PRBCs and FFP have been administered. One unit of single-donor apheresis platelets is equivalent to 6 units of pooled platelets.

Each unit of FFP increases the fibrinogen level by approximately 15 mg/dL. Large volumes of FFP may be needed to maintain fibrinogen levels >100 mg/dL. Cryoprecipitate, administered as 5-unit pooled packs, allows for administration of fibrinogen in a much smaller volume. At our institution, when the massive obstetric hemorrhage protocol is activated, the blood bank continuously prepares and sends 4 units of PRBCs, 4 units of FFP, 1 unit single-donor apheresis platelets, and 5 units of pooled cryoprecipitate until the protocol is deactivated.

Hypothermia, which may lead to coagulopathy and acidemia, should be avoided by infusing PRBCs and FFP through a warmer. A rapid infusion system should be used when large volumes of blood and blood products are administered; this allows for rapid infusion with very efficient warming of the blood and blood products.

The use of a cell saver should also be considered because it decreases the total number of banked PRBC units administered. Numerous studies have demonstrated the safety of a cell saver, with no reports of amniotic fluid embolism attributed to the use of cell salvaged blood.

If excessive bleeding is anticipated, a balloon catheter can be placed in the internal iliac artery before the scheduled surgical procedure. If needed, inflation of the balloon markedly decreases flow to the uterine arteries. However, the presence of a significant collateral uterine circulation makes the effectiveness of this intervention questionable. The following treatment adjuncts for hemorrhage secondary to uterine hypotonia have decreased the need for hysterectomy:

- Uterine artery embolization
- Intrauterine balloon tamponade
- Placement of a uterine constrictive suture (i.e., B-Lynch suture)

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CASE 57

# Anesthesia for Nonobstetric Surgery during Pregnancy

Yaakov Beilin, MD

## QUESTIONS

1. What is the incidence of nonobstetric surgery in pregnant patients?
2. What are the anesthetic concerns in a pregnant patient?
3. Describe the physiologic changes during pregnancy and the impact they have on anesthesia.
4. What is a teratogen, and which anesthetic agents are known teratogens?
5. What precautions should be taken to avoid intrauterine fetal asphyxia?
6. How is preterm labor prevented?
7. What monitors should be used when anesthetizing a pregnant patient?
8. What are the special considerations for laparoscopic surgery?
9. What general recommendations can be made when anesthetizing a pregnant patient for nonobstetric surgery?

A 32-year-old woman who was 17 weeks pregnant presented to the emergency department complaining of abdominal pain, nausea, and vomiting. After physical examination, a presumptive diagnosis of appendicitis was made, and an emergency appendectomy was scheduled.

### 1. What is the incidence of nonobstetric surgery in pregnant patients?

The incidence of nonobstetric surgery during pregnancy is 0.3%–2%. There are approximately 4 million deliveries per year in the United States, which means that 80,000 pregnant women require surgery annually. This figure may be an underestimate because it does not account for surgery performed before clinical recognition of pregnancy. Appendectomy is the most common nonobstetric operation performed during pregnancy. However, almost every type of surgical procedure has been successfully performed in pregnant patients, including open heart procedures with cardiopulmonary bypass, neurosurgical procedures requiring hypotensive techniques and hypothermia, and liver transplantation.

### 2. What are the anesthetic concerns in a pregnant patient?

Anesthetizing a pregnant patient is one of the only times an anesthesiologist must consider two patients simultaneously. Maternal considerations result from the physiologic changes of pregnancy that affect almost every organ system (Table 57-1). To provide safe anesthesia to a pregnant patient, one must not only understand the physiologic changes but also know when they occur during the gestational period and what impact they have on the administration of anesthesia. Fetal concerns include the possible teratogenic effects of anesthetic agents, avoidance of intrauterine fetal asphyxia, and prevention of premature labor.

### 3. Describe the physiologic changes during pregnancy and the impact they have on anesthesia.

#### *Respiratory System*

As a result of increased progesterone levels during the first trimester, minute ventilation is increased by almost 50% and remains at this level for the remainder of the pregnancy. The increase in minute ventilation leads to a decrease in arterial carbon dioxide tension ($PaCO_2$) to approximately 30 mm Hg. Arterial pH remains unchanged because of a compensatory increase in renal excretion of bicarbonate ions. At term, alveolar ventilation is increased by 70% because anatomic dead space does not change significantly during pregnancy. After the fifth month of pregnancy, the functional residual capacity, expiratory reserve volume, and residual volume all are decreased by about 20% because of the gravid uterus pushing on the diaphragm. Vital capacity is not appreciably changed from prepregnancy levels.

#### *Anesthetic Implications*

Increased alveolar ventilation and decreased functional residual capacity lead to a more rapid uptake and excretion of inhaled anesthetics. The decrease in functional

TABLE 57-1 **Physiologic Changes of Pregnancy**

| | |
|---|---|
| **Respiratory** | |
| Minute ventilation | Increases by 50% |
| Tidal volume | Increases by 40% |
| Respiratory rate | Increases by 10% |
| Oxygen consumption | Increases by 20% |
| $PaO_2$ | Increases by 10 mm Hg |
| Dead space | No change |
| Alveolar ventilation | Increases by 70% |
| $PaCO_2$ | Decreases by 10 mm Hg |
| Arterial pH | No change |
| Serum $HCO_3^-$ | Decreases by 4 mEq/L |
| Functional residual capacity | Decreases by 20% |
| Expiratory reserve volume | Decreases by 20% |
| Residual volume | Decreases by 20% |
| Vital capacity | No change |
| **Cardiovascular** | |
| Cardiac output | Increases by 30%–40% |
| Heart rate | Increases by 15% |
| Stroke volume | Increases by 30% |
| Total peripheral resistance | Decreases by 15% |
| Femoral venous pressure | Increases by 15% |
| Central venous pressure | No change |
| Systolic blood pressure | Decreases by 0%–15% |
| Diastolic blood pressure | Decreases by 10%–20% |
| Intravascular volume | Increases by 35% |
| Plasma volume | Increases by 45% |
| Red blood cell volume | Increases by 20% |
| **Gastrointestinal** | |
| Motility | Decreases |
| Stomach position | More cephalad and horizontal |
| Transaminases | Increases |
| Alkaline phosphatase | Increases |
| Pseudocholinesterase | Decreases by 20% |
| **Hematologic** | |
| Hemoglobin | Decreases |
| Coagulation factors | Increase |
| Platelet count | Decreases by 20% |
| Lymphocyte function | Decreases |
| **Renal** | |
| Renal blood flow | Increases |
| Glomerular filtration rate | Increases |
| Serum creatinine and BUN | Decrease |
| Creatinine clearance | Increases |
| Glucosuria | 1–10 g/day |
| Proteinuria | 300 mg/day |
| **Nervous system** | |
| MAC | Decreases by 40% |
| Endorphin levels | Increase |

*BUN,* Blood urea nitrogen; *$HCO_3^-$*, bicarbonate; *MAC,* minimum alveolar concentration; *$PaCO_2$,* arterial carbon dioxide tension; *$PaO_2$,* arterial oxygen tension.

residual capacity in conjunction with increases in cardiac output, metabolic rate, and oxygen consumption make the pregnant patient more susceptible to arterial hypoxemia during periods of apnea or airway obstruction.

Edema, weight gain, and increase in breast size may make tracheal intubation technically difficult. An array of laryngoscope blades and handles and other emergency airway management equipment should be available. Capillary engorgement of the mucosal lining of the upper airway accompanies pregnancy. Extreme care is mandated during manipulation of the airway, and a smaller than normal tracheal tube needs to be used. The use of a nasal airway and nasotracheal intubation should be avoided.

### *Cardiovascular System*

Cardiac output is increased by 30%–40% during the first trimester. This increase in cardiac output is primarily related to an increase in stroke volume (30%) and secondarily related to an increase in heart rate (15%). Cardiac output increases slightly further during the second trimester, and this increase lasts throughout the pregnancy.

Blood pressure normally decreases during pregnancy because of a 15% decrease in systemic vascular resistance. Near term, 10%–15% of patients have a dramatic reduction in blood pressure in the supine position, often associated with diaphoresis, nausea, vomiting, pallor, and changes in cerebration. This condition is known as supine hypotensive syndrome and is caused by compression of the inferior vena cava and aorta by the gravid uterus. Other manifestations of the syndrome are decreases in renal and uteroplacental blood flow from compression of the aorta.

Intravascular volume is increased by 35% during pregnancy. Because plasma volume increases by a greater percentage than red blood cell volume (45% and 20%), there is a relative anemia during pregnancy. Nevertheless, a hemoglobin concentration <11 g/dL is considered abnormal.

### Anesthetic Implications

Increases in cardiac output hasten the speed of intravenous induction of anesthesia. Also, it is critical to displace the uterus 15–30 degrees toward the left to avoid supine hypotensive syndrome and hypotension.

### Gastrointestinal System

Traditionally, gastric emptying was considered prolonged in a pregnant woman by the end of the first trimester. This delayed emptying was thought to be related to progesterone and mechanical anatomic changes as the stomach is displaced upward by the enlarging uterus. More recent data using acetaminophen absorption (Wong, 2002) do not support this conclusion, and gastric emptying may not be prolonged until the woman is in active labor. Although gastric emptying is not delayed, gastric pressure increases secondary to the gravid uterus, gastric secretions are more acidic, and lower esophageal sphincter tone is impaired.

### Anesthetic Implications

Although studies suggest that pregnant women are not at increased risk for pulmonary aspiration, any woman with symptoms of acid reflux such as heartburn, a common finding in pregnancy, should be considered at risk for pulmonary aspiration. If the patient is considered at risk, a nonparticulate antacid, $H_2$ receptor blocker, and metoclopramide should be used to decrease the acidity and volume of the gastric contents, and general anesthesia with tracheal intubation should be conducted with a rapid-sequence induction, cricoid pressure, and tracheal intubation.

### Hepatic System

Tests of liver function (aspartate aminotransferase, lactic acid dehydrogenase, alkaline phosphatase, and cholesterol) are commonly increased during pregnancy. These increases do not indicate abnormal liver function. Pseudocholinesterase activity declines 20% during the first trimester and remains stable during the remainder of the pregnancy.

### Anesthetic Implications

Decreased pseudocholinesterase activity could prolong the effect of succinylcholine but apnea is rarely a problem after a standard dose used for tracheal intubation. Similarly, prolonged activity of ester-linked local anesthetics has not been a problem.

### Hematologic System and Blood Constituents

Pregnancy does not significantly alter the lymphocyte count, but lymphocyte function is depressed, which can decrease maternal resistance to infection. The risk of upper respiratory infections is increased, which may complicate airway management during general anesthesia.

The platelet count decreases by about 20% during pregnancy, but this is not usually of clinical significance. Circulating levels of coagulation factors increase significantly during pregnancy leading to the hypercoagulable state of pregnancy.

### Anesthetic Implications

The increased risk of upper airway infections may complicate airway management during general anesthesia. Increased coagulability may predispose a pregnant patient to thromboembolic events including pulmonary embolism. Venous thromboembolic prophylaxis should be considered in the perioperative period.

### Renal System

Renal blood flow and glomerular filtration rate are increased during the first trimester, leading to an increase in creatinine clearance and a decrease in serum creatinine. During the third trimester, renal blood flow and glomerular filtration rate decrease toward prepregnant levels because of compression of the aorta by the enlarging uterus. As a result of progesterone, renal calyces and pelves dilate during the third month of pregnancy. During the third trimester, they dilate further because of ureteral compression. This dilation may lead to stasis and urinary tract infections.

### Anesthetic Implications

Bladder catheterization, which may predispose a patient to urinary tract infections, should be avoided, if possible. Although not generally related to the anesthesia, care should be taken not to overhydrate the patient to try to obviate the need for catheterization.

### Central Nervous System

The minimum alveolar concentration for inhaled anesthetics is decreased by 40% during pregnancy; this is related to a progesterone and endorphin effect. Compression of the inferior vena cava by the gravid uterus leads to dilation of the azygos system and the epidural veins. Epidural venous engorgement decreases the size of the epidural and intrathecal spaces.

### Anesthetic Implications

The decrease in minimum alveolar concentration along with an increase in alveolar ventilation places a pregnant patient at risk for anesthetic overdose. The decreased size of the epidural and intrathecal spaces as a result of epidural venous engorgement explains why the doses of drugs used during a major conduction block must be decreased. An alternative explanation is that progesterone may increase the sensitivity of nerve cells to local anesthetics because neuraxial drug requirements decrease before uterine enlargement.

## 4. What is a teratogen, and which anesthetic agents are known teratogens?

A teratogen is a substance that produces an increase in the incidence of a congenital defect that cannot be attributed to chance. To produce a defect, the teratogen

must be administered in a sufficient dose at a critical point in development. In humans, this critical point is during organogenesis, which is approximately 15–60 days of gestational age. However, the central nervous system does not fully develop until after birth, and the critical time for this system may extend beyond gestation.

Three approaches have been employed to study the effects of anesthetic agents or anesthesia in pregnant patients: (1) animal studies, (2) studies of operating room personnel with long-term exposure to trace concentrations of inhaled anesthetics, and (3) studies of women who underwent surgery while pregnant.

The results of animal studies are of limited value because of (1) species variation; (2) the fact that the doses of anesthetic agents used in animal studies were usually far greater than doses used clinically; and (3) other factors such as hypercarbia, hypothermia, and hypoxemia (known teratogens) either were not measured or were not controlled in the study. Species variation is particularly important. Thalidomide has no known teratogenic effects on rats and was approved by the U.S. Food and Drug Administration (FDA) for use in humans. It is now known that thalidomide is teratogenic in humans.

The FDA has established a risk classification system to assist physicians in weighing the risks and benefits when choosing therapeutic agents for pregnant women (Table 57-2). Most anesthetic agents, including intravenous induction agents, local anesthetics, opioids, and neuromuscular blocking drugs, have been assigned a category B or C classification (Table 57-3).

The use of two common agents, benzodiazepines and nitrous oxide, in pregnant women is controversial. Some investigators in retrospective studies noted an association between diazepam taken in the first 6 weeks of pregnancy and cleft palate. Although this finding has been questioned by the results of a prospective study, diazepam and other benzodiazepines are classified by the FDA as category D drugs and should be avoided, if possible.

TABLE 57-2 **U.S. Food and Drug Administration Category Ratings of Drugs during Pregnancy**

| Category | |
|---|---|
| A | Controlled studies demonstrate no risk<br>Well-controlled studies in humans have not demonstrated risk to the fetus |
| B | No evidence of risks in humans<br>Either animal studies have found a risk but human studies have not, or animal studies are negative, but adequate human studies have not been done |
| C | Risk cannot be ruled out<br>Human studies have not been adequately performed, and animal studies are positive or have not been conducted; potential benefits may justify risk |
| D | Potential evidence of risk; confirmed evidence of human risk; however, benefits may be acceptable despite the known risk (i.e., no other medication is available to treat a life-threatening situation) |
| X | Contraindicated in pregnancy<br>Human or animal studies have shown fetal risk that clearly outweighs any possible benefit to the patient |

TABLE 57-3 **U.S. Food and Drug Administration Category Ratings of Specific Anesthetic Agents**

| Anesthetic Agent | Classification |
|---|---|
| **Induction agents** | |
| Etomidate | C |
| Ketamine | C |
| Methohexital | B |
| Propofol | B |
| Thiopental | C |
| **Inhaled agents** | |
| Desflurane | B |
| Enflurane | B |
| Halothane | C |
| Isoflurane | C |
| Sevoflurane | B |
| **Local anesthetics** | |
| Chloroprocaine | C |
| Bupivacaine | C |
| Lidocaine | B |
| Ropivacaine | B |
| Tetracaine | C |
| Cocaine | X |
| **Opioids** | |
| Alfentanil | C |
| Fentanyl | C |
| Sufentanil | C |
| Meperidine | B |
| Morphine | C |
| **Neuromuscular blocking drugs** | |
| Atracurium | C |
| Cisatracurium | B |
| Curare | C |
| Mivacurium | C |
| Pancuronium | C |
| Rocuronium | B |
| Succinylcholine | C |
| Vecuronium | C |
| **Benzodiazepines** | |
| Diazepam | D |
| Midazolam | D |

Nitrous oxide is a known teratogen in mammals and rapidly crosses the human placenta. The proposed mechanism is that nitrous oxide oxidizes vitamin $B_{12}$, which cannot function as a cofactor for the enzyme methionine synthetase. Methionine synthetase is needed for the formation of thymidine, a subunit of DNA. However, pretreatment of rats exposed to nitrous oxide with folinic acid, which bypasses the methionine synthetase step in DNA synthesis, does not prevent congenital abnormalities. In addition, suppression of methionine synthetase occurs at low concentrations of nitrous oxide—concentrations found to be safe in animal studies. Despite these theoretical concerns, nitrous oxide has not been found to be associated with congenital abnormalities in humans. The FDA has not given nitrous oxide a category classification because it is a medical gas and not directly regulated by the FDA.

Numerous epidemiologic studies have been performed to determine the health hazards, including birth defects and spontaneous abortions, of pregnant women with long-term exposure to anesthetic gases. All the studies found similar results. The authors of the largest study, sponsored by the American Society of Anesthesiologists (ASA) (1974), sent questionnaires to 73,496 individuals who may have been exposed to anesthetic gases to gather information about the extent of their exposure and reproductive outcome. The study population included the entire membership of the ASA, the American Association of Nurse Anesthetists, the Association of Operating Room Nurses, and the Association of Operating Room Technicians. The investigators found that operating room personnel had an increased risk of spontaneous abortions and congenital abnormalities. They recommended that a means to scavenge trace anesthetic gases should be mandatory in all operating rooms, which is the current standard. However, all these studies were later criticized for their lack of a control group, low response rate to questionnaires, recall bias, and statistical inaccuracies.

There have also been several retrospective studies of pregnant patients who had undergone surgery to determine whether there is an association between anesthesia and surgery and congenital defects, spontaneous abortions, or fetal demise. All studies found similar results. In the largest study, Mazze and Kallen (1989) linked the data from three Swedish health registries: the Medical Birth Registry, the Registry of Congenital Malformations, and the Hospital Discharge Registry for the 9-year period 1973–1981. They examined the data for four adverse outcomes including congenital defects, stillborn infants, infants born alive but who died within 7 days, and infants with a birth weight <1500 g and <2500 g. They found 5405 of 720,000 women had undergone surgery during their pregnancy. In their data set, most procedures were performed during the first trimester (41.6%), and the incidence decreased during the second (34.8%) and third (23.5%) trimesters. There was no increase in infants with congenital abnormalities or stillborn births among patients who underwent surgery while pregnant during any trimester. However, the number of infants born with a birth weight <1500 g and <2500 g and the number of infants who died within 7 days of birth were greater in patients who underwent surgery while pregnant; this was true during all three trimesters. These risks could not be linked to either the specific anesthetic agents or the anesthetic technique. Most operations (54%) were performed under general anesthesia, and nitrous oxide was used in 98% of the general anesthetics. The increased risk to the fetus may be due to the condition that necessitated surgery in the first place, with the highest rate occurring with gynecologic procedures. These data are very important because they clearly demonstrate that anesthetic agents are not teratogenic and that the greatest risk is premature labor with the delivery of a low-birth-weight infant. The data suggest that the anesthetic agents are not responsible for the major complication of surgery: premature labor and early delivery of the fetus.

## 5. What precautions should be taken to avoid intrauterine fetal asphyxia?

Intrauterine fetal asphyxia is avoided by maintaining normal maternal arterial oxygen tension ($PaO_2$), $PaCO_2$, and uterine blood flow. Maternal hypoxemia may lead to fetal hypoxemia and fetal demise. General anesthesia is a particular risk to pregnant patients because management of the airway can be difficult, and the rate of hemoglobin oxygen desaturation is increased owing to the decreased functional residual capacity and increased oxygen consumption. However, care also must be taken during a regional anesthetic because a high segmental level of anesthesia during a major conduction block, a toxic local anesthetic reaction, or oversedation can also lead to a hypoxic event. High inspired oxygen tension does not adversely affect the fetus even if 100% oxygen is administered.

Maternal hypercapnia and hypocapnia can be detrimental to the fetus. Severe hypocapnia produced by excessive positive pressure ventilation may increase mean intrathoracic pressure, decrease venous return, and lead to a decrease in uterine blood flow. In addition, maternal alkalosis, as produced by hyperventilation, decreases uterine blood flow by direct vasoconstriction and decreases oxygen delivery by shifting the maternal oxyhemoglobin dissociation curve to the left. Severe hypercapnia is detrimental because it is associated with fetal acidosis and myocardial depression.

Both drugs and anesthetic procedures affect uterine blood flow. Placental blood flow is directly proportional to the net perfusion pressure across the intervillous space and inversely proportional to the resistance. Perfusion pressure is decreased by hypotension, which may be due to the use of an epidural or spinal anesthetic, aortocaval compression in the supine position, or hemorrhage. Vasoconstriction secondary to the use of α-adrenergic drugs, decreased $PaCO_2$, or increased catecholamines (e.g., occurs during pain, apprehension, or light anesthesia) increases vascular resistance and decreases uteroplacental blood flow.

## 6. How is preterm labor prevented?

Premature labor, preterm delivery, and delivery of an infant <1500 g are the most significant risks to the fetus. Medications that have α-adrenergic agonist properties (e.g., ketamine and phenylephrine) can increase uterine

vascular tone and should be avoided, if possible. The potent inhaled anesthetic agents decrease uterine tone and inhibit uterine contractions and may be beneficial. However, no study has documented that any particular anesthetic agent or technique is associated with a higher or lower incidence of miscarriage or preterm labor. The greatest risk for preterm labor occurs when there is uterine manipulation, as occurs during gynecologic procedures. The lowest risk for preterm labor occurs during the second trimester.

### 7. What monitors should be used when anesthetizing a pregnant patient?

In addition to the routine intraoperative monitors, the fetal heart rate (FHR) and uterine tone should be monitored, if possible. Using a Doppler apparatus, FHR monitoring becomes feasible after week 16 of pregnancy. An external tocodynamometer can be used if the uterus is at or above the level of the umbilicus. The monitor may be technically difficult or impossible to use during an intraabdominal procedure or in an obese patient. It is important that someone proficient in fetal monitoring be present throughout the case to interpret the uterine/fetal tracings. Also, there should be a plan regarding how to proceed in the event of fetal distress. Before 23–24 weeks of gestation when the fetus is not viable, optimization of the maternal condition, by increasing the blood pressure or increasing the inspired oxygen concentration, may improve the fetal condition. After 23–24 weeks of gestation, in addition to attempts at correcting the intrauterine milieu, emergent cesarean delivery should be part of the plan. FHR and uterine tone monitoring should continue into the postoperative period.

### 8. What are the special considerations for laparoscopic surgery?

Previously considered an absolute contraindication during pregnancy, laparoscopic surgery is now commonly performed during pregnancy. Outcomes in patients who have surgery laparoscopically and patients who undergo a traditional laparotomy are the same. Specific anesthetic considerations during laparoscopy include maintaining normocarbia because carbon dioxide is commonly used to maintain a pneumoperitoneum. Surgical concerns include caution during placement of the trocars, which can be accomplished as an open technique, and maintaining low pneumoperitoneum pressures (<15 mm Hg) so that uterine perfusion is maintained.

### 9. What general recommendations can be made when anesthetizing a pregnant patient for nonobstetric surgery?

Whenever possible, anesthesia and surgery should be avoided during the first trimester, the period of organogenesis (Box 57-1). Before initiating an anesthetic, an obstetrician should be consulted, and FHR tones should be documented. Precautions against aspiration should be taken if the woman has signs of acid reflux by administering a clear nonparticulate oral antacid, $H_2$ receptor blocker, and metoclopramide. If possible, apprehension should be allayed by personal reassurance rather than with premedication. The patient should be informed that there is no known risk to the fetus regarding congenital malformations but that there is an increased risk of miscarriage or premature labor. The patient should be transported to the operating room with left uterine displacement to avoid aortocaval compression.

**BOX 57-1 Recommendations for Anesthetizing Pregnant Patients for Nonobstetric Surgery**

- Avoid surgery during first trimester, if possible
- Document FHR tones before surgery
- Monitor uterine tone and FHR tones during surgery, if possible
- Continue monitoring FHR and uterine tone in postoperative period
- Avoid premedication
- Transport with left uterine displacement
- Regional anesthesia is recommended when possible
- Provide aspiration prophylaxis after first trimester if indicated
  - Nonparticulate antacid
  - $H_2$ Blocker
  - Metoclopramide
- Regional anesthesia:
  - Treat hypotension with fluid administration, ephedrine, or phenylephrine
- General anesthesia:
  - Denitrogenate with 100% oxygen
  - Employ rapid sequence with cricoid pressure induction if indicated
  - Use drugs with history of relative safety
  - Ensure adequate oxygenation
  - Maintain normocarbia

In addition to the routine intraoperative monitors, the FHR and uterine tone should be monitored and should continue to be monitored into the postoperative period. The type of anesthesia is determined by maternal indications, the site and nature of the surgery, and the anesthesiologist's experience. The dose of all anesthetic agents for general or regional anesthesia should be reduced. Unless otherwise contraindicated, local or regional anesthesia may be preferable to general anesthesia to avoid the risk of aspiration and to decrease fetal drug exposure.

The greatest risk of spinal or epidural anesthesia is hypotension, which reduces uteroplacental perfusion. Prevention of hypotension is difficult because prehydration does not reliably reduce the incidence of hypotension. If hypotension occurs, ephedrine or phenylephrine can be used, and there may be a benefit to phenylephrine. The key is not which drug is chosen but that hypotension, if it occurs, is treated quickly.

General anesthesia should be preceded by careful evaluation of the airway, denitrogenation, and a rapid-sequence induction with the application of cricoid pressure,

if indicated by the emergent nature of the surgery or if signs of acid reflux are present. Because tracheal intubation may be technically difficult, an array of laryngoscope blades, handles, and other emergency airway management equipment should be available. The use of a nasal airway and nasotracheal intubation should be avoided. A high concentration of oxygen should be used (at least 50%), and $PaCO_2$ should be maintained at normal pregnancy levels (30–35 mm Hg). End-tidal carbon dioxide ($ETCO_2$) is an excellent approximation of $PaCO_2$ in a pregnant patient because the $PaCO_2$-$ETCO_2$ gradient decreases during pregnancy.

Cardiopulmonary bypass, hypothermia, and hypotensive techniques all have been performed successfully during pregnancy. These techniques should not be withheld if they are needed.

Epidural or subarachnoid opioids are an excellent choice for postoperative pain management because they cause minimal sedation, and smaller doses can be used compared with the intramuscular or intravenous routes. Nonsteroidal antiinflammatory drugs should be avoided because they may cause premature closure of the ductus arteriosus.

Regardless of the technique, maintenance of a normal intrauterine physiologic milieu throughout the perioperative period, including the avoidance of hypotension, hypoxemia, hypercarbia, hypocarbia, and hypothermia, is the key to a successful outcome.

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CASE 58

# Thrombocytopenia in Pregnancy

**Yaakov Beilin, MD**

## QUESTIONS

1. What is the concern when placing an epidural catheter if the platelet count is low?
2. Who is at risk for developing an epidural hematoma?
3. What is considered a low platelet count from the perspective of epidural catheter placement, and why is there controversy regarding choosing a lowest "safe" platelet count?
4. What is the expected platelet count during pregnancy?
5. Describe coagulation and the role platelets play in the process.
6. What are causes of thrombocytopenia during pregnancy?
7. What tests are available to evaluate platelet function?
8. Describe the thromboelastogram and its limitations.
9. Describe the platelet function analyzer and its limitations.
10. What is the overall risk of epidural hematoma?
11. Are there any cases of epidural hematoma in a parturient with thrombocytopenia?
12. What is the evidence that initiating an epidural anesthetic in a patient with a low platelet count may be safe?
13. How do you evaluate a patient who has a low platelet count?
14. What are practical recommendations regarding neuraxial anesthesia in a parturient who presents with a low platelet count?
15. What is low-molecular-weight heparin, and how does it compare with and differ from standard heparin?
16. Why do some pregnant women take low-molecular-weight heparin?
17. What has been the anesthetic experience with low-molecular-weight heparin and neuraxial anesthesia?
18. What are the unique recommendations for anesthetizing a parturient taking low-molecular-weight heparin?

A 22-year-old woman presented to the labor and delivery suite at 40 weeks' gestation with mild uterine contractions. The obstetricians decided to augment labor with oxytocin and requested an epidural anesthetic for labor analgesia. The patient's past medical history was significant for miscarriage during a previous pregnancy. Until 2 weeks ago, she had been receiving enoxaparin (Lovenox) injections, 30 mg twice a day. Her laboratory data were within normal limits except for a platelet count of 76,000 $mm^{-3}$.

### 1. What is the concern when placing an epidural catheter if the platelet count is low?

The concern when placing an epidural catheter in the face of a low platelet count is that if either the needle or the catheter punctured a blood vessel, the blood would not clot, leading to an epidural hematoma.

### 2. Who is at risk for developing an epidural hematoma?

Anyone who receives a spinal or epidural anesthetic is at risk for developing an epidural hematoma. Epidural hematoma is an extremely rare event and is generally associated with patients who have disorders of hemostasis. A patient with a clinically active coagulopathy is considered to have an absolute contraindication to regional anesthesia. However, many gray areas exist, and this is especially true in patients with thrombocytopenia.

### 3. What is considered a low platelet count from the perspective of epidural catheter placement, and why is there controversy regarding choosing a lowest "safe" platelet count?

An epidural hematoma is a potentially catastrophic complication, which can lead to permanent paralysis. It is prudent to practice in a conservative manner and refrain from epidural anesthesia if the patient is at increased risk of developing this complication. In 1988, Cousins and Bromage recommended against epidural anesthesia if the platelet count is $<100{,}000$ $mm^{-3}$. However, this recommendation has been widely disputed. Thrombocytopenia is the most common hematologic disorder during pregnancy. Choosing an absolute platelet count below which it is considered too dangerous to place a neuraxial anesthetic may dictate the use of general anesthesia, which carries its own risks in a parturient. A review of pregnancy-related deaths found that fatality rates for parturients administered general anesthesia for cesarean delivery were much

greater than fatality rates of parturients who received neuraxial anesthesia. Refraining from neuraxial anesthesia during labor and delivery commits the patient, at a minimum, to a painful labor. It is possible that later in the course of labor the woman may require a cesarean delivery, and then general anesthesia would likely be needed.

### 4. What is the expected platelet count during pregnancy?

Platelet count decreases by approximately 20% during normal pregnancy; most platelet counts remain >150,000 $mm^{-3}$. However, approximately 7% of all parturients present with a platelet count <150,000 $mm^{-3}$, and 0.5%–1% present with a platelet count <100,000 $mm^{-3}$.

### 5. Describe coagulation and the role that platelets play in the process.

Clotting can be thought of as occurring in two phases: primary and secondary hemostasis. Primary hemostasis is the creation of the initial platelet plug, and secondary hemostasis is the creation of the stable fibrin clot. Platelets play an important role in both processes. Generally, blood vessels prevent platelet adhesion by releasing a potent vasodilator, prostacyclin. After vessel wall injury, prostacyclin levels decrease, and platelets adhere to the vessel wall. Adhesion leads to activation and degranulation with release of adenosine diphosphate (ADP), serotonin, and thromboxane, which leads to platelet aggregation. Further aggregation leads to formation of a platelet plug. This plug is unstable and requires fibrin formation (secondary hemostasis), which occurs by activation of the intrinsic or extrinsic coagulation system. Platelets provide the phospholipid membrane on which the coagulation cascade occurs. Platelet abnormalities can be qualitative or quantitative and are the most common hematologic disorders during pregnancy.

### 6. What are the causes of thrombocytopenia during pregnancy?

Most cases (99%) of thrombocytopenia during pregnancy are related to one of three causes: hypertensive disorders such as preeclampsia, gestational thrombocytopenia, or idiopathic thrombocytopenic purpura (ITP). When evaluating a parturient with thrombocytopenia, there are two specific issues to consider. The first concern is whether the disorder is static or dynamic (Table 58-1). If the disorder is static, as occurs during gestational thrombocytopenia or ITP, the platelet count is usually stable. If the disorder is dynamic, as occurs during preeclampsia, the platelet count may change rapidly, and it is important to obtain serial platelet counts. The second issue is whether platelet function is normal or abnormal. Platelet function is typically normal in gestational thrombocytopenia and ITP and may be abnormal in preeclampsia.

### 7. What tests are available to evaluate platelet function?

A patient who presents with a platelet disorder is difficult to evaluate with standard laboratory tests because both platelet quantity and quality must be assessed. Tests of platelet function have been criticized for being difficult to perform, lacking reproducibility, and being of questionable clinical relevance. The ideal test would be easy to perform, would be inexpensive, and would not require specialized equipment, with results that could be reproduced and correlate with outcome. Bedside tests of coagulation include the thromboelastogram (Thrombelastograph; Haemoscope Corporation, Skokie, IL) and the platelet function analyzer (PFA-100; Dade Behring, Newark, DE).

TABLE 58-1 **Static versus Dynamic Thrombocytopenia**

| Disorder | Incidence | Process | Platelet Function |
|---|---|---|---|
| Gestational | 74% | Static | Normal |
| ITP | 4% | Static | Normal |
| Preeclampsia | 21% | Dynamic | Abnormal |

*ITP,* Idiopathic thrombocytopenic purpura

### 8. Describe the thromboelastogram and its limitations.

The thromboelastogram measures all phases of coagulation and fibrinolysis by using <1 mL of a whole blood sample to measure the shear elasticity of clotting blood. Blood is placed in a cylindrical cup that oscillates. A pin is suspended in the blood by a torsion wire and is monitored for motion. The torque of the rotating cup affects the pin only after fibrin-platelet bonding has linked the cup and pin together. The strength of the developing clot affects the magnitude of the pin motion such that strong clots move the pin directly in phase with the cup and weak clots do not. The resulting profile is a measure of the time it takes for the first fibrin strand to form, the kinetics of the clot, strength of the clot, and breakdown of the clot (Figure 58-1). The maximum amplitude (MA) has been found to correlate best with platelet function.

Orlikowski et al. (1996) measured platelet counts, thromboelastogram parameters, and bleeding times in healthy pregnant women and in women with preeclampsia. They found that the MA remains normal (53 mm) until the platelet count decreases to <54,000 $mm^{-3}$ (95% confidence limit, 40,000–75,000 $mm^{-3}$). Based on their study, they suggested that a platelet count of 75,000 $mm^{-3}$ should be associated with adequate hemostasis. However, there is no clinical evidence that a normal MA correlates with safe epidural anesthesia.

### 9. Describe the platelet function analyzer and its limitations.

The platelet function analyzer is specific for platelet function, the primary hematologic disorder of parturients. The machine simulates the in vivo hemostatic mechanism of platelet function by accelerating citrated

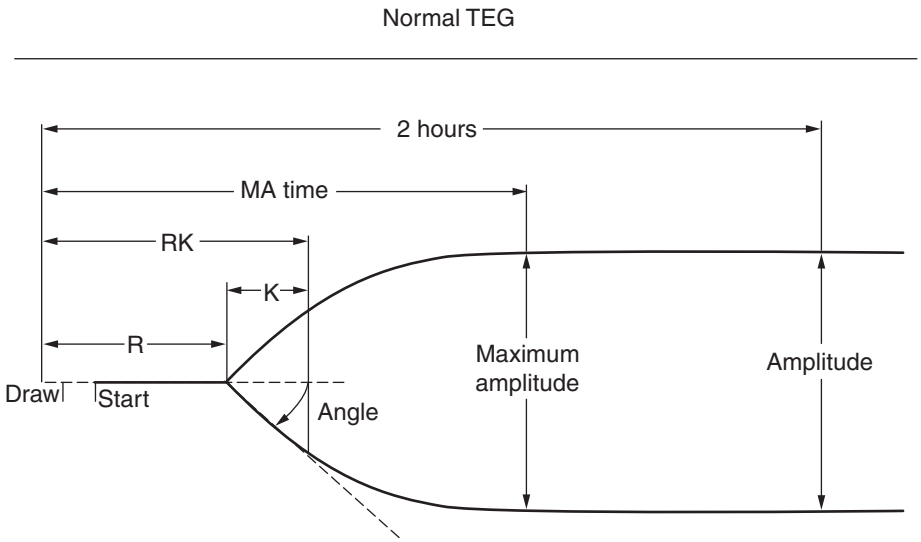


**FIGURE 58-1** ■ Thromboelastogram (TEG). *R* is time until the onset of clotting. *K* is time until the tracing amplitude reaches 20 mm. The angle between the tangent line drawn from the curve to the split point and the horizontal line of the tracing is measured in degrees. *MA* is the maximum amplitude, a measure of clotting strength. MA correlates best with platelet function.

whole blood through a 150-mm aperture in a collagen membrane. The collagen membrane is coated with one of two platelet activators: epinephrine or ADP. The cartridges are named for the platelet activator that coats them, CEPI or CADP. The time taken for the aperture to close is called the closure time. Reference range for the CEPI cartridge is 78–199 seconds and for the CADP cartridge is 55–137 seconds. This machine can be used as a screening tool for patients who present with unknown coagulopathies and is sensitive for the detection of von Willebrand disease. Studies in parturients have focused on defining the expected closure time in pregnancy and if there is a closure time that correlates with significant thrombocytopenia. Similar to the limitations of the thromboelastogram, there are no clinical studies defining specific closure times that correlate with epidural hematoma.

## 10. What is the overall risk of epidural hematoma?

The overall risk of spinal or epidural hematoma after neuraxial anesthesia is 1:150,000–250,000. Vandermeulen et al. (1994) reviewed the literature and found 61 cases of anesthesia-related epidural hematoma. Most cases (68%) occurred in patients with coagulopathies, and 75% of all patients with hematoma had an epidural rather than a spinal anesthetic. Of patients who received an epidural anesthetic, 88% had an epidural catheter inserted, and almost 50% of those patients developed an epidural hematoma after catheter removal.

## 11. Are there any cases of epidural hematoma in a parturient with thrombocytopenia?

There is one case in the literature of a woman with preeclampsia with a platelet count of 71,000 $mm^{-3}$ who received an epidural catheter for cesarean delivery and developed an epidural hematoma. The epidural catheter was placed without complication. The patient had a seizure in the postanesthesia care unit 1 hour after the procedure. There was no seizure activity in her lower extremities, and a computed tomography scan revealed an epidural collection. A laminectomy was performed 6 hours after epidural catheter placement, at which time 4 mL of blood was drained from the epidural space. The patient experienced a complete recovery. It is unlikely 4 mL of blood was sufficient to cause her symptoms, and it is more likely the symptoms were related to residual local anesthetic, but this cannot be proven.

## 12. What is the evidence that initiating an epidural anesthetic in a patient with a low platelet count may be safe?

The safety of initiating epidural anesthesia with a platelet count $<100{,}000$ $mm^{-3}$ is supported by three retrospective studies. In the largest study, Beilin et al. (1997) reviewed the medical records of 15,919 consecutive parturients during a 3-year period. Among 80 women who presented with a platelet count $<100{,}000$ $mm^{-3}$, 30 received an epidural anesthetic without sequelae. The lowest platelet count in the study was 69,000 $mm^{-3}$. These 30 women had certain characteristics in common. The platelet count did not decrease around the time of epidural catheter placement, and there was no clinical evidence of bleeding. In that study, five women were denied an epidural anesthetic because of a decreasing platelet count, and two women were denied an epidural anesthetic because of evidence of bruising.

## 13. How do you evaluate a patient who has a low platelet count?

A routine platelet count is unnecessary in an otherwise healthy parturient and should be drawn based on patient history, physical examination, and clinical signs. If the platelet count is found to be low, it is important to confirm

the result with a manual count. Automated counters can be unreliable, especially at lower platelet levels. The patient history and physical examination are key components when deciding whether to proceed with regional anesthesia in parturients with thrombocytopenia. Consultation with a hematologist, preferably before labor, can also help with assessing the etiology of thrombocytopenia and determining whether the platelets are functioning adequately. If there is a history of easy bruising or if the patient has petechiae or ecchymosis, regional anesthesia should not be offered. If the patient has no bleeding history, our general practice is to obtain at least one additional platelet count as close in time to epidural catheter placement as possible to ensure that it is not decreasing further. This additional platelet count is especially important for disease processes that are dynamic, such as preeclampsia. We do not obtain any bedside tests of platelet function, and we do not have any absolute platelet count cutoff. A patient with a stable platelet count of 50,000 $mm^{-3}$, as seen in ITP, is probably at lower risk than a patient with a platelet count of 75,000 $mm^{-3}$ that is rapidly decreasing, as seen in preeclampsia. Generally, I place an epidural catheter in women with stable platelet counts of approximately 75,000 $mm^{-3}$. Other physicians are comfortable with lower platelet counts, especially in women with ITP. There is no absolute cutoff, and the risks of epidural placement versus general anesthesia have to be individualized. Informed consent must be obtained.

### 14. What are practical recommendations regarding neuraxial anesthesia in a parturient who presents with a low platelet count?

If the decision is made to proceed with neuraxial anesthesia, a subarachnoid block using a small-caliber spinal needle is preferable to epidural anesthesia. This block is not always possible, especially for women in labor who require repeated doses of local anesthetic.

Epidural anesthetics should be placed using a midline technique. The lowest concentration of local anesthetic necessary to produce analgesia while preserving motor function is recommended. Patients should be examined every 1–2 hours for motor block, and these examinations should continue until after the anesthetic has worn off and the catheter has been removed. In this way, if the patient develops a motor block out of proportion to what one would expect or if the anesthetic has a prolonged duration of action, the patient can be immediately assessed with magnetic resonance imaging for the development of an epidural hematoma. Immediate evaluation is necessary because an emergent laminectomy and decompression must be performed within 6–12 hours to preserve function. If patients develop a coagulopathy with an indwelling epidural catheter, the catheter should be removed only after the coagulation parameters are corrected.

### 15. What is low-molecular-weight heparin, and how does it compare with and differ from standard heparin?

Standard unfractionated heparin (UH) is a mixture of linear polysaccharide chains, with a molecular weight of 5000–30,000. Heparin acts as an anticoagulant by binding to antithrombin III and potentiates the inhibition of factors IIa (thrombin), IXa, Xa, XIa, and XIIa. A specific pentasaccharide sequence on the heparin chain has a high-affinity binding site for antithrombin III; only about 30% of the heparin molecule has this sequence. To catalyze inhibition of factor Xa, only the pentasaccharide binding sequence is necessary. However, to catalyze inhibition of factor IIa, a heparin molecule must contain both this high-affinity pentasaccharide sequence and an additional chain of at least 13 sugars. UH is highly sulfated and negatively charged. As a result, it has a great affinity for plasma and vascular matrix proteins and has $<30\%$ bioavailability. Low-molecular-weight heparin (LMWH) is produced by chemical or enzymatic depolymerization of standard heparin, which produces shorter polysaccharide chains of 13–22 sugars and a molecular weight of 4000–6000. LMWH has the same anti-Xa activity as standard heparin with less anti-IIa (thrombin) activity. The concentration of LMWH is referred to in international standards and expressed as anti-Xa units per millimeter. The reduced molecular size leads to lower binding of plasma and endothelial cell proteins; this results in $>90\%$ bioavailability after subcutaneous injection, a longer plasma half-life (4–6 hours vs. 0.5–1 hour for standard heparin), and a predictable and reproducible dose response. Laboratory monitoring is not required. The peak LMWH anti-Xa activity occurs 3–4 hours after subcutaneous injection, and anti-Xa levels are approximately 50% of peak levels at 12 hours. LMWH excretion is almost solely via the kidneys. Protamine sulfate is able to neutralize 100% of anti-IIa activity but only 60%–70% of anti-Xa activity and is not effective at neutralizing LMWH effects.

### 16. Why do some pregnant women take low-molecular-weight heparin?

Pregnancy induces a state of hypercoagulability, but thromboembolic complications are rare. However, some parturients require anticoagulant medication during the antepartum period, such as patients with disorders of hemostasis, mechanical heart prostheses, or at high risk for venous thromboembolism. Additionally, anticoagulant medication is used in women with a history of fetal loss related to thrombophilia and hypercoagulable syndromes, such as antithrombin III deficiency, antiphospholipid syndrome, and protein C or S deficiency. Warfarin causes abnormal fetal development and congenital malformations during the first trimester, such as nasal hypoplasia and skeletal dysplasias. It also increases the risk of maternal and fetal hemorrhage when given during the peripartum period. Heparin and LMWH do not cross the placenta, are not teratogenic, and are unlikely to cause fetal hemorrhage. LMWH has gained widespread use in pregnancy and has certain advantages over UH. UH and LMWH have similar hemorrhagic complication rates and antithrombotic efficacy. However, LMWH, in contrast to UH, does not require laboratory monitoring because the response is predictable. Also, there is less risk of serious complications with LMWH, such as heparin-induced thrombocytopenia and osteoporosis.

**BOX 58-1 Summary of Recommendations of Consensus Conference Convened by the American Society of Regional Anesthesia and Pain Medicine Regarding Anticoagulants and Neuraxial Anesthesia and Analgesia, 2010**

1. The decision to perform a neuraxial block when a patient is receiving LMWH must be made on an individual basis by weighing the risk of spinal hematoma with the benefits of regional anesthesia for a specific patient.
2. Monitoring of the anti-Xa level is not recommended because it is not predictive of the risk of bleeding.
3. Concomitant medications known to potentiate bleeding, such as antiplatelet agents or oral anticoagulants, create an additional risk for the development of spinal hematoma.
4. If blood is seen during needle or catheter placement, the first dose of LMWH should be delayed for 24 hours.
5. If a patient is receiving LMWH preoperatively, neuraxial anesthesia should occur at least 10–12 hours after the last LMWH dose. Patients receiving high doses of LMWH, such as enoxaparin 1 mg/kg twice a day, require waiting longer (e.g., 24 hours).
6. A single-shot spinal technique may be the safest choice for neuraxial anesthesia.
7. The first dose of LMWH should be given ≥24 hours after neuraxial anesthesia. Indwelling catheters should be removed before initiation of LMWH; the first LMWH dose may be given 2 hours after catheter removal.
8. If a patient is receiving LMWH and has an indwelling catheter, the catheter should not be removed for at least 10–12 hours after the last dose of LMWH.

## 17. What has been the anesthetic experience with low-molecular-weight heparin and neuraxial anesthesia?

The release of LMWH for general use in the United States in May 1993 sparked a new challenge for anesthesiologists. Previously, spinal or epidural hematoma was a rare occurrence, reportedly <1 in 150,000–220,000. Enoxaparin, the first LMWH to be approved by the U.S. Food and Drug Administration (FDA), had been used for many years in Europe. However, the approved dosing schedule of enoxaparin was 30 mg (3000 units) every 12 hours in the United States as opposed to 40 mg (4000 units) once daily in Europe. Within 1 year of its introduction in the United States, two cases of epidural hematoma were voluntarily reported through the MedWatch system. The warning section of the drug label was revised, and a letter from the manufacturer was issued to practitioners to alert them to the risk of spinal hematoma in patients undergoing neuraxial anesthesia while receiving LMWH. Despite these warnings, 40 cases of perioperative neuraxial hematoma in patients on LMWH were voluntarily reported between May 1993 and November 1997. A FDA Health Advisory was issued in December 1997.

The actual risk of spinal or epidural hematoma in patients receiving LMWH while undergoing neuraxial anesthesia is difficult to estimate. There are likely additional, unreported cases. The reported incidences of spinal or epidural hematoma in patients receiving LMWH may be approximately 1 in 3000 for continuous epidural anesthesia and 1 in 40,000 for spinal anesthesia. Of the 40 cases of spinal or epidural hematoma associated with LMWH in conjunction with neuraxial anesthesia, 2 patients received epidural steroid injections; 6 underwent spinal anesthesia, 1 of which was continuous spinal anesthesia; 23 had continuous epidural anesthesia; 6 underwent unspecified techniques; and 3 had general anesthesia after attempted or failed neuraxial anesthesia. Also, some patients had additional risk factors for the development of spinal or epidural hematoma, such as difficult needle placement or administration of antiplatelet or anticoagulant medication. None of the patients was pregnant.

## 18. What are the unique recommendations for anesthetizing a parturient taking low-molecular-weight heparin?

Neuraxial anesthesia can be safely administered to a patient receiving LMWH if certain guidelines and precautions are met. The American Society of Regional Anesthesia and Pain Medicine (ASRA) convened a consensus conference on neuraxial anesthesia in 1998. The committee reconvened for a second consensus conference in 2002 and a third meeting in 2009. Following these meetings, recommendations regarding the administration of neuraxial anesthesia to patients receiving anticoagulation therapy were developed. These recommendations are summarized in Box 58-1.

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SECTION 11

# PEDIATRICS

CASE 59

# Abdominal Wall Defects

Renee L. Davis, MD

QUESTIONS

1. What are the differences between gastroschisis and omphalocele?
2. What are the preoperative concerns for these two defects?
3. How would you manage this neonate intraoperatively?
4. What is the surgical treatment for gastroschisis and omphalocele?

A 2-day-old, 3-kg neonate, born at 36 weeks' gestation, was brought to the operating room for surgical repair of an abdominal wall defect. The defect was at the base of the umbilicus and had a membranous covering.

## 1. What are the differences between gastroschisis and omphalocele?

Gastroschisis and omphalocele differ in their embryologic origin, location, and associated congenital anomalies. Fetal ultrasonography during the first trimester can distinguish the two defects from each other. Specificity for identifying gastroschisis and omphalocele by ultrasound is 95%, but sensitivity is only 60%–75%. Maternal alpha fetoprotein (AFP) levels may suggest a diagnosis of omphalocele or gastroschisis. High levels of AFP obtained during amniocentesis are associated not only with neural tube defects but also with abdominal wall defects.

At 5–10 weeks of gestational age, the midgut is extruded into the extraembryonic coelom. By 10 weeks of gestational age, the midgut normally returns to the abdominal cavity. Omphalocele results from failure of intestinal contents to migrate from the yolk sac into the abdominal cavity. Amnion covers the omphalocele and protects the abdominal contents from infection and loss of intracellular fluid. The bowel is morphologically and usually functionally normal. Omphalocele is located at the base of the umbilical cord and includes not only the intestines but also often parts of the liver and other organs. Omphalocele has a high association with congenital anomalies such as cardiac, craniofacial, and urologic defects and chromosomal abnormalities. Omphalocele associated with macroglossia, organomegaly, hypoglycemia, and mental retardation is known as Beckwith-Wiedemann syndrome. Omphalocele is also associated with advanced maternal age. Most mothers of infants with omphalocele are >30 years of age.

In contrast to omphalocele, gastroschisis develops later in fetal life, after the intestines have returned to the abdominal cavity, and has a higher incidence of prematurity. Gastroschisis develops from occlusion of the omphalomesenteric artery, resulting in ischemia and atrophy of abdominal wall layers. The abdominal wall defect, which is commonly located to the right of the umbilicus, permits abdominal viscera to herniate. The degree of herniation outside the peritoneal cavity varies from slight to major. There is no membranous covering of the intestines in gastroschisis resulting in loss of extracellular fluid and risk of infection. The intestines are edematous, dilated, inflamed, and functionally abnormal. Gut malrotation and volvulus are associated with gastroschisis. Gastroschisis is a neonatal emergency that requires immediate or urgent surgical intervention. Risk factors for gastroschisis include maternal age <20 years, maternal cigarette smoking, maternal illicit drug use, and maternal use of over-the-counter vasoactive drugs. Although no congenital anomalies are associated with gastroschisis, intestinal abnormalities such as malrotation, volvulus, and atresia can occur (Table 59-1).

## 2. What are the preoperative concerns for these two defects?

Management of neonates with these defects preoperatively focuses on reducing fluid losses and preventing infection, hypothermia, and trauma to the viscera. A warm moistened sterile dressing should be applied to the exposed viscera, and a sterile clear plastic bag should envelope the lower body of the infant to minimize temperature and fluid losses.

Neonates with abdominal wall defects are assessed for associated congenital anomalies, particularly cardiac and urologic problems. For preterm infants, respiratory abnormalities should be ascertained. Adequate intravenous access is established for fluid resuscitation. An arterial catheter may be necessary for frequent blood sampling, and a central venous catheter may be used to aid in fluid management. Significant electrolyte imbalances and fluid deficits should be corrected preoperatively. Neonates with gastroschisis may require multiple boluses of 20 mL/kg of balanced salt solution to replace evaporative and third space losses. Albumin is occasionally required for intravascular volume expansion.

TABLE 59-1 **Comparison of Omphalocele and Gastroschisis**

| | Omphalocele | Gastroschisis |
|---|---|---|
| Etiology | Failure of gut migration from yolk sac to abdominal cavity | Occlusion of omphalomesenteric artery |
| Incidence | 1:3000–1:10,000 | 1:15,000–1:30,000 |
| Epidemiology | Advanced maternal age | Young maternal age |
| Gender | Male > Female | Associated with maternal smoking and illicit drug use<br>Male = Female |
| Location | Base of umbilical cord<br>Peritoneal covering | Periumbilical (usually to the right of umbilical cord)<br>No peritoneal covering |
| Anomalies | High association with congenital anomalies<br>Beckwith-Wiedemann syndrome<br>Chromosomal abnormalities | Malrotation<br>Volvulus<br>Atresia |

### 3. How would you manage this neonate intraoperatively?

The operating room should be warmed, and a forced air warming blanket should be placed on the operating room table. Standard American Society of Anesthesiologists monitors should be placed, and gastric decompression should be performed to prevent distention and aspiration. A rapid-sequence induction with cricoid pressure followed by intubation or an awake intubation should be performed. The choice of intravenous induction agent depends on the medical condition and volume status of the neonate. Muscle relaxation can be achieved with either succinylcholine or a double dose of rocuronium (1.2 mg/kg). When succinylcholine is administered, many anesthesiologists precede it with an anticholinergic (e.g., atropine) because neonates have an immature sympathetic nervous system putting them at risk of developing bradycardia during suctioning, induction, and laryngoscopy and after succinylcholine administration. Rocuronium provides adequate intubating conditions within 60–90 seconds, although significant desaturation may occur requiring positive pressure breaths before intubation. Laryngoscopy is performed with either a Miller No. 0 or 1 laryngoscope blade, and a 3.0–3.5 uncuffed tracheal tube or a 3.0 cuffed tube is placed. An air leak of 20–30 cm $H_2O$ is desirable.

Nitrous oxide should be avoided because it diffuses into intestines (closed space) faster than nitrogen escapes into the circulation, resulting in intestinal distention. A mixture of air and oxygen should be used to maintain oxygen saturation between 95%–100% and arterial oxygen tension ($PaO_2$) <100 mm Hg.

Intraoperative fluid management should consist of maintenance fluid, replacement of third space loss, and blood to match losses as needed. Maintenance fluid volume is determined based on the patient's weight (Table 59-2).

Surgery is associated with the transfer of isotonic fluids from the intravascular space to a nonfunctional extravascular compartment. This nonfunctional compartment is referred to as third space loss. Replacement of third space loss should begin with balanced salt solutions at 8–15 mL/kg per hour, although a neonate with omphalocele or gastroschisis may require 5–10 times this amount. Although hypoglycemia is a concern in a neonate with diminished glycogen stores, *only* maintenance fluids should contain glucose, whereas balanced salt solutions are used for third space losses. The amount of maintenance glucose needed may be reduced during surgical procedures because of catecholamine release that tends to increase blood glucose.

TABLE 59-2 **Maintenance Fluid Requirement**

| Patient's Weight (kg) | Hourly Fluid Requirement |
|---|---|
| <10 | 4 mL/kg per hour |
| 11–20 | 40 mL + 2 mL/kg per hour for each kg between 11 and 20 kg |
| >20 | 60 mL + 1 mL/kg per hour for each kg >20 kg |

Maintenance anesthesia can be accomplished with various intravenous drugs and volatile anesthetics. The exact selections are determined by the neonate's medical condition and comorbidities. Muscle paralysis providing for maximal abdominal relaxation is important because primary closure of the defect is preferable.

The decision to transfuse blood should be based on the patient's blood volume (Table 59-3), preoperative hematocrit, and maximum allowable blood loss. Maximum allowable blood loss is a function of the patient's total blood volume, starting hematocrit, and the lowest acceptable hematocrit taking into account the patient's age and comorbidities, as follows:

$$\text{MABL} = \frac{\text{EBV} \times \text{HCT}_\text{S} - \text{HCT}_\text{L}}{\text{HCT}_\text{S}}$$

where *MABL* is maximum allowable blood loss, *EBV* is estimated blood volume, $HCT_S$ is starting hematocrit, and $HCT_L$ is lowest acceptable hematocrit.

TABLE 59-3 **Estimated Blood Volume**

| Age | EBV (mL/kg) |
|---|---|
| Preterm | 100 |
| Full-term | 90 |
| Infant | 80 |
| >1 year | 70 |

*EBV,* Estimated blood volume.

If blood loss is replaced with crystalloid, 3 mL of crystalloid should be administered for each 1 mL of blood lost. However, if replacing blood loss with blood, the replacement should be 1 mL of transfused blood for each 1 mL of blood lost. Frequent assessment of volume status consisting of clinical examination, vital signs, urine output, and laboratory values should be done throughout the case.

### 4. What is the surgical treatment for gastroschisis and omphalocele?

The surgical treatment for gastroschisis and omphalocele is either primary or staged closure. If the abdominal wall defect is small, complete reduction and repair is possible. Depending on comorbidities, the patient's trachea may be extubated at the end of the procedure. If a large defect is closed primarily, mechanical ventilation with muscle relaxation should be continued into the postoperative period. Mechanical ventilation may be required for 3–7 days.

A tight primary closure could increase intraabdominal pressure, decreasing ventilatory reserves. Changes in peak airway pressure should be monitored during abdominal closure. Increased intraabdominal pressure could decrease perfusion to intestines, kidneys, and liver. Impaired organ function may alter drug metabolism and lead to prolonged drug effects. A decrease in urine output may be secondary to decreased intravascular volume or decreased renal perfusion. Additionally, a decrease in venous return from the lower body may occur. Visualization of the lower extremity and pulse oximetry of the foot can aid in monitoring circulation to the lower extremity during closure.

The decision to close the defect primarily can be aided by measuring intragastric pressure. A pressure <20 mm Hg should allow for successful closure without excessive intraabdominal pressure. Other measurements such as changes in central venous pressure, peak airway pressure, and end-tidal carbon dioxide can be used to assist in the decision to close the abdomen primarily or not.

If the defect is large, underdevelopment of the abdominal muscles and peritoneum may preclude return of abdominal viscera to the peritoneal cavity and preclude primary closure. In this case, a prosthetic silo is placed to cover the exposed viscera. The size of the silo is reduced in stages every 2–3 days in the intensive care unit. This gradual reduction allows the abdominal cavity to accommodate viscera without resulting in an excessive intraabdominal pressure that would impede ventilation and impair organ perfusion. After most of the intraabdominal contents are reduced, the patient is brought to the operating room for closure of the defect. At the end of this procedure, if there are no significant comorbidities, the tracheal tube can be removed.

There has been a subset of gastroschisis patients more recently for whom a silo was placed in the neonatal intensive care unit. Reduction of intraabdominal contents occurred on a daily basis, and the neonate was brought to the operating room only for closure of the abdominal defect.

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CASE 60

# Congenital Diaphragmatic Hernia

**Francine S. Yudkowitz, MD, FAAP**

## QUESTIONS

1. Describe the embryology and pathophysiology of congenital diaphragmatic hernia.
2. What are the clinical features of congenital diaphragmatic hernia?
3. How is congenital diaphragmatic hernia diagnosed?
4. What is the preoperative management of a neonate with congenital diaphragmatic hernia?
5. What is permissive hypercapnia?
6. What are the anesthetic considerations for neonates with congenital diaphragmatic hernia?
7. What problems may occur intraoperatively and postoperatively?
8. Describe the techniques for fetal surgery.

A full-term, 3-kg infant born vaginally was noted to be cyanotic despite being given blow-by 100% oxygen and adequate respiratory effort. On closer inspection, the infant was observed to have a scaphoid abdomen. On physical examination, there were no breath sounds on the left, and the heart sounds were shifted to the right. The trachea was intubated, and the neonate was brought to the neonatal intensive care unit (NICU) for further evaluation and management.

### 1. Describe the embryology and pathophysiology of congenital diaphragmatic hernia.

The incidence of congenital diaphragmatic hernia (CDH) is 1 in 2000 to 1 in 5000 live births. There may be associated congenital anomalies of the central nervous, gastrointestinal, genitourinary, and cardiovascular systems. Chromosomal anomalies also may be present. In the fetus, during the first month of life, there is a single pleuroperitoneal cavity. During the second month, the pleuroperitoneal membrane begins to form, separating the pleural and peritoneal cavities. The last portion of this membrane to form is the posterolateral portion; the right side closes before the left side. The fetal gut is outside the pleuroperitoneal cavity in the yolk sac during the first month of fetal life and returns to the peritoneal cavity during the second month of development. If the gut returns before full closure of the pleuroperitoneal membrane, any or all portions of the gut may migrate up into the pleural cavity. There are three sites where migration of the gut may occur:

- Posterolateral (foramen of Bochdalek)
- Anteromedial (foramen of Morgagni)
- Esophageal hiatus

The most common site of migration (80%) is through the posterolateral portion, the left side more commonly than the right. Approximately 1% of diaphragmatic hernias occur through the anteromedial portion, and the remaining cases occur through the esophageal hiatus (Table 60-1).

Lung development is impaired by the presence of abdominal contents in the pleural cavity during fetal growth. The degree of impairment of lung development is determined by both the amount of abdominal contents in the pleural cavity and the time of migration. The greater the amount of abdominal contents in the pleural cavity and the earlier the migration, the greater the degree of pulmonary hypoplasia that is present at birth. Not only is the ipsilateral lung affected, but also there are developmental changes in the contralateral lung. These changes include the following:

- Decreased number of bronchi and alveoli
- Smaller pulmonary artery
- Inappropriately muscularized pulmonary arteries
- Decreased cross-sectional area of pulmonary artery branches

The physiologic changes that occur secondary to developmental changes in the lung are an increase in pulmonary vascular resistance (PVR) and persistent pulmonary hypertension. Decreased pulmonary blood flow and right-to-left shunting through the foramen ovale and ductus arteriosus contribute to progressive hypoxia and acidosis. These physiologic changes can be divided into two components: (1) irreversible (owing to pulmonary hypoplasia and abnormal vasculature) and (2) reversible (owing to vasoconstriction of abnormal muscularized arteries). The greater the irreversible component, the poorer the prognosis. To date, there is no method available to determine accurately which component is predominant.

Although compression of the lung by abdominal contents in the pleural cavity is detrimental, it does not contribute significantly to hypoxia and acidosis. CDH is no longer considered a surgical emergency. The initial management of these neonates is directed at improving oxygenation and ventilation. Surgery should be considered only after stabilization of the neonate's condition.

TABLE 60-1 **Types of Diaphragmatic Hernia**

| Type | Location | Frequency |
|---|---|---|
| Foramen of Bochdalek | Posteromedial | 80% |
| Foramen of Morgagni | Anteromedial | 1% |
| Esophageal hiatus | | 19% |

In a stable neonate, surgery is usually scheduled in the next 24–48 hours.

### 2. What are the clinical features of congenital diaphragmatic hernia?

The manifesting symptom of CDH is respiratory distress, with tachypnea and cyanosis, in the neonatal period (Box 60-1). On visual inspection, the abdomen may appear scaphoid and the thorax barrel-shaped. On physical examination, breath sounds are absent on the affected side (most commonly the left side), and the cardiac impulse is shifted to the opposite side of the defect (most commonly the right side). Bowel sounds on the affected side are an uncommon finding.

The onset of respiratory symptoms correlates well with the degree of lung hypoplasia and with prognosis. The earlier the symptoms manifest, the greater the degree of lung hypoplasia is present. Neonates presenting in the first hour of life have the highest mortality.

### 3. How is congenital diaphragmatic hernia diagnosed?

The diagnosis of CDH may be made prenatally or postnatally. With the increased use of ultrasonography in the prenatal period, prenatal diagnosis of CDH is more common. Findings consistent with a diagnosis of CDH are polyhydramnios, visualization of the fetal stomach in the thorax, and shift of the mediastinum away from the side of the hernia. A poor prognosis can be anticipated if the liver is seen in the thorax and there is a low lung-to-head ratio.

Postnatally, the diagnosis should be considered if the above-described clinical features are present. Definitive diagnosis is made by chest radiograph showing abdominal contents in the thoracic cavity.

### 4. What is the preoperative management of a neonate with congenital diaphragmatic hernia?

In the delivery room, when the diagnosis of CDH is suspected, mask ventilation should be avoided to prevent distention of the abdominal organs in the thorax, which would further impair oxygenation and ventilation (Box 60-2). The trachea should be intubated, and inflation pressures should be limited to <40 cm $H_2O$ to avoid causing a pneumothorax. A pneumothorax is most likely to occur in the contralateral lung, which is where most of the gas exchange occurs. An orogastric tube should be inserted to assist in deflation of the stomach. If transfer to the NICU is delayed, an arterial and intravenous catheter should be inserted to guide therapy and to administer pharmacologic agents. If possible, the arterial catheter should be placed in the right radial artery so that preductal oxygenation is measured.

Measures both to prevent further increases in PVR and to promote a decrease in PVR, increasing pulmonary blood flow, should be instituted. These measures include increased oxygenation, hypocarbia, alkalosis, avoidance of sympathetic stimulation, and normothermia (Box 60-3). Pharmacologic vasodilator therapy may be necessary. Tolazoline is most commonly used for this purpose. However, systemic hypotension may be associated with its use, and volume replacement and pharmacologic support of the systemic blood pressure may be necessary. Fluid replacement should be performed judiciously to avoid volume overload and pulmonary edema. Inhaled nitric oxide, a specific pulmonary vasodilator, has been used in these patients with variable results. The benefit of nitric oxide is that systemic hypotension is avoided. If these measures do not improve the neonate's condition, extracorporeal membrane oxygenation (ECMO) may be used. ECMO provides the neonate with adequate gas exchange while allowing the lungs to rest and mature.

### 5. What is permissive hypercapnia?

Permissive hypercapnia is an alternative modality in the treatment of neonates with CDH. Conventional ventilatory management resulted in pulmonary barotrauma secondary to high inspiratory pressures needed to achieve adequate ventilation and oxygenation. In permissive hypercapnia, the arterial carbon dioxide tension ($PaCO_2$)

**BOX 60-1 Clinical Features of Congenital Diaphragmatic Hernia**

- Tachypnea
- Cyanosis
- Scaphoid abdomen
- Barrel chest
- Absence of breath sounds on affected side
- Heart sounds shifted to opposite side of defect
- Bowel sounds in thorax (uncommon finding)

**BOX 60-2 Delivery Room Management**

- Avoid bag and mask ventilation
- Perform tracheal intubation
- Maintain peak inspiratory pressures <40 cm $H_2O$
- Insert orogastric tube
- Transfer to NICU for stabilization

**BOX 60-3 Factors Adversely Affecting Pulmonary Vascular Resistance**

- Hypoxia
- Hypercarbia
- Acidosis
- Hypothermia
- Sympathetic stimulation

is allowed to increase, while maintaining adequate oxygenation and acid-base balance. The benefit of this technique is that lower peak inspiratory pressures are used resulting in less pulmonary barotrauma. The goal during permissive hypercapnia is to maintain a preductal oxygen saturation of >90%. Acid-base balance is maintained with either bicarbonate or tris(hydroxymethyl) aminomethane (THAM). With this technique, PVR may not be maximally lowered, but it may allow for sufficient pulmonary blood flow to achieve adequate oxygenation. If the above-mentioned goals are unattainable, conventional treatment modalities for reducing PVR should be instituted.

## 6. What are the anesthetic considerations for neonates with congenital diaphragmatic hernia?

Surgery may be scheduled after the patient is stabilized. Most surgeons prefer a transabdominal approach. The abdominal organs are reduced, and the diaphragm is repaired either primarily or with a synthetic patch. In most cases, the abdominal wall can be closed primarily, but in some instances a Silastic pouch may be created.

In the last decade, thoracoscopic repair has gained increasing popularity. However, this method of repair is associated with a longer duration of surgery and a higher rate of recurrence. Insufflation of carbon dioxide to 3 mm Hg was sufficient to reduce the intrathoracic viscera into the abdomen. No clinically significant increase in $PaCO_2$ occurred.

Anesthetic management of patients (Box 60-4) includes continuation of preoperative measures to improve oxygenation and ventilation and to promote a decrease in PVR. To reduce excessive ventilator pressures, small tidal volumes and rapid respiratory rates may be necessary. If permissive hypercapnia was employed, these measures should be continued intraoperatively. Pharmacologic infusions should be continued. Arterial blood gases should be monitored frequently, and any changes in ventilation, oxygenation, and acid-base balance should be treated expeditiously. It is important to avoid hypoxia and acidosis, which would lead to an increase in PVR that would be very difficult to reverse. Measures to prevent hypothermia are also important in the management of these patients.

All anesthetic agents may be used in these neonates with the exception of nitrous oxide. Nitrous oxide may cause intestinal distention, which could compromise the neonate and impede abdominal closure. However, depending on the neonate's cardiovascular stability, inhalation agents may not be tolerated well. In most cases, an oxygen–opioid–muscle relaxant combination would be optimal.

**BOX 60-4 Anesthetic Management**

- Prevent increases in PVR
  - Adequate oxygenation
  - Hyperventilation
  - Alkalosis
- Maintain normothermia
- Continue pharmacologic infusions
- Avoid nitrous oxide

## 7. What problems may occur intraoperatively and postoperatively?

Meticulous attention should be paid to adequate oxygenation and ventilation of these neonates. There is an increased risk for pneumothorax, especially on the contralateral side. If this should occur, it would be life-threatening. Use of ventilation pressures >40 cm $H_2O$ should be avoided so as not to cause a pneumothorax. No attempt should be made to inflate the contralateral lung manually because of this potentially life-threatening risk. A diagnosis of pneumothorax should be considered when any abrupt change in the neonate's condition occurs during surgery. When in doubt of the diagnosis, a needle should be inserted into the contralateral chest. This maneuver both diagnoses the presence of a pneumothorax and treats pneumothorax. A chest tube should be placed after the diagnosis is made.

Postoperatively, these neonates may continue to require oxygen and ventilatory support. Pulmonary hypertension may persist, and there may be continued clinical deterioration despite surgical correction. This deterioration is due to the severe pulmonary hypoplasia that existed preoperatively and the change in pulmonary mechanics after surgery.

## 8. Describe the techniques for fetal surgery.

Two techniques for fetal correction of CDH have been described. The first technique is surgical correction of the diaphragmatic defect and reduction of the abdominal contents into the abdominal cavity. This technique cannot be performed if the liver is in the thoracic cavity because it would result in compromised flow through the umbilical vein. The second technique is tracheal occlusion, which has been shown to result in lung development. However, this technique has been fraught with problems and is not widely used.

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CASE 61

# Tracheoesophageal Fistula

Michael Chietero, MD

QUESTIONS



A 1-day-old, 3.3-kg neonate presented to the operating room for repair of tracheoesophageal fistula (TEF). The patient was born at 38 weeks gestation by normal vaginal delivery.

## 1. What is a tracheoesophageal fistula?

TEF is a congenital malformation involving esophageal atresia (EA) combined with a fistula connecting the esophagus to the trachea. These abnormalities can occur in various combinations. The most common classification system of TEFs is Gross' classification (Figure 61-1). Table 61-1 describes the various types of TEF and their approximate incidence. The most common type, EA with a distal fistula (Gross type C), accounts for approximately 80% of cases.

The incidence of EA and TEF is approximately 1 in 3000 births. Embryologically, the trachea and esophagus both originate from the ventral diverticulum of the primitive foregut. They normally become separated by the esophagotracheal septum. Because the trachea is situated anterior to the esophagus, the fistula is located on the posterior aspect of the trachea and usually just proximal to the carina.

## 2. What is the typical presentation of a patient with a tracheoesophageal fistula?

In contrast to other congenital anomalies, it is difficult to diagnose TEF in utero. Polyhydramnios is often present because EA prevents the fetus from swallowing amniotic fluid. At delivery, an orogastric tube cannot be passed into the stomach. Typically, the orogastric tube passes only to a distance of approximately 10 cm from the gums. In most cases, the diagnosis is initially suspected at the first feeding, when the neonate presents with coughing, choking, and cyanosis (the "three Cs"). Excessive salivation and respiratory distress can also occur.

Confirmation of the diagnosis is made radiographically when a radiopaque orogastric catheter is seen curled in the proximal esophageal pouch. The presence of air in the stomach and intestines on radiography signifies the presence of a fistula between the trachea and distal esophagus (Gross types C and D). Absence of air in the stomach occurs with cases of EA without a distal fistula (Gross types A and B). The "H"-type fistula (TEF without atresia, Gross type E) usually manifests later in life, most commonly with choking during feedings and recurrent pneumonitis.

## 3. What are the preoperative concerns in patients with tracheoesophageal fistula?

There is a 30%–50% incidence of associated anomalies in infants with EA and TEF. Particular combinations have been described, termed VATER association or, more exactly, VACTERL association (Table 61-2).

The approximate incidence of associated anomalies is shown in Table 61-3. The prevalence of congenital heart disease often necessitates an electrocardiogram (ECG) and echocardiogram preoperatively. In addition, because renal anomalies can also occur, evaluation of renal function should be documented. Finally, because of the potential for vertebral malformations, a lumbar ultrasound may be indicated if a sacral dimple is present. A lumbar ultrasound is especially indicated if a thoracic epidural catheter placed via the caudal route is planned for postoperative analgesia.

Pulmonary complications can have important implications for the anesthesiologist. Atelectasis from gastric distention and aspiration from regurgitation are common pulmonary complications; both lead to reduced pulmonary compliance and ventilation/perfusion ($\dot{V}/\dot{Q}$) mismatching. Preoperative management of patients with TEF primarily involves preventing pulmonary complications until surgery is performed. Management includes the following:

- Cessation of feeding
- Positioning the infant slightly head up (30 degrees) to minimize regurgitation of gastric contents through the fistula
- Intermittent suctioning of the proximal esophageal pouch catheter

There is also an increased incidence of prematurity in patients with TEF, especially in patients who have

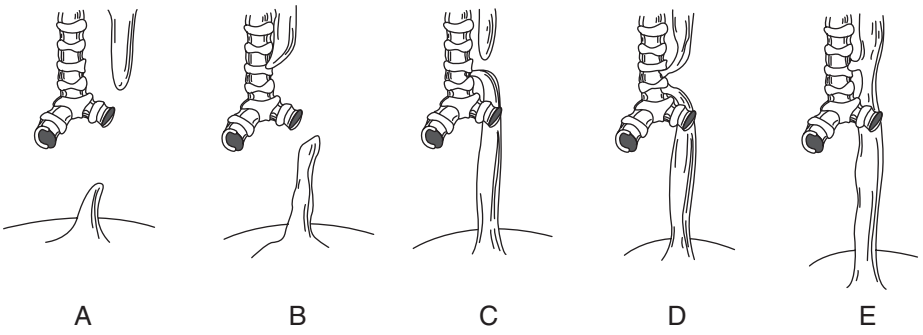


**FIGURE 61-1 ■ A-E,** Gross' classification of TEF. (From Gregory GA. Pediatric anesthesia, 4th ed. New York: Churchill Livingstone; 2002.)

TABLE 61-1 **Type and Incidence of Esophageal Atresia and Tracheoesophageal Fistula**

| Type | Incidence (%) | Description |
|---|---|---|
| A | 10 | EA without fistula |
| B | 1 | EA with proximal fistula |
| C | 80 | EA with distal fistula |
| D | 2 | "K" type, EA with proximal and distal fistula |
| E | 7 | "H" type, fistula without atresia |

*EA,* esophageal atresia.

TABLE 61-2 **VACTERL Association**

| | |
|---|---|
| V | Vertebral (vertebral malformations, hemivertebrae) |
| A | Anal (imperforate anus, also midgut malrotation, Meckel diverticulum) |
| C | Cardiac (VSD, PDA, TOF, ASD, right-sided aortic arch, coarctation of aorta) |
| T | Trachea (TEF) |
| E | Esophagus (EA) |
| R | Renal (renal agenesis, hydronephrosis, renal lobulation) |
| L | Limb (radial aplasia, polydactyly, wrist anomalies) |

*ASD,* atrial septal defect; *EA,* esophageal atresia; *PDA,* patent ductus arteriosus; *TEF,* tracheoesophageal fistula; *TOF,* tetralogy of Fallot; *VSD,* ventricular septal defect.

TABLE 61-3 **Incidence of Associated Anomalies**

| Anomaly | Incidence (%) |
|---|---|
| Cardiovascular | 35 |
| Musculoskeletal | 30 |
| Gastrointestinal | 20 |
| Genitourinary | 10 |
| Craniofacial | 4 |

associated anomalies. All the concerns of prematurity are applicable to this situation (see Chapter 64).

### 4. How are patients with tracheoesophageal fistula managed intraoperatively?

Optimal surgical management is a one-stage repair in which the fistula is ligated, and the proximal and distal ends of the esophagus are anastomosed primarily. The approach is typically through a right thoracotomy incision, with the patient in the left lateral decubitus position. In the presence of a right aortic arch, a left thoracotomy may be performed. The repair can also be performed thoracoscopically. Staged repair may be necessary in cases where the gap between atretic esopheageal pouches is too long for primary closure.

Anesthetic management includes warming the operating room and warming blankets. Standard American Society of Anesthesiologists monitors are applied. If one is not already present, an intravenous catheter is placed before induction. Invasive blood pressure monitoring may be necessary in high-risk infants or in infants undergoing thoracoscopic repair. A precordial stethoscope should be securely positioned in the left axilla for detection of intraoperative airway obstruction. The esophageal pouch is suctioned, and the patient is preoxygenated. Atropine, 0.02 mg/kg, may be administered intravenously to prevent bradycardia during laryngoscopy.

In the past, a gastrostomy tube was placed to decompress the stomach. However, this maneuver essentially created a bronchocutaneous fistula, which could result in further loss of tidal volume during positive pressure ventilation. If sufficient tidal volume was lost, the gastrostomy tube would be clamped. Previously a common practice, gastrostomy tubes are usually omitted in current practice because the gastrostomy may increase the incidence of gastroesophageal reflux later in life. If gastrostomy is performed, it is usually accomplished under local anesthesia before induction. The gastrostomy can then be used to aid in placing the endotracheal tube (ETT). If gastric distention does not impair ventilation, the surgeon may perform gastrostomy after induction of general anesthesia.

Optimal anesthetic management of these patients calls for maintenance of spontaneous ventilation until the fistula is ligated. Positive pressure ventilation is best avoided, if possible, because it can result in insufflation of the stomach via the fistula or loss of ventilation through the gastrostomy; this is especially true in patients with either large fistulas or poor pulmonary compliance. Gastric distention may compromise ventilation and may lead to aspiration of gastric contents via the fistula. However,

maintaining spontaneous ventilation during intubation, thoracotomy, or thoracoscopy, can be challenging, and many cases go well with gentle positive pressure ventilation by hand without significant gastric distention.

Awake intubation is the safest approach. It allows airway reflexes to be maintained and allows appropriate positioning of the ETT without positive pressure ventilation. During laryngoscopy, supplemental oxygen can be administered via a side port found on certain laryngoscope blades (oxyscope). However, awake intubation may be difficult and traumatic in vigorous infants. Alternatively, inhalation or intravenous induction may be performed without muscle relaxation, allowing for spontaneous breathing. If a muscle relaxant is used, care must be taken during positive pressure ventilation to avoid excessive insufflation of the stomach via the fistula.

Placement and positioning of the ETT can be difficult. To avoid intubating the fistula, which is located on the posterior aspect of the trachea, the ETT should be inserted with the bevel facing posteriorly. After intubation, the ETT (without a Murphy eye) is rotated so that the bevel is facing anteriorly to avoid ventilating the fistula.

Because the fistula is usually located just proximal to the carina, positioning the ETT so that it is above the carina but still occluding the fistula is often challenging. One commonly used method is to insert the ETT into the right main stem bronchus and then gradually withdrawing it until breath sounds are heard on the left. However, this does not always ensure that the ETT occludes the fistula. If a gastrostomy tube is in place, the distal end can be submerged in a beaker of water; if bubbling occurs, there is leakage through the fistula. The ETT is advanced until the bubbling ceases while still maintaining left-sided breath sounds. The gastrostomy tube may be left to water seal during surgery, which allows continued monitoring for ventilation through the fistula.

A better method of confirming placement of the ETT is with a fiberoptic bronchoscope. After intubation, the fiberoptic bronchoscope is passed through the ETT, and the carina is visualized. On withdrawal of the bronchoscope, if the fistula is not visualized, the ETT is appropriately positioned. If the fistula is visualized, the ETT is advanced making sure that its tip remains above the carina. Alternatively, the ETT can be placed, with the aid of the fiberoptic scope, into the left main stem bronchus, and the patient can be managed with one-lung ventilation. This alternative provides a still operative field during surgery, which is particularly beneficial with thoracoscopy.

Sometimes with a large fistula that is located at or distal to the carina, placement of the ETT to avoid ventilating the fistula is impossible. In this situation, the fistula may need to be occluded with a Fogarty balloon catheter placed from above with the help of a bronchoscope or from below through the gastrostomy.

Once positioned, the Fogarty catheter should be carefully secured because it can dislodge easily. After the patient is positioned in the left lateral decubitus position, reconfirmation of the position of the ETT and the Fogarty catheter may be necessary.

Maintenance of anesthesia can be accomplished with inhalation anesthesia, typically with the judicious addition of opioids. The administration of muscle relaxants should be delayed until the fistula is ligated.

**BOX 61-1 Intraoperative Concerns**

- Operating room setup
  - Warm room
  - Warming blanket
  - Fluid warmer
  - Arterial catheter (?)
- Intubation
  - Awake versus after induction
  - Maintain spontaneous ventilation
  - Positioning of ETT
    - Proximal to carina, occluding the fistula
    - Right main stem intubation and withdrawal
    - Left main stem intubation with one-lung ventilation
  - Confirmation
    - Fiberoptic bronchoscopy
    - Gastrostomy to water seal
- Occlusion of fistula
  - Fogarty catheter via trachea or through gastrostomy
- Loss of breath sounds and end-tidal carbon dioxide tracing
  - Secretions or blood in ETT
  - Kinking of the trachea during surgical manipulation

Loss of breath sounds and the end-tidal carbon dioxide tracing commonly occurs during surgery secondary to airway obstruction. This may be due to the accumulation of secretions or blood in the ETT. More often, however, it results from kinking of the trachea during surgical manipulation. The surgeon should immediately be instructed to release the surgical traction (Box 61-1).

### 5. What are the postoperative concerns in patients with tracheoesophageal fistula?

Postoperative management of patients with TEF depends on the degree of pulmonary dysfunction and the presence of associated anomalies. In healthy, vigorous infants, extubation of the trachea at the completion of surgery is not only possible but also desirable to decrease stress at the surgical anastomosis. More compromised patients, such as patients with complex congenital heart disease, preoperative pulmonary complications, prematurity, and low birth weight, may require postoperative intubation and ventilation.

Postoperative pain management may be accomplished by either neuraxial analgesia or intravenous opioids. For neuraxial analgesia, a thoracic epidural catheter is placed via the caudal approach. Position of the catheter should be confirmed radiographically before starting an infusion of local anesthetic and opiate solution. Postoperative survival in healthy infants approaches 100% but may be affected by prematurity, severity of pulmonary dysfunction, and associated anomalies.

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CASE 62

# Pyloric Stenosis

**Francine S. Yudkowitz, MD, FAAP**

QUESTIONS

1. What is pyloric stenosis?
2. What is the clinical presentation of pyloric stenosis?
3. How is the diagnosis made?
4. What metabolic derangements are associated with pyloric stenosis, and how are they treated?
5. What is the surgical treatment for pyloric stenosis?
6. What are the anesthetic considerations for patients with pyloric stenosis?

A 4-week-old infant presented for pyloromyotomy. The patient had a 3-day history of nonbilious, projectile vomiting.

## 1. What is pyloric stenosis?

Pyloric stenosis is caused by circular muscular hypertrophy at the pylorus. It produces gastric outlet obstruction. Pyloric stenosis usually manifests between 2 and 6 weeks of age but can manifest earlier. There is a higher incidence in male infants.

## 2. What is the clinical presentation of pyloric stenosis?

Symptoms may begin with regurgitation, which progresses to nonbilious, projectile vomiting. Jaundice may occur in 5% of infants secondary to hepatic gluconyltransferase deficiency. Jaundice usually resolves after treatment.

## 3. How is the diagnosis made?

On physical examination, an olive-like mass can be palpated in the epigastrium just right of the midline. The diagnosis can be confirmed either by ultrasound or by barium swallow. However, barium swallow adds to the risk of aspiration pneumonitis in the perioperative period.

## 4. What metabolic derangements are associated with pyloric stenosis, and how are they treated?

Vomiting from pyloric stenosis usually leads to hypovolemia and a hypochloremic, hypokalemic metabolic alkalosis. Because the vomitus consists only of gastric contents, hydrogen, sodium, potassium, and chloride ions are lost. Initially, the renal response is to maintain acid-base balance. Alkaline urine is excreted because the bicarbonate load presented to the kidneys exceeds the absorption capability of the proximal tubules. Because sodium is excreted along with the bicarbonate, urinary sodium concentrations cannot be relied on as an indirect measure of the volume status. Chloride is reabsorbed in exchange for bicarbonate leading to minimal urinary chloride concentrations.

As the infant becomes more dehydrated, the renal response is aimed at maintaining intravascular volume. Aldosterone is secreted, which results in conservation of sodium and loss of potassium. In the distal tubule, sodium is conserved at the expense of hydrogen, and an acidic urine is excreted.

The degree of dehydration should be assessed to guide fluid resuscitation. Sodium chloride is the isotonic fluid of choice for resuscitation. It may be necessary to correct hypovolemia rapidly with 10–20 mL/kg of normal saline if the patient is exhibiting signs of shock. Glucose should be administered as well. These infants may have depleted glycogen stores in the liver leading to the development of hypoglycemia if glucose is not provided.

Hypovolemia, electrolyte imbalance, and acid-base derangements should be corrected before surgical intervention. The presence of normal plasma chloride levels suggests that there is adequate fluid and electrolyte resuscitation.

## 5. What is the surgical treatment for pyloric stenosis?

The surgical treatment of pyloric stenosis is laparoscopic pyloromyotomy, in which the circular muscles of the pylorus are spread apart. Occasionally, duodenal perforation may occur, which is easily sutured closed. This complication may slightly delay the start of oral feeds after surgery.

## 6. What are the anesthetic considerations for patients with pyloric stenosis?

Pyloric stenosis is a medical and not a surgical emergency. Before the start of anesthesia, hypovolemia, electrolyte

imbalances, and acid-base derangements should be completely corrected. Before induction, the stomach should be suctioned with a large-bore (14F) orogastric tube while placing the infant in supine, right lateral, and left lateral positions to decrease the risk of regurgitation and aspiration. If a smaller sized orogastric or nasogastric tube is already present, it should be replaced.

Although inhalation induction has been described for these patients, most anesthesiologists would consider them as having a "full stomach." Consequently, either a rapid-sequence induction with cricoid pressure or an awake intubation would be indicated. Although awake intubation is a viable option, it is associated with oxygen desaturation, bradycardia, longer time to intubation, and reduced first attempt success rates. It does not provide any advantage over a rapid-sequence induction. Maintenance of anesthesia can be accomplished either by inhalation or by a balanced technique. Muscle relaxants are not necessary. The use of opioids may not be necessary because the surgeon usually infiltrates the surgical wound with local anesthetic, which provides adequate analgesia postoperatively. In addition, opioids may increase the risk for postoperative apnea that may occur secondary to changes in cerebrospinal fluid pH and hyperventilation. Glucose infusion should be administered during the procedure to avoid hypoglycemia. Extubation should be done only when the infant is awake and protective airway reflexes are reestablished.

Depending on the postconceptual age of the infant, apnea monitoring may be necessary postoperatively.

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CASE 63

# Congenital Heart Disease

**Ingrid B. Hollinger, MD**

QUESTIONS



A 5-week-old infant was scheduled for bilateral inguinal herniorrhaphy. On preoperative evaluation, the infant was noted to be tachypneic and tachycardic. A IV/VI systolic murmur was heard at the left sternal border.

## 1. What is the incidence of congenital heart disease?

The incidence of congenital heart disease (CHD) is approximately 6 to 8 in 1000 live births. It is the most common congenital malformation. The incidence of CHD has increased as a result of improvements in diagnostic testing, increased awareness, and improved medical treatments of critically ill infants. Approximately 40,000 children are born each year with CHD in the United States. The most common CHD lesions manifest with a systolic murmur (Table 63-1). The main consequences of significant CHD are congestive heart failure and cyanosis.

## 2. What is the differential diagnosis for a systolic murmur?

Systolic murmurs can be either innocent or pathologic. Innocent murmurs are soft flow murmurs without physiologic consequences. Pathologic murmurs are loud, pansystolic or late systolic, and are associated with cardiac anomalies. The most common lesions associated with a systolic murmur in young infants are ventricular septal defect (VSD) and patent ductus arteriosus (PDA). These infants have signs of mild congestive heart failure (i.e., tachypnea and tachycardia) and should undergo a cardiology evaluation before surgery. Transthoracic echocardiography is presently the fastest, most accurate, and least invasive diagnostic tool to establish an exact anatomic diagnosis in most patients with CHD.

## 3. What are the general anesthetic considerations for common congenital cardiac lesions?

### *Extracardiac Defects*

Associated extracardiac defects are present in 5–50% of children with CHD. In 17–18%, the defect is part of a syndrome or chromosomal anomaly. Genitourinary tract anomalies are among the most common lesions and are present in 4–15% of patients with CHD. Major chromosomal anomalies with associated cardiac lesions of anesthetic significance are Down (trisomy 21), Turner, Noonan, and DiGeorge syndromes.

### *Prevention of Air Embolism*

All patients with shunt lesions (i.e., communication between the pulmonary and systemic circulation), regardless of the presence or absence of pulmonary outflow obstruction or usual shunting pattern, are at risk for air emboli to the systemic circulation. Shunts are often bidirectional, and owing to the earlier relaxation of the left ventricle compared with the right ventricle, a left-to-right shunt may transiently reverse during this portion of the cardiac cycle. On sudden obstruction to right ventricular output secondary to air embolism, a left-to-right shunt converts to a right-to-left shunt pattern. The following precautions should be followed whenever caring for a patient with a shunt lesion:

- Intravenous (IV) tubing should be meticulously debubbled and then rechecked after warming the operating room. Warming could allow nitrogen to come out of solution in the IV fluid, forming additional hazardous bubbles.
- All IV lines should be connected while free flowing.
- All syringes should be cleared of air, and before injecting into an IV line, a small amount of fluid should

TABLE 63-1 **Frequency of Most Common Congenital Cardiac Lesions**

| Lesion | % |
|---|---|
| Ventricular septal defect | 25 |
| Atrial septal defect | 12 |
| Patent ductus arteriosus | 12 |
| Pulmonic stenosis | 9 |
| Tetralogy of Fallot | 8 |
| Coarctation of the aorta | 7 |
| Aortic stenosis | 5 |
| Transposition of the great arteries | 5 |

be aspirated into the syringe to clear the needle and injection port of air. A recommended technique is to dilute medications in a 10-mL syringe such that each milliliter contains the calculated dose. In this way, aspiration of IV fluid into the syringe would not significantly change the medication concentration; this is in contrast to aspirating fluid into a small volume of undiluted medication.

### *Endocarditis Prophylaxis*

According to the American College of Cardiology/American Heart Association (ACC/AHA) guidelines, endocarditis prophylaxis is required for the prevention of bacterial endocarditis before any surgical, diagnostic, or dental procedure that may result in bacteremia for the following patients:

- Patients with unrepaired cyanotic CHD (including palliative shunts and conduits)
- Patients with completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first 6 months after the procedure
- Patients with repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization)

Endocarditis prophylaxis is not needed for routine tracheal intubation or flexible bronchoscopy. It is not needed for diagnostic procedures involving the gastrointestinal tract (e.g., esophagogastroduodenoscopy, colonoscopy) and the genitourinary tract unless a urinary tract infection is present. The only dental procedures that require endocarditis prophylaxis are procedures that involve (1) manipulation of gingival tissue or the periapical region of teeth or (2) perforation of the oral mucosa.

It is recommended that patients with the above-noted CHD lesions receive endocarditis prophylaxis for procedures involving the respiratory tract, skin structures, or musculoskeletal tissues that are infected. Current medication regimens for endocarditis prophylaxis are listed in Table 63-2.

TABLE 63-2 **Medication Regimens for Endocarditis Prophylaxis**

| Route | Medication | Dose |
|---|---|---|
| **Oral** | Amoxicillin | 50 mg/kg<br>Maximum 2 g |
| | ***Allergic to Penicillins:*** | |
| | Cephalexin | 50 mg/kg<br>Maximum 2 g |
| | Clindamycin | 20 mg/kg<br>Maximum 600 mg |
| | Azithromycin or Clarithromycin | 15 mg/kg<br>Maximum 500 mg |
| **Intravenous/ Intramuscular** | Ampicillin<br>or<br>Cefazolin or Ceftriaxone | 50 mg/kg<br>Maximum 2 g<br>50 mg/kg<br>Maximum 1 g |
| | ***Allergic to Penicillins:*** | |
| | Cefazolin or Ceftriaxone | 50 mg/kg<br>Maximum 1 g |
| | Clindamycin | 20 mg/kg<br>Maximum 600 mg |

*Note:* Antibiotics should be given 30-60 minutes before procedure start. If dose was not given, may administer up to 2 hours after the procedure finished.

Modifed from Wilson W, Taubert KA, Gewitz M, et al.: Prevention of Infective Endocarditis: Guidelines From the American Heart Association: A Guideline From the American Heart Association 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 116:1736-1754, 2007.

## 4. What are common intracardiac lesions with left-to-right shunting?

Common intracardiac lesions with left-to-right shunting include all forms of atrial septal defects (ASDs), VSDs, PDA, and other large aortopulmonary connections. The magnitude and direction of the shunt depend on the difference between the outflow resistances of the two connections and the size of the defect. Exceptions are communications between the left ventricle and right atrium where obligatory shunting of blood occurs owing to the large pressure difference that exists between these two cardiac chambers.

### *Atrial Septal Defects*

In ASDs located in the area of the fossa ovalis (i.e., ASD secundum), shunting occurs between low-pressure circulations. Despite a large shunt volume resulting in marked increase in pulmonary blood flow, pulmonary artery pressure remains low over many years. These patients are generally asymptomatic throughout childhood and adolescence but may develop mild pulmonary hypertension in the third and fourth decades of life. In this lesion, the right ventricle is volume-overloaded. The main anesthetic concern in asymptomatic patients is prevention of systemic embolization from injection of air or debris from IV tubing. These ASDs are closed electively during childhood either surgically or with an intracardiac device. Device closure has become the preferred approach. Size of available devices and delivery systems precludes percutaneous closure in patients weighing <15 kg. There is a risk of late device erosion through the cardiac wall with large devices.

### *Ventricular Septal Defects*

Small VSDs restrict the amount of left-to-right shunting and limit the hemodynamic consequences. With a large defect (i.e., approximating the size of the normal age-appropriate aortic orifice or larger), there is no restriction to flow, and shunting depends largely on the relative ratio of pulmonary vascular resistance (PVR) to systemic vascular resistance (SVR). In the early neonatal period, PVR is high and patients do not exhibit signs or symptoms related to the VSD. As PVR declines during the second and third weeks of life, left-to-right shunting increases, and larger volumes of blood traverse the pulmonary circulation. Substantially more blood returns to the left heart creating congestive heart failure (CHF) secondary to volume overload of the left ventricle. In this lesion, the pulmonary vascular bed is exposed to increased blood flow and systemic blood pressure.

An estimated 25–50% of all small to moderate-sized VSDs close spontaneously, generally during the first year of life. Many VSDs become smaller throughout life and are benign. Probably <5% of large VSDs undergo spontaneous closure. Surgery is indicated for primary closure of the defect during the first year of life in infants with CHF and failure to thrive despite medical therapy. Failure to close a large VSD leads to progressive pulmonary vascular obstructive disease, particularly after the second year of life.

Before the development of pulmonary vascular disease, the volume of the shunt may be manipulated by changing PVR or SVR or both. High oxygen concentrations, hyperventilation, and alkalosis lead to pulmonary vasodilation and may cause massive increases in left-to-right shunting. With the limited cardiac output of the small infant, this increase in left-to-right shunting can lead to severe systemic underperfusion and cardiovascular collapse. Similarly, an increase in afterload leads to an increase in left-to-right shunting, as long as PVR is less than SVR. Most patients with large shunts receive anticongestive medications (e.g., digoxin, furosemide) and an afterload-reducing agent (e.g., angiotensin-converting enzyme inhibitor) before cardiac surgery or if managed medically only.

### *Patent Ductus Arteriosus*

Large PDAs have a similar clinical presentation to large VSDs and are managed surgically or with device closure to protect the pulmonary vascular bed. Small PDAs are closed percutaneously with coils or devices to prevent endarteritis of the PDA. Because of the size of the delivery system, percutaneous closure is not performed in infants <6 months old or weighing <6 kg. In premature infants, a PDA is not considered CHD. The ductus arteriosus often does not close in a premature infant because of insensitivity to the factors that would normally stimulate closure when the infant is born full-term. Pharmacologic closure of the PDA can be attempted with prostaglandin inhibitors (e.g., indomethacin) unless it is contraindicated. If closure is not achieved after three doses or if there is a contraindication to treatment, surgical closure is indicated.

## 5. What are the anesthetic considerations for left-to-right shunting lesions?

A left-to-right shunt influences the uptake of inhalation anesthetic agents only minimally, unless cardiac output is depressed, in which case induction is accelerated. However, induction with IV agents is delayed because much of the injected drug is recirculated to the lung. Agents that cause myocardial depression are poorly tolerated in infants with limited cardiac reserve. Infants with large left-to-right shunts have chronically congested lungs with decreased compliance, increased closing volume, and increased airway resistance. The airway should be secured and ventilation should be controlled during general anesthesia. It is important to maintain a relatively high PVR to avoid increasing pulmonary congestion from increased pulmonary blood flow. Inspired oxygen concentrations should be kept to a minimum that provides adequate oxygen saturation, and ventilation parameters should be aimed at maintaining normocarbia or mild hypercarbia. Prevention of paradoxical air embolism from IV sets is of paramount importance. Although mild afterload reduction leads to increased systemic output and a reduction in left-to-right shunting, excessive systemic vasodilation in the presence of a high PVR can lead to significant right-to-left shunting resulting in cyanosis. Ketamine, opioid and muscle relaxant techniques, and low-dose inhalation anesthesia

**BOX 63-1 Anesthetic Considerations for Left-to-Right Shunting Lesions**

- Airway management
  - Intubation
  - Mechanical ventilation
- Prevent paradoxical air embolism
  - Debubble all IV sets
  - Check IV sets for rebubbling in warm operating room
  - Connect IV tubing while fluid flowing
  - After attaching syringe to IV line, before injection of medications, aspirate to remove air bubbles
- Maintain relatively high PVR
  - Minimize inspired oxygen concentration to maintain normal oxygen saturations
  - Normocarbia to mild hypercarbia
- Prevent significant decrease in SVR
  - Ketamine
  - Opioid and muscle relaxant
  - Low-dose isoflurane or sevoflurane
- Anesthesia induction
  - Inhalation induction minimally affected
  - IV induction delayed
- Endocarditis prophylaxis
  - First 6 months after ASD, VSD, or PDA repair
  - >6 months if residual defect at or near repair

with isoflurane or sevoflurane are usually well tolerated. Endocarditis prophylaxis is required only for the first 6 months after ASD, VSD, and PDA repair, unless there is a residual defect at or near the site of repair (Box 63-1).

## 6. What are common intracardiac lesions with right-to-left shunting and reduced pulmonary blood flow?

### *Tetralogy of Fallot*

The combination of VSD, pulmonary valvular or right ventricular infundibular stenosis, right ventricular hypertrophy, and a large overriding aorta is known as tetralogy of Fallot (TOF). It is the most common cyanotic defect seen after the first year of life, accounting for 10% of all congenital cardiac lesions.

The degree of right ventricular outflow or pulmonic obstruction determines the onset and severity of cyanosis. If obstruction is severe, cyanosis appears with closure of the ductus arteriosus in the neonatal period. Prostaglandin $E_1$ (by keeping the ductus arteriosus open) may be used to stabilize the patient before surgical intervention. Many infants do not develop symptoms until 3–6 months of age, and even then these infants may not appear cyanotic at rest. However, episodes of severe cyanosis with hyperventilation and acidosis, known as hypercyanotic spells (or "tet" spells), may occur. These episodes are caused by severe infundibular spasm, probably induced by changes in venous return and SVR. Reduction in peripheral vascular tone leads to decreased pulmonary blood flow because blood tends to be shunted to the systemic circulation. Decreased venous return further decreases pulmonary blood flow. In older children, squatting may improve symptoms through an increase in venous return from the lower extremities and by increasing SVR. Hypercyanotic spells may occur perioperatively because of the dynamic nature of the muscular infundibular obstruction. The treatment of hypercyanotic spells is based on the goals of decreasing infundibular spasm, by decreasing contractility and heart rate, and increasing preload. Another goal (especially in fixed right ventricular outflow obstruction) is to increase SVR to decrease right-to-left shunting across the VSD. Strategies to prevent and treat these complications are outlined in Table 63-3.

Maintenance of cardiac output is essential because the oxygen content of blood is low. Bradycardia is very poorly tolerated for this reason. In patients with systemic-to-pulmonary shunts, adequate systemic blood pressure is necessary to maintain pulmonary perfusion, besides reducing right-to-left shunting at the cardiac level. In TOF, both ventricles work at systemic pressure, but volume overload does not occur, and CHF is rare.

Arterial oxygen saturation generally increases on induction of anesthesia in cyanotic patients. This increase is probably secondary to the reduction in oxygen consumption during anesthesia and the subsequent increase in venous oxygen saturation.

Monitoring blood pressure may become problematic in patients with previous shunting procedures using the subclavian arteries. The contralateral arm should be used for invasive or noninvasive monitoring. For major surgery, intraarterial pressure or central venous pressure (CVP) or both should be measured directly. This measurement also allows blood sampling for blood gas and acid-base measurements. Because the major myocardial

TABLE 63-3 **Management of Hypercyanotic Spells**

| Prevention | Treatment |
|---|---|
| Preanesthetic sedation | Prevent and relieve airway obstruction |
| Continued β-adrenergic blockade | 100% oxygen |
| Maintain adequate anesthetic depth | Deepen anesthesia/provide sedation |
| Avoid hypovolemia | Administer fluid bolus |
| Avoid afterload reduction | Increase SVR: phenylephrine 1–2 μg/kg |
| | Esmolol 100–200 μg/kg/min |
| | Aortic compression |

*SVR,* Systemic vascular resistance.

stress rests on the right ventricle in these patients, CVP can be used to assess cardiac performance.

The patient should arrive in the operating room well sedated. Preoperative fluid restriction should be minimized or maintenance IV fluid should be administered to prevent hemoconcentration and hypovolemia. Smooth anesthetic induction is important to prevent increases in oxygen demand or hypercyanotic spells. The agents used should have minimal peripheral vasodilating effects. Mild myocardial depression is desirable because it may relieve infundibular obstruction. For this reason, halothane was the preferred inhalation agent for these patients. Because halothane is no longer readily available, sevoflurane titrated carefully is the best alternative. If IV agents are used, they should be carefully titrated to prevent a relative overdose. IV barbiturate requirements may be halved. Ketamine can be used safely, particularly in very sick patients, because it maintains SVR and does not precipitate hypercyanotic spells.

Endocarditis prophylaxis is required if TOF is uncorrected or shunted or if residual defects remain despite corrective surgery.

### *Complex Lesions and Transposition of the Great Arteries*

Patients with complex lesions and transposition of the great arteries (TGA) will have undergone repair or palliation before elective noncardiac surgery. These situations are discussed subsequently.

**BOX 63-2 Anesthetic Considerations for Right-to-Left Shunting Lesions**

- Prevent paradoxical air embolism
  - Debubble all IV lines
  - Check IV lines for rebubbling in warm operating room
  - Connect IV line while fluid flowing
  - After attaching syringe to IV line, before injection of medications, aspirate to remove any air bubbles
- Avoid dehydration
  - Clear liquids until 2 hours before surgery
  - IV maintenance fluids
- Polycythemia
  - Hemodilute to hematocrit of <65% (target 55–60%)
- Cardiac
  - Maintain adequate systemic blood pressure
  - Bradycardia poorly tolerated
- Pulmonary
  - Cyanosis
    - Blunted response to hypoxia
  - Ventilation/perfusion abnormalities
    - Positive pressure ventilation may increase dead space ventilation
    - Moderate degree of hyperventilation necessary to maintain normocarbia
    - Increased gradient between arterial and $ETCO_2$
- Induction
  - Prolonged with poorly soluble inhalation anesthetics
  - Accelerated with IV agents

*$ETCO_2$*, End-tidal carbon dioxide.

### 7. What are the anesthetic considerations for right-to-left shunting lesions with reduced pulmonary blood flow?

Similar to patients with left-to-right shunt lesions, all patients with right-to-left shunts are at increased risk of systemic embolization of air or blood clots from IV sets. In older cyanotic patients with severe polycythemia, isovolemic hemodilution to a hematocrit of <65% (goal is hematocrit 55–60%) should be performed before elective surgery; this improves cardiac output, peripheral perfusion, and oxygen transport. Coagulation defects commonly found in polycythemic patients also may be improved. However, hemodilution to normal hematocrit levels may be very dangerous because oxygen transport would be seriously limited. Routine hemodilution to control hematocrit is no longer recommended because it leads to microcytic anemia secondary to iron deficiency.

Dehydration must be avoided in these patients at all times. Prolonged fasting should be avoided by administration of clear liquids until 2 hours before surgery or administration of maintenance IV fluids.

Patients with cyanosis have a blunted response to hypoxia, which may persist after correction of the underlying lesion. In patients with reduced pulmonary blood flow, marked ventilation/perfusion inequalities exist. Positive pressure ventilation may exacerbate this problem, leading to increases in dead space ventilation and arterial carbon dioxide tension ($PaCO_2$). To maintain normal $PaCO_2$ in the presence of severely reduced pulmonary blood flow, a moderate degree of hyperventilation is required. Capnography underestimates $PaCO_2$ in these patients because only part of the cardiac output reaches the pulmonary circulation for gas exchange. The greater the right-to-left shunt, the greater the $PaCO_2$-to-end-tidal carbon dioxide ($ETCO_2$) gradient. A markedly increased $PaCO_2$ may be present despite a normal $ETCO_2$.

The presence of a right-to-left shunt prolongs inhalation induction with poorly soluble inhalation anesthetics. This prolonged induction may be offset by the presence of a surgically created systemic-to-pulmonary shunt. Inhalation induction time with highly soluble agents may be nearly normal because these patients usually hyperventilate to maintain a normal $PaCO_2$. In contrast, the onset of IV agents is accelerated because a significant portion of the drug bypasses the lungs (Box 63-2).

### 8. What surgical options are available for congenital heart disease?

The type of CHD determines whether a true anatomic (i.e., restore normal cardiovascular anatomy) or palliative (i.e., attempt to establish normal cardiovascular physiology) repair is possible. Even after surgical repair, there may be residual defects or short-term or long-term sequelae.

True anatomic repair, in which further surgery is not anticipated, consists of ligation of a PDA or suture closure of an ASD. Closure of a simple VSD, resection of a coarctation of the aorta with end-to-end anastomosis, and the arterial switch operation for correction of TGA also result in normal anatomy but are accompanied by late sequelae in some patients.

In the following conditions, anatomic repair is attempted but results in residual defects or requires use of prosthetic materials:

- TOF
- Atrioventricular (AV) canal defect
- Obstructive valvular lesions
- Lesions requiring insertion of a conduit between the ventricle and respective artery (usually the right ventricle and pulmonary artery)
- Valve replacement

In patients in whom anatomic repair is not feasible, palliative repair is attempted to try to establish normal cardiovascular physiology. Included in this group is the initial repair of TGA by the Mustard or Senning operation. In this procedure, blood flow is redirected at the atrial level (i.e., atrial switch) where pulmonary venous blood is directed to the aorta and systemic venous blood is directed to the pulmonary artery. Also included in this group are cardiac malformations that result in only one functional ventricle that supports the pulmonic and systemic circulation. This heterogeneous group of lesions requires several staged surgical interventions until the final Fontan operation, which results in separation of the two circulations but without a pulmonary ventricle.

One of the most common sequelae after surgery for CHD is arrhythmia (Box 63-3). Supraventricular arrhythmias are the most common arrhythmias and can be life-threatening under certain conditions (e.g., atrial flutter after Fontan operation). They are particularly common after repairs with extensive atrial suture lines or elevated atrial pressures or both. Atrial arrhythmias may be either tachycardias or bradycardias. These arrhythmias are often refractory to medical therapy and may require ablation or pacemaker insertion. After Senning or Mustard procedure for TGA, only 20–40% of patients are in sinus rhythm 5–10 years following surgery. After the Fontan procedure performed with direct atrial-to-pulmonary artery anastomoses, there is at least a 30% incidence of atrial arrhythmias. Newer Fontan surgical approaches, either lateral tunnel or extracardiac conduits, attempt to diminish the incidence of late arrhythmias. Atrial arrhythmias also are seen in 5–10% of patients after repair of a secundum ASD, particularly following repair at an older age. Supraventricular arrhythmias are associated with a 2–8% incidence of sudden death.

Ventricular arrhythmias, although less common in the postoperative period, are frequently more significant because they may indicate an underlying residual defect and may be the harbinger of sudden death. Ventricular premature beats can be seen with right ventriculotomy or resection, elevated intracavitary pressure (as seen with valvular stenosis), and cardiomyopathies with diastolic dysfunction. Cardiomyopathies with diastolic dysfunction can be seen after surgery with suboptimal myocardial preservation or when pressure and volume overload of the ventricle were present for a long time before corrective surgery, particularly if associated with an increased hematocrit.

Occasionally, the stress of anesthesia and surgery may unmask an underlying rhythm disturbance. New ventricular extrasystoles observed during anesthesia in a patient with previous TOF repair should be brought to the cardiologist's attention so that appropriate follow-up can occur. TOF repair has the highest association of ventricular arrhythmias and sudden death in the long-term after repair, particularly in patients operated on later in life and in earlier series. To prevent this complication, an implantable cardioverter-defibrillator may be required.

**BOX 63-3 Arrhythmias after Congenital Heart Disease Procedures**

- Atrial arrhythmias
  - Senning or Mustard procedure
  - Fontan
  - Secundum ASD
- Ventricular arrhythmias
  - Right ventriculotomy
  - Right ventricular resection
  - Elevated intracavitary pressure
- Cardiomyopathies with diastolic dysfunction

## 9. Describe the surgical repair and sequelae of specific congenital cardiac lesions.

### *Atrial Septal Defects*

Secundum ASD is associated with a 30% incidence of mitral valve prolapse. Patients need to be followed for the development of mitral regurgitation, which occurs in 5–10% of patients, or ventricular arrhythmias. Early and late atrial arrhythmias occur after ASD repair, particularly if the patient was >20 years old at the time of repair, in which case it could be present even before surgery. Development of paroxysmal or chronic atrial fibrillation requires anticoagulation therapy to prevent systemic embolization. The risk of late development (i.e., 25–30 years after repair) of atrial flutter or fibrillation is 4% if repair is done before age 10 years and 58% if repair is done after age 40 years. The presence of a large left-to-right shunt before surgery is an additional risk factor for the development of late atrial arrhythmias. The most commonly observed arrhythmias after repair of sinus venosus defects are sinus node dysfunction and sick sinus syndrome, which occur in at least 10% of patients.

### *Ventricular Septal Defect*

The incidence of residual VSD after surgery is <5%. Patients with subarterial VSD may have aortic insufficiency, which is an indication to close even a small defect. In 3% of cases, regurgitation is progressive. After VSD repair, many patients (30–65%) have a right bundle-branch block (RBBB) on electrocardiogram (ECG). Previously, when a right ventriculotomy was commonly performed, serious ventricular arrhythmias were seen in at least 34% of patients, with a 1–2% incidence of sudden death. Complete heart block is one of the risk factors of VSD closure, but with improved surgical techniques the incidence is <2%. Complete heart block is also seen after device closure of a perimembranous VSD where it can develop late and cause

sudden death. It is also a late sequela of patients who exhibit bifascicular block after surgery (i.e., RBBB and left anterior hemiblock). Most patients whose defects are closed before age 2 years have normal cardiovascular function. However, they have a greater risk for arrhythmias compared with the normal population. Patients operated on later in life may have persistence of depressed myocardial reserve and progressive pulmonary hypertension.

### Coarctation of the Aorta

In 50% of patients with coarctation of the aorta, other associated cardiac lesions are present. Bicuspid aortic valve is seen in 85% of patients, and 3–10% have berry aneurysms of the circle of Willis. Coarctation of the aorta occurs in 35% of patients with Turner syndrome.

The technique of repair of coarctation of the aorta has changed over the years. The preferred technique at the present time is resection of the coarcted aorta and end-to-end anastomosis. Older repairs included patch aortoplasty, subclavian flap aortoplasty, and interposition graft. Patch aortoplasty has been abandoned because it is associated with a high incidence of aortic aneurysm formation that expands rapidly and has led to aortic rupture and death. Subclavian flap aortoplasty is still used occasionally. Blood pressure measurements in the left arm may be unreliable after this procedure. Bridging grafts are occasionally used in older patients with repeated coarctations. Repair in infancy is associated with a 15–20% incidence of repeat coarctation, which can be managed effectively with balloon angioplasty. Balloon angioplasty is not effective for primary coarctation in the newborn. However, it can be performed in older patients, in whom a stent can be placed in the dilated coarctation site to maintain the diameter. A long-term sequela of balloon angioplasty is the development of an aortic aneurysm at the angioplasty site (2–14%).

Patients with repaired coarctation of the aorta are at risk for development of late hypertension in the absence of repeat coarctation. Age at repair is the strongest predictor for this complication. Repair after age of 5 years has a 75% incidence of systolic hypertension at 25-year follow-up. Long-term survivors have an accelerated risk of coronary artery disease, myocardial infarction, and premature death. In addition, because of the high incidence of bicuspid aortic valve, 7–10% of patients develop aortic valvular disease requiring aortic valve replacement. In the perioperative period, patients who are normotensive at rest may develop significant hypertension with minimal stimulation; this may be due to underlying hypertensive disease or unrecognized repeat coarctation.

### Atrioventricular Septal Defects

AV septal defects are the most common cardiac defect associated with Down syndrome. The complete form results in severe CHF and pulmonary hypertension. The defect is usually repaired in infancy because of symptoms and to prevent development of obstructive pulmonary vascular disease. Primum ASDs manifest similar to secundum ASD, unless associated with significant mitral regurgitation. Although the cleft mitral valve is competent in most patients, 10–15% of patients have mitral valve regurgitation at the time of initial surgery. Because of the abnormality of the mitral valve, long-term mitral insufficiency remains a serious problem after repair of primum ASDs and complete canals. In >60% of patients followed long-term after repair of partial AV septal defects, evidence of mitral regurgitation is found that may require eventual mitral valve replacement. After repair of complete AV septal defect in infancy, the incidence of mitral regurgitation requiring reintervention is approximately 7%. First-degree heart block is seen in 50% of patients after repair. Malignant tachyarrhythmias may develop as patients age.

### Tetralogy of Fallot

Older TOF repairs have resulted in right ventricular dysfunction secondary to pulmonary insufficiency and a high incidence of arrhythmias from extensive right ventriculotomies. Incomplete relief of right ventricular outflow obstruction, demonstrated by a right-ventricle-to-left ventricle systolic pressure ratio >0.5, is an independent predictor of late mortality after repair. Repair at an older age is also associated with higher long-term mortality, as is the presence of a large outflow patch. Most patients are symptom-free after repair. However, in the survivors of the earlier repairs, there is a 6% incidence of sudden death, or 0.3% per patient year, and at least 10% incidence of inducible ventricular tachycardia requiring implantation of a cardioverter-defibrillator. Nearly one third of patients at late follow-up have atrial tachycardias, which can also cause sudden death. Most patients have a RBBB on ECG.

The presence of ventricular ectopy must be thoroughly evaluated preoperatively. The presence of residual lesions, VSD, or right ventricular hypertension should be identified before any procedure. Sympathetic stress in the setting of right ventricular hypertension and an old ventriculotomy scar increase the propensity for ventricular dysrhythmias. Patients with significant pulmonary insufficiency may not tolerate rapid fluid shifts. Vascular access may be difficult in patients with multiple previous cardiovascular procedures. Patients with residual shunts are at risk for paradoxical emboli.

### Transposition of the Great Arteries

TGA represents 5–7% of all congenital cardiac defects and is the most common cause of cyanotic CHD in newborns. In TGA, the aorta arises from the right ventricle and the pulmonary artery from the left, creating two parallel circulations. Survival past the neonatal period is impossible unless some mixing between the circulations occurs, through a PDA, ASD, or VSD. If insufficient mixing is present, these critically ill and severely cyanotic infants must undergo emergent balloon atrioseptostomy to create an ASD and allow for better mixing. Before surgical interventions, 90% of patients died within the first year of life. Surgical interventions are aimed at improving mixing, redirecting flow of systemic venous or pulmonary venous return to pulmonary artery or

aorta, or anatomically correcting the problem. The initial physiologic repair for this condition was "switching" the blood return at the atrial level with the help of an intraatrial baffle, the Mustard and Senning procedures. This repair resulted in the right ventricle becoming the systemic ventricle and extensive suture lines in the atria. There is now >40-year follow-up available for these patients. The 20-year survival rate is 80%, but late morbidity is common. Sinus rhythm is present in <20% of patients, and >10% of patients have developed right ventricular failure requiring either transplantation or conversion to an arterial switch. The intraatrial baffle leads to systemic venous obstruction in 10–20% of patients, which may not be clinically apparent except for mild facial swelling. Monitoring of the CVP may be quite misleading under these circumstances and may cause superior vena cava (SVC) syndrome. Both the Mustard and the Senning procedures resulted in obstruction of the right pulmonary vein owing to baffle shrinkage in 5–10% of patients, frequently requiring reoperation because of unilateral pulmonary venous hypertension. However, the most serious long-term complication is the severe arrhythmias that follow both procedures. Sinus node dysfunction or atrial flutter (25%) can result in sudden death. Late right ventricular dysfunction leads to ventricular tachycardia. Patients may be receiving multiple antiarrhythmic drugs and may require pacemaker implantation to prevent complications from this therapy. Pacemakers are necessary in patients with sick sinus syndrome. Tachyarrhythmias are presently treated with radiofrequency ablation, if possible, but may require an implantable antitachycardia device. After the Mustard procedure, 50% of patients have a pacemaker by age 30 years.

Because of the disappointing long-term results of the atrial switch procedures, anatomic correction at the arterial level has been the preferred approach since the mid-1980s. It involves transection of both great vessels with relocation of the aorta above the pulmonary valve and the left ventricle and relocation of the pulmonary artery above the aortic valve and the right ventricle. The coronary arteries are disconnected and relocated to the neoaorta. Long-term follow-up of >30 years is now available. There is a significant reduction in arrhythmias, better systemic ventricular function, and better exercise tolerance. In the initial series, supravalvular pulmonary stenosis occurred in >10% of patients requiring dilation or reoperation. With modifications in the surgical technique, this complication has become rare. Aortic insufficiency, which may eventually require aortic valve replacement, occurs in long-term survivors. In addition, 1–3% of patients have asymptomatic occlusion of one coronary artery on follow-up coronary angiography. Patients after atrial switch procedures may have limited cardiac reserve. They also may have difficult central access problems. The course of central lines on the chest film appears quite abnormal because the catheter traverses from the SVC along the baffle into the mitral valve, left ventricle, and pulmonary artery. After the arterial switch procedure, patients should be evaluated for supravalvular stenosis and may be at risk for development of myocardial ischemia secondary to coronary stenosis. These patients are otherwise similar to a person with a structurally normal heart.

### *Single Ventricle and the Fontan Operation*

A multitude of complex congenital cardiac lesions have only one functional ventricle to support the pulmonary and systemic circulation or can be repaired only by converting them to single-ventricle physiology. Common lesions that are "repaired" in this way include tricuspid atresia, double inlet left or right ventricle, hypoplastic left heart syndrome (HLHS), and pulmonary atresia with intact septum and hypoplastic right ventricle. In infancy, these patients undergo a procedure to balance pulmonary blood flow between the systemic circulation and the pulmonary circulation. This procedure involves either the creation of an aortopulmonary shunt for pulmonary perfusion or banding of the pulmonary artery to restrict excessive flow. In HLHS, the aorta is reconstructed during the same procedure (i.e., Norwood stage 1).

A hybrid approach has been advocated to avoid either a shunting procedure or a Norwood stage 1 in the newborn period. For ductus dependent lesions requiring an aortopulmonary shunt, a stent is inserted in the ductus in the catheterization laboratory, avoiding a surgical procedure. For HLHS, bilateral pulmonary artery banding is performed via median sternotomy, and a stent is inserted in the ductus in an antegrade direction. At about 6 months of age, to relieve the volume load on the single ventricle, the venous return from the upper extremity is diverted directly into the lung by anastomosis of the SVC to the pulmonary artery (bidirectional Glenn operation). The pulmonary valve is occluded or the pulmonary band is left in situ (pulsatile Glenn operation). The PDA or aortopulmonary shunt is ligated. Aortic arch reconstruction is performed during the same surgery after a neonatal hybrid procedure.

All patients remain cyanotic after these procedures. Because all blood mixes in the single ventricle, with balanced flow to the systemic and pulmonary vascular bed and normal cardiac output, oxygen saturation is between 80% and 85%. In the final stage procedure (Fontan), complete separation of the two circulations is achieved by diversion of the inferior vena cava (IVC) blood to the pulmonary artery. There have been several modifications of this procedure over the years. At the present time, the IVC is channeled either through an intraatrial lateral baffle or via an extracardiac conduit to the pulmonary artery. Because pulmonary blood flow and cardiac output depend on a pressure gradient between the CVP and the mean pulmonary or intrathoracic pressure, PVR has to be low and myocardial function relatively normal to avoid excessively high CVP. Patients have limited potential to increase cardiac output because of limited flow across the venous channels. A fenestration is created between the IVC channel and the right atrium to allow decompression of high venous pressure. Because the fenestration creates a right-to-left shunt, cardiac output is maintained at the expense of full oxygenation.

These patients are at risk for several long-term problems, as follows:

- Persistently elevated CVP leads to protein-losing enteropathy in 5–13% of patients >10 years old.
- Persistent pleural effusions.

- Atrial suture lines and atrial distention lead to a high incidence of atrial tachyarrhythmias. Atrial flutter occurs in 40–50% of patients 15 years after the procedure.
- If the single ventricle is a right ventricle, ventricular function deteriorates progressively.
- Abnormal cardiac function is present in 50% of patients 10 years after the repair.
- The 15-year survival rate is 60–73%.
- Spontaneous thrombosis requiring long-term low-dose anticoagulation.
- Afterload-reducing agents are required to protect myocardial function and to maintain low left atrial pressure.
- Sinus rhythm is important to maintain cardiac output.
- Reduced exercise tolerance is present.

Key considerations for anesthetic management are the following:

- A thorough preoperative cardiac evaluation should be performed including echocardiography to assess function of the AV valve and ventricle.
- Maintenance of adequate preload and sinus rhythm is important.
- Cardiodepressant drugs should be avoided.
- Spontaneous ventilation should be maintained if possible to minimize increases in intrathoracic pressure.
- Controlled ventilation should be adjusted to keep positive intrathoracic pressure to a minimum.
- CVP catheters should be used only when absolutely indicated because of the risk of thrombosis and obstruction to venous return.
- Neuraxial anesthesia should be carefully titrated to allow for adjustment for acute decreases in preload and afterload.
- Endocarditis prophylaxis is indicated in the presence of a shunt or with a fenestration.
- Paradoxical emboli are a risk in the presence of a fenestration or baffle leak.

The surgical repair and sequelae of specific congenital heart lesions are summarized in Box 63-4.

## BOX 63-4 Complications and Sequelae of the Repaired Heart

- Atrial septal defect
  - Associated conditions
    - Mitral valve prolapse
  - Mitral regurgitation
  - Ventricular arrhythmias
  - Atrial arrhythmias
    - Repair at older age
    - Large left-to-right shunts
  - Sinus venosus repair
    - Sinus node dysfunction
    - Sick sinus syndrome
- Ventricular septal defect
  - Residual defect
  - Right bundle branch block
  - Complete heart block
    - Reduced incidence with improved surgical techniques
    - Device closure of perimembranous defect
    - RBBB and left anterior hemiblock after surgery
  - Repair at older age
    - Depressed myocardial reserve
    - Progressive pulmonary hypertension
- Coarctation of the aorta
  - Associated conditions
    - Bicuspid aortic valve—develop aortic valvular disease
    - Berry aneurysm
    - Turner syndrome
  - Repeat coarctation
  - Balloon angioplasty
    - Aneurysm at angioplasty site
  - Hypertension
    - Incidence increases with later age at time of repair
  - Accelerated risk of coronary artery disease
  - Myocardial infarction
  - Premature death
- Atrioventricular septal defects
  - Associated conditions
    - Down syndrome
  - Mitral regurgitation
  - First-degree heart block
  - Malignant tachyarrhythmias
- Tetralogy of Fallot
  - Late mortality
    - Right ventricle-to-left ventricle systolic pressure ratio >0.5
    - Repaired at older age
    - Large outflow patch
  - Inducible ventricular tachyarrhythmias
    - May require internal cardioverter-defibrillator
  - Atrial tachycardia
  - Right bundle branch block
  - Preoperative evaluation
    - Ventricular ectopy
    - Residual lesions
    - Ventricular septal defect
    - Right ventricular hypertension
  - Anesthetic considerations
    - Pulmonary insufficiency—fluid shifts poorly tolerated
    - Difficult vascular access
    - Paradoxical emboli
- Transposition of the great arteries
  - Mustard/Senning
    - Right ventricular failure—ventricular tachyarrhythmias
    - Systemic venous obstruction
    - Right pulmonary vein obstruction
    - Unilateral pulmonary venous hypertension
    - Atrial/ventricular arrhythmias
  - Arterial switch
    - Supravalvular pulmonary stenosis
    - Aortic insufficiency
    - Coronary artery occlusion
- Single ventricle and Fontan operation
  - Elevated central venous pressure
  - Protein-losing enteropathy
  - Pleural effusion
  - Atrial tachyarrhythmias
  - Spontaneous thrombosis
  - Paradoxical emboli

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CASE 64

# Preterm Infant

**Scott D. Lipson, MD**

## QUESTIONS

1. How does prematurity affect survival, and how is it classified?
2. What unique developmental considerations must be taken into account when caring for preterm or term neonates?
3. What specific medical problems affect preterm neonates?
4. What pharmacologic differences must be considered in preterm and term neonates?
5. What intraoperative monitors and temperature-regulating measures should be used for this former preterm neonate?
6. What are the goals for oxygen administration intraoperatively?
7. Is this patient a candidate for discharge to home immediately after surgery?
8. Would a regional anesthetic allow for this patient to be discharged home earlier?

A 20-week-old infant who was born at 25 weeks gestational age presented for right inguinal hernia repair before discharge home from the neonatal intensive care unit (NICU).

### 1. How does prematurity affect survival, and how is it classified?

There are >500,000 preterm births in the United States each year, accounting for >1 in every 8 births. The rate of premature birth in the United States has increased >35% since the 1980s. This increase is due in large part to greater numbers of fertility treatments, resulting in increasing numbers of multiple births and an older maternal population, both of which can lead to premature deliveries. Survival rate for preterm infants born at 23 weeks gestational age is 11%–33%; survival for infants born at 25 weeks gestational age is 55%–75%. Morbidity among survivors of both of these groups is still around 50%.

NICU care has also improved over this period, which means preterm infants are surviving longer. Because preterm infants are at increased risk for numerous congenital and acquired complications, many need anesthetic care either in the operating room (OR) or in off-site locations.

Newborns are classified by gestational age as follows:

| | |
|---|---|
| Full-term infant | 38–42 weeks |
| Postterm infant | >42 weeks |
| Preterm infant | <37 weeks |
| Micropremature infant | <26 weeks (or weight <800 g) |
| Extremely low gestational age newborn (ELGAN) | 23–27 weeks |

Preterm infants weighing <1000 g are classified further as extremely low birth weight.

### 2. What unique developmental considerations must be taken into account when caring for preterm or term neonates?

#### *Circulation*

After delivery, the neonatal circulation undergoes numerous changes as it transitions from fetal circulation to adult-type circulation over the first days to weeks of life (Table 64-1). Pulmonary vascular resistance (PVR) decreases rapidly on the first day of life, and pulmonary blood flow increases. Pressure on the left side of the heart increases with an increase in pulmonary venous return and systemic vascular resistance. These changes, along with higher oxygen levels, promote functional closure of two in utero connections between the right and left sides of the circulation. Mechanical closure continues over weeks to months. During this transitional period, the circulation can alternate between fetal and adult because shunts can reopen under certain conditions. Close attention must be paid to changes in hemodynamics during anesthesia and surgical stress because they can induce circulatory changes that can trigger shunt reopening. Numerous factors can increase the risk of prolonged transitional circulation, including prematurity, elevated PVR, acidosis, hypothermia, meconium aspiration, and congenital heart disease (CHD).

#### *Cardiovascular*

Myocardium in infants is stiff and poorly compliant secondary to poorly developed contractile cellular mass compared with older children. Stroke volume is relatively fixed making the increased cardiac output predominately rate dependent. Because the infant heart normally functions at the top of the Frank-Starling curve, changes in volume or afterload are poorly tolerated. Preoperative

TABLE 64-1 **Anatomic and Physiologic Differences and Their Implications**

| Organ System | Difference | Implications |
|---|---|---|
| Cardiac | Noncompliant myocardium | Functioning at upper end of Starling curve<br>Stroke volume fixed<br>No cardiac reserve<br>Hypovolemia and hypervolemia poorly tolerated |
| | Cardiac output | Heart rate dependent |
| | Immature sympathetic system | "Vagotonic"—bradycardia with hypoxia or laryngoscopy |
| | Decreased calcium storage in sarcoplasmic reticulum | Cardiac depression with decreased calcium levels or anesthetic agents |
| Pulmonary | Decreased lung compliance, increased chest wall compliance | Increased work of breathing |
| | Increased closing volume | Small airway closure during normal tidal volume breathing |
| | Increased minute ventilation | Secondary to increased respiratory rate |
| | Increased oxygen consumption | Rapid oxygen desaturation during apnea or airway obstruction |
| | Increased $\dot{V}_A$/FRC | Rapid oxygen desaturation during apnea or airway obstruction |
| | Decreased type I muscle fibers in diaphragm and intercostal muscles | Early respiratory fatigue with increased work of breathing (e.g., airway obstruction, general anesthesia)<br>Tracheal intubation during general anesthesia |
| Airway | Large occiput | Neck flexion leads to airway obstruction<br>Roll under shoulder |
| | Relatively large tongue | Difficult mask ventilation<br>May need oral airway |
| | Cephalad larynx | Difficult visualization of vocal cords<br>Straight laryngoscope blade necessary |
| | Floppy epiglottis | Obstructing view of vocal cords<br>Straight laryngoscope blade to lift epiglottis |
| | Vocal cords slanted | Tracheal tube hung up at anterior commissure |
| | Cricoid cartilage narrowest portion of airway | Perform leak test of tracheal tube<br>$<$30 cm $H_2O$ or greater than peak airway pressure<br>Postextubation stridor |
| Renal | Decreased GFR | Decreased ability to excrete saline or water loads<br>Decreased excretion of medications |
| Hepatic | Decreased glycogen stores<br>Decreased enzyme systems | Perioperative glucose maintenance<br>Decreased drug metabolism |
| Gastrointestinal | Decreased lower esophageal sphincter tone | Gastroesophageal reflux |
| Thermogenesis | Nonshivering thermogenesis | Increase in circulating norepinephrine increases PVR |
| Hematologic | Hemoglobin F | Increased affinity for oxygen<br>Inefficient delivery of oxygen to tissues<br>Transfusion threshold increased |

*GFR,* Glomerular filtration rate; *PVR,* pulmonary vascular resistance; $\dot{V}_A$*/FRC,* alveolar ventilation-to-functional residual capacity ratio.

fasting and other perioperative fluid deficits must be accounted for.

The neonate has a poorly developed sympathetic nervous system, which is unable to compensate for periods of stress with changes in heart rate, preload, or afterload. Infants are considered "vagotonic" because of the imbalance between the immature sympathetic and developed parasympathetic systems. Infants often respond initially with bradycardia when they become hypoxic or stimulated, such as during laryngoscopy. Neonatal sarcoplasmic reticulum has reduced calcium storage ability, making the heart susceptible to cardiac depression from changes in calcium levels or from the depressant effects of anesthetic agents.

### *Pulmonary*

Lung development continues in utero much later than other organs. The lungs cannot function on their own ex utero until 34–36 week gestational age, when lung volume, surface area for gas exchange, and surfactant production to help keep small airways open all have developed adequately. Alveolar maturation continues postnatally, increasing in size and number, for approximately 8 years. The relatively small number and size of neonatal alveoli lead to reduced lung compliance and small airways prone to closure. In contrast, the cartilaginous neonatal rib cage makes the chest wall highly compliant. As a result, the ribs provide less support to maintain open alveoli. The work of breathing is increased with the subsequent breath to reexpand these

closed airways. These factors cause a higher closing volume, with small airway closure during normal tidal volume.

Minute ventilation (or alveolar ventilation) is higher than in adults secondary to an increased respiratory rate because tidal volume on a per kilogram basis is the same as in adults. The alveolar ventilation-to-functional residual capacity ratio is higher because of the increased alveolar ventilation (5:1 vs. 1.5:1 in adults). Additionally, oxygen consumption is increased twofold to threefold. These factors, limited oxygen stores and increased oxygen demand, lead to rapid oxyhemoglobin desaturation during periods of apnea or airway obstruction.

The diaphragm and intercostal muscles are composed of two types of muscle fibers. Type I fibers are fatigue-resistant, and type II fibers are fatigue-prone and less energy efficient. The neonate has a decreased amount of type I fibers, resulting in an increased work of breathing and early fatigue if airway obstruction occurs. Under general anesthesia, there is a further increase in chest wall compliance because of muscle relaxation. At end expiration, the lungs reach a lower volume. Consequently, it takes more work to open airways during the next breath. For this reason, tracheal intubation is indicated during general anesthesia.

The respiratory drive to hypoxia or hypercarbia is not yet developed. Both stimuli induce respiratory depression and breath holding.

### Pediatric Airway

The neonatal airway has numerous anatomic differences that must be accounted for. Infants have a proportionally larger head and tongue with a shorter trachea and neck than adults. The large tongue may make mask ventilation difficult and necessitate use of an oral airway to relieve airway obstruction. The neonate's upper airway is susceptible to closure, especially if the head is flexed when lying supine owing to the relatively large occiput. Use of a shoulder roll may help open the airway and improve visualization of the glottic region. The larynx is located more cephalad (C4 vs. adult level of C5) with an epiglottis that is short, omega-shaped, and angled over the glottic opening. The larynx in a preterm infant is even more cephalad, located at the C3 level. These differences make straight laryngoscope blades especially useful in the neonatal period. The narrowest portion of the airway is the cricoid cartilage, necessitating performance of a leak test around a cuffed or uncuffed endotracheal tube, with an ideal leak $<30$ cm $H_2O$ but greater than peak airway pressures. The anterior attachment of the vocal cords in infants is more caudad than the posterior attachment, in contrast to the adult vocal cords that are perpendicular to the tracheal axis. When placing the tracheal tube, it often becomes hung up at the anterior commissure. This situation is particularly problematic when performing nasal intubations. When placing the tracheal tube, every effort should be made to introduce it through the posterior aspect of the vocal cords.

### Kidneys

Glomerular filtration rate (GFR) and tubular function reach maturation around 5 months of age, although this is delayed in premature infants. GFR is approximately 40% of adult values in neonates and even lower in preterm infants, with GFR values proportional to gestational age. This decreased GFR results in decreased creatinine clearance; immature diluting and concentrating ability; and impaired sodium, glucose, and bicarbonate management in neonates. These problems are worse in preterm infants. Decreased GFR impairs excretion of saline, excessive water, and medications. Renal function approaches adult values around 2 years of age.

### Liver

The liver builds up its glycogen stores primarily in the last trimester of fetal life; this means preterm infants have missed much and ELGANs have missed nearly all of their intrauterine glycogen storage time. Although term infants are susceptible to hypoglycemia, this is especially a concern in preterm neonates. Glucose hemostasis management is imperative in the perioperative setting. Maintenance glucose requirement for preterm infants is 8–10 mg/kg per minute, whereas in full-term neonates it is 5–8 mg/kg per minute.

The liver is the primary site for drug metabolism, which is slower in neonates, owing in part to relatively lower hepatic blood flow. Decreased metabolism in this population is secondary to deficiencies of many of the enzymes required for oxidation, reduction, hydrolysis, and conjugation of medications. Many enzymes still need to be exposed to toxins or drugs, which serve to stimulate and induce further development of these enzymatic pathways.

### Gastrointestinal

There is an increased incidence of gastroesophageal reflux in infants until age 4–5 months, with the rate particularly high in preterm infants, secondary to decreased lower esophageal sphincter tone.

### Thermoregulation

Heat loss to the environment is particularly high in the neonatal period because of thin skin, poor fat stores, and a high surface-to-weight ratio. Fully developed epidermis is present only after 32 weeks gestational age, making preterm newborn skin a large source of heat and water loss. Evaporative loss of water can be 5–6 mL/kg per hour. Cold is poorly tolerated because it increases oxygen consumption and leads to metabolic acidosis. In contrast to adults, neonates are unable to preserve or generate heat by peripheral vasoconstriction and shivering. Neonates produce heat by nonshivering thermogenesis that occurs predominately in brown fat that is rich in mitochondria. Brown fat is located between the scapulae, in the axillae and mediastinum, and around the adrenal glands. Increased sympathetic output results in an increase in circulating norepinephrine and thyroid-stimulating hormone that uncouples oxidative phosphorylation in brown fat, generating heat. Approximately 25% of the cardiac output is diverted to brown fat resulting in direct warming of the blood. This process uses vital energy stores in neonates and takes a high

caloric toll. Circulating norepinephrine increases PVR. Neonates left exposed to room air can lose 150 kcal per minute. Anesthetic agents negatively affect nonshivering thermogenesis.

### Hematologic Development

In utero, the predominant hemoglobin is fetal hemoglobin (HbF), which is characterized by high affinity for oxygen. HbF is 50% saturated with oxygen ($P_{50}$) at 19 mm Hg. The $P_{50}$ of adult hemoglobin (HbA) is 27 mm Hg. In utero, HbF efficiently delivers oxygen to the relatively hypoxic tissues. However, ex utero, when tissue oxygen levels increase, HbF delivers oxygen less efficiently than HbA. Transfusion thresholds are higher in infants who have predominantly HbF compared with infants whose hemoglobin has converted to HbA. A preterm infant who received blood transfusions in the NICU would have predominantly HbA depending on the total amount transfused. Transfusion thresholds should be considered based on the HbA profile.

Normal hemoglobin values at birth are as follows:

| | |
|---|---|
| Full-term newborn | 14–20 g/dL |
| Preterm newborn, 32–36 weeks gestational age | 13–14 g/dL |
| Preterm newborn, 28–32 weeks gestational age | 12–13 g/dL |

Physiologic anemia occurs at 9–12 weeks in full-term infants, with a nadir of 9–11 g/dL, and at 4–8 weeks in preterm infants, with a nadir of 7–9 g/dL. After 12 weeks, hemoglobin levels normalize around 12 g/dL for the first 2 years, although preterm infants may take 1 year to reach this level. Oxygen delivery is not compromised during these hemoglobin level changes because during the transition from HbF to HbA, the oxygen-hemoglobin dissociation curve shifts to the right. Additionally, 2,3-diphosphoglycerate levels increase, which shifts the oxyhemoglobin curve to the right, allowing better offloading of oxygen to tissues.

## 3. What specific medical problems affect preterm neonates?

### Cardiovascular

Preterm neonates are more likely to have CHD, the combination of which increases morbidity in this subset of infants. Preterm neonates are at particular risk for patent ductus arteriosus (PDA), which occurs in >50% of ELGANs. The degree of shunting through the PDA is a function of size, fluid status, and gradient between the PVR and systemic vascular resistance. Significant left-to-right shunting puts these newborns at risk for congestive heart failure and pulmonary edema. Subsequent systemic hypoperfusion increases the risk of gastrointestinal ischemia causing necrotizing enterocolitis, intraventricular hemorrhage (IVH), and renal insufficiency.

Preoperative understanding of the cardiac anatomy and physiology in infants with CHD is critical to managing intraoperative hemodynamics. Equally important is awareness of the presence of right-to-left shunts that allow entrained air to bypass the lungs and enter the cerebral and coronary circulations. Debubbling of intravenous tubing and careful injection of medications to avoid introducing air into the intravenous line are important measures to avoid this catastrophic event.

### Lung Disease

Infant respiratory distress syndrome (IRDS), formerly known as hyaline membrane disease, occurs in preterm infants secondary to immature surfactant production and impaired structural support of lung tissue. IRDS is the number one cause of mortality in preterm newborns. The incidence of IRDS is inversely related to gestational age, with about 50% of newborns of 26–28 weeks gestational age affected compared with approximately 25% of newborns of 30 weeks gestational age affected. IRDS manifests shortly after birth as progressive respiratory failure with tachypnea, increased work of breathing, grunting, tachycardia, cyanosis, and hypercarbia. It is commonly treated with ventilatory support, progressing as needed from continuous positive airway pressure to endotracheal intubation with exogenous surfactant administration and to high-frequency oscillatory ventilation and extracorporeal membrane oxygenation in extreme circumstances.

Before 34–36 weeks of gestational age, many preterm neonates often need some degree of respiratory support, whether or not they are classified with IRDS. However, these life-sustaining measures often disrupt lung development and may lead to bronchopulmonary dysplasia (BPD) and chronic lung disease. In mild cases, disruption of alveolar and vascular growth is seen. In more extreme cases, inflammation and scarring of the lungs with alveolar septal injury and interstitial fibrosis occurs. Intubation and supplemental oxygen may be needed; however, attempts to limit the use of both have been shown to decrease the severity of BPD. Continuous positive airway pressure may be used instead of intubation, when appropriate. Anesthetic care of preterm neonates usually necessitates intubation and mechanical ventilation. Lung protective ventilation strategies used in the NICU should be used during anesthetic care when appropriate. These strategies include a target peak inspiratory pressure of 14–18 cm $H_2O$ and tidal volumes of 4–6 mL/kg with slightly higher respiratory rates than normal to achieve normal minute ventilation. Positive end expiratory pressure of 4–5 cm $H_2O$ should also be used.

Many preterm neonates are poor candidates for tracheal extubation in the OR, especially if they are at risk for postoperative apnea. Leaving the tracheal tube in place should also be considered if the infant is going directly from the OR to a distant NICU. Because of the detrimental effects of prolonged mechanical ventilation in these patients, the anesthetic should be tailored to allow for early tracheal extubation when in the NICU.

### Airway

Preterm infants, who more often require tracheal intubation, can develop subglottic stenosis, which may or may not be clinically evident. A heightened awareness to the possible presence of subglottic stenosis is important, especially if tracheal intubation is planned. It may be necessary to place a smaller endotracheal tube to avoid excessive tracheal pressure leading to edema and postextubation stridor.

### Central Nervous System

Preterm infants are susceptible to IVH secondary to an immature cerebral circulatory system with poorly developed autoregulatory capabilities. Hemorrhage develops during changes in perfusion resulting in hypoxic ischemia, during which lack of blood flow leads to cell death and breakdown of blood vessel walls. This process causes further cell injury; the development of IVH serves as a marker of neurologic insult.

Preterm infants are particularly susceptible to IVH in the first week of life, although it may occur later at a time of physiologic stress. Immature cerebral autoregulating capability makes maintaining hemodynamic stability especially important. Development of IVH may be noted by sudden clinical deterioration without an obvious cause. This clinical deterioration may include hypotension, changes in heart rate, altered mental status, or respiratory acidosis. IVH is graded based on location and amount of bleeding. Grades I–II are often clinically insignificant, whereas grades III–IV characterize hemorrhage that may block the flow of cerebrospinal fluid, leading to hydrocephalus and development of long-term neurologic insult.

### Retinopathy of Prematurity

Retinopathy of prematurity (ROP) is the result of narrowing and destruction of retinal blood vessels. Fibrovascular proliferation can lead to hemorrhage, retinal detachment, and blindness. Administration of supplemental oxygen to preterm or full-term neonates <44 weeks of postconceptual age (PCA) has been associated with the development of ROP. PCA is calculated by adding the gestational age and the chronologic age. For example, a neonate born at 32 weeks of gestation who is now 10 weeks old is 42 weeks PCA. However, there are many reports of ROP occurring in infants never exposed to supplemental oxygen, in full-term infants, and in newborns with cyanotic CHD who received supplemental oxygen that did not lead to hyperoxia. These reports suggest that development of ROP is multifactorial. Other implicated causes of ROP include genetic predisposition, maternal diabetes, hypercarbia, hypotension, and exposure to fluctuating levels of oxygen. It is unclear if brief exposure to supplemental oxygen, such as occurs in the OR, increases the risk of ROP. However, given the long implicated role of oxygen in the development of ROP in preterm neonates <44 weeks PCA, it is prudent to limit supplemental oxygen administration where clinically appropriate. However, oxygen should never be denied when needed or during high-risk periods (e.g., induction, extubation).

## 4. What pharmacologic differences must be considered in preterm and term neonates?

The minimum alveolar concentration (MAC) of inhaled anesthetics changes throughout development in pediatric patients. MAC is lower in preterm infants than full-term infants. The MAC value increases from preterm values until 3–6 months of life when they reach their peak. Values for MAC then decrease, reaching a plateau around 1 year of life. Thereafter, MAC decreases by a small amount with each subsequent decade of life. The rate of rise and fall of volatile anesthetics are much faster in infants than in older children and adults. There are numerous factors contributing to this difference including a higher respiratory rate and cardiac index. These factors combined with a minimal fat reservoir for accumulation of volatile agent allow for anesthetics to be eliminated much faster, even after prolonged use.

Infants and preterm neonates in particular have proportionally higher total body water content. Fat and muscle content is much lower proportionately and increases with age. These factors have numerous implications for intravenous medication administration. Water-soluble medications (e.g., succinylcholine) need a larger initial dose per kilogram to reach a desired blood level. Drugs dependent on redistribution into fat stores for termination of effect (e.g., propofol) have a prolonged clinical effect. Immature neonatal kidney and hepatic function, compounded by larger volumes of distribution, can cause delayed drug excretion. Slowed drug metabolism and altered protein binding in neonates and especially preterm infants leads to substantial individual patient variability in response to drugs. These conditions produce wide swings in the duration of action for many drugs. Consequently, careful titration of all medications is necessary when treating preterm and full-term neonates.

Because preterm and full-term infants are "vagotonic," many practitioners administer an anticholinergic, usually atropine, before tracheal intubation. The dose of atropine in a neonate is 0.02 mg/kg and of glycopyrrolate is 0.01 mg/kg. Anticholinergics help dry secretions, which in the small neonatal airway can take up a proportionally much larger space leading to airway obstruction. This prophylactic dose is often given to infants <6 months old.

## 5. What intraoperative monitors and temperature-regulating measures should be used for this former preterm neonate?

Preterm neonates need special monitoring considerations beyond the standard American Society of Anesthesiologists monitoring guidelines. A preterm neonate's skin is very fragile and friable. Wires from monitors may traumatize the skin if the patient is lying on the wires or if they are pulling across the infant's skin. If monitor lines are too taut, they can obstruct blood flow or pull limbs or digits in unintended directions. Neonatal pulse oximetry

and electrocardiogram (ECG) leads use special adhesive material with a limited area of skin contact to minimize skin trauma with application and removal. Oxygen saturation, if a PDA is present, should be monitored both in preductal and postductal locations, to assess shunting or circulatory changes intraoperatively. The only location for monitoring preductal oxygen saturation in the presence of normal cardiac anatomy is the right upper extremity. However, variant cardiac anatomy may necessitate a different location. Postductal oxygen saturation can be monitored in any other limb. Blood pressure cuffs should be size appropriate and need to be programmed to neonatal settings because overly high inflation pressures can fracture poorly ossified and calcified bones. Small tidal volumes may make end-tidal capnography and tidal volume measurements less accurate. Low dead space capnography adapters and placement as close to the tracheal tube as possible may help improve the accuracy of these measurements. The use of invasive intraarterial or central venous monitors must take into consideration the difficulty of placement and the risk of potential disruption of distal blood flow with resultant ischemia versus the benefits of these monitors (Box 64-1).

Temperature monitoring and regulation is critical throughout anesthetic care for full-term neonates and even more so for preterm neonates. Thin skin, limited fat, and inability to shiver or tolerate cold stress highlight the need for tight temperature management during anesthesia. Anesthetics cause redistribution and loss of central heat and inhibit temperature regulation by impairing nonshivering thermogenesis. A radiant heating lamp can be used during times of maximum exposure (e.g., induction, line placement). Intraoperatively, heat loss can be minimized by use of warming blankets, increasing the temperature of the OR to 80° F, and keeping the infant's exposed surfaces (including the head) covered. Humidification of inspired gas limits evaporative heat loss, while helping to reduce atelectasis. Heat loss can be minimized during transport by using a warming incubator (Box 64-2).

**BOX 64-1 Monitoring Considerations for Preterm Infants**

- Monitoring cables and leads
  - Keep away from skin to avoid abrasions and skin trauma
  - Taut leads can cause perfusion compromise
  - Pulling can lead to dislocation of digits or limbs
- PDA
  - Consider monitoring preductal and postductal oxygen saturation
- Blood pressure
  - Appropriate cuff size
  - Limit inflation pressures to avoid trauma to limb
- End-tidal carbon dioxide and tidal volume measurements
  - Use low dead space adapters
  - Monitor close to endotracheal tube
- Intraarterial and central venous pressure catheters
  - Consider risk versus benefit

**BOX 64-2 Methods of Preventing Heat Loss in the Operating Room**

- Conductive heat loss
  - Forced air warming blanket
  - Increase operating room temperature
- Convection heat loss
  - Forced air warming blanket
  - Cover exposed areas of patient
  - Transport in heated incubator
- Evaporative heat loss
  - Humidification of inspired gas
  - Plastic wrap on infant
- Radiation
  - Double-shelled Isolette for transport
  - Radiant heating lamp during induction and emergence

## 6. What are the goals for oxygen administration intraoperatively?

Oxygen saturation by pulse oximetry ($SpO_2$) >93% in preterm neonates is associated with ROP, BPD, and brain injury with compromised neurodevelopment. Even brief exposures (minutes) to hyperoxia have been associated with an increased incidence of long-term complications. Hyperoxia causes oxidative stress and production of oxygen free radicals. Preterm neonates are deficient in antioxidant enzyme systems at birth and have low levels of antioxidants, such as vitamins C and E. Without these natural defense mechanisms, preterm neonates are at increased risk from supplemental oxygen that results in hyperoxia. However, oxygen supplementation provides added safety during key events in anesthetic care (e.g., intubation, extubation) and should not be withheld when necessary. If deemed safe, oxygen supplementation can be limited with the use of oxygen/air mixtures, with the goal of maintaining $SpO_2$ <95%.

## 7. Is this patient a candidate for discharge to home immediately after surgery?

Premature infants who are <55–60 weeks PCA are at increased risk for episodes of apnea after surgery. This risk is inversely related to gestational age at birth. These apneic episodes may be the result of physical airway obstruction or central apnea or a combination of both. All former preterm infants either should have surgery delayed until after 60 weeks PCA if the procedure is elective (e.g., circumcision requiring anesthesia) or should be admitted overnight for apnea monitoring. Exactly how long it is necessary to continue monitoring is unclear; apneic episodes have occurred >12 hours after anesthesia. The most conservative approach is the safest route in this fragile population, and it is reasonable to admit all former preterm infants <60 weeks PCA to a monitored setting for at least 12 hours of apnea-free monitoring. Full-term infants who are <44 weeks PCA have also been found to be at risk for postoperative apnea episodes, although at a lower risk. Elective surgery in these patients should also be delayed until after 44 weeks PCA. If the procedure is urgent or emergent, these

infants should be admitted and monitored with the same guidelines as ex-preterm neonates who are <60 weeks PCA.

The only parameter that consistently relates to postoperative apnea episodes is hemoglobin <10 g/dL. A preoperative hematocrit should be obtained if the decision to delay surgery would be based on hemoglobin level. Caffeine administered intravenously may decrease the incidence of postoperative apnea, but it does not preclude the need to admit infants at risk for apnea monitoring.

### 8. Would a regional anesthetic allow for this patient to be discharged home earlier?

A spinal anesthetic would be appropriate for this case. A spinal anesthetic offers the benefit of avoiding tracheal intubation and mechanical ventilation in a former preterm infant who may have underlying lung disease, BPD, or subglottic stenosis. It also precludes the need for medications that cause respiratory depression and would theoretically eliminate or decrease the risk of postoperative apnea. However, a Cochrane database review found no decrease in apneic episodes if sedatives were given before administering a spinal anesthetic. If sedation was avoided entirely, there was a statistically significant decrease in apneic episodes, although not a total elimination. The fact that apneic episodes still occurred, although less frequently, justifies the need for postoperative apnea monitoring. However, this need for monitoring does not negate the benefit of regional techniques in preterm infants who have chronic lung disease and for whom tracheal intubation is best avoided.

The duration of surgical anesthesia from spinal techniques is approximately 60 minutes in neonates because of their larger cerebrospinal fluid volume per kilogram and a more rapid cerebrospinal fluid turnover. The duration may vary slightly depending on the local anesthetic administered. Because of the relatively short duration, spinal anesthesia should be considered only in cases in which the surgeon can complete the procedure in this time frame. To maximize the time the surgeon has to perform the procedure, the surgeon should be present at the time of block and immediately ready to operate.

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CASE 65

# Adenotonsillectomy

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## QUESTIONS

1. What are the indications for adenotonsillectomy?
2. What is the pathophysiology of obstructive sleep apnea, and how is it diagnosed?
3. What should be included in the preoperative evaluation for adenotonsillectomy?
4. Is premedication recommended for this child?
5. Describe the intraoperative management for adenotonsillectomy.
6. What are the anticipated postoperative problems?
7. Which patients should be admitted postoperatively?
8. How is a patient with postadenotonsillectomy bleeding managed?

A 3-year-old girl with obstructive sleep apnea presented for adenotonsillectomy (AT). She had a 3-day history of a runny nose and a productive cough.

### 1. What are the indications for adenotonsillectomy?

The most common indication for adenotonsillectomy (AT) in pediatric patients is sleep-disordered breathing. Obstructive sleep apnea (OSA) is an extreme form of sleep-disordered breathing. Other indications include recurrent pharyngitis, peritonsillar abscess, dysphagia, asymmetric tonsillar hypertrophy, halitosis, and post-transplant lymphoproliferative disorder. Indications for adenoidectomy without tonsillectomy are adenoidal hypertrophy, chronic sinusitis, adenoiditis, and recurrent otitis media.

### 2. What is the pathophysiology of obstructive sleep apnea, and how is it diagnosed?

Respiration involves chest wall expansion and diaphragm descension, both of which create negative intrapleural pressure. This negative pressure is distributed throughout the lower and upper airway. Negative pressure in the pharynx tends to draw soft tissues inward, predisposing to upper airway obstruction. During sleep, airway patency is maintained despite a decrease in pharyngeal muscle tone. This situation may be altered in the presence of neuromuscular hypotonia or craniofacial abnormalities or when alcohol or sedatives are taken (Box 65-1). Tonsillar hypertrophy exacerbates upper airway obstruction in two ways. First, it encroaches on the airway, narrowing its cross-sectional area. Second, when the cross-sectional area is reduced sufficiently, airflow through the stenosed pharynx increases, which produces reduced pressure inside the pharynx by the Bernoulli effect. The additional decrease in pharyngeal pressure draws soft tissues farther into the airway and exacerbates upper airway obstruction. Patients with neuromuscular or craniofacial disorders are at increased risk for OSA, especially if tonsillar hypertrophy coexists.

Airway obstruction results in hypoxia and hypercarbia that trigger the brainstem arousal reflex causing increased pharyngeal tone. When pharyngeal dilator muscles contract, soft tissues are moved out of the airway lumen, and airway patency is improved. This series of events occurs many times during sleep, disrupting the normal sleep cycle. Symptoms consist of snoring, breathing pauses, gasping, and use of accessory respiratory muscles. Enuresis and excessive sweating may also occur. If the sleep cycle is significantly disturbed, daytime somnolence is present as well.

Chronic hypoxia and hypercarbia lead to pulmonary vasoconstriction and pulmonary hypertension. Right atrial enlargement, right ventricular hypertrophy, and ultimately right-sided heart failure (cor pulmonale) develop if OSA is not treated early (Figure 65-1). Polycythemia may occur in response to chronic hypoxia.

The "gold standard" for the diagnosis of OSA is polysomnography. Polysomnography is an overnight sleep study during which electroencephalogram, electromyogram, electrocardiogram (ECG), pulse oximetry, airflow, and thoracic and abdominal movements are monitored. The number of obstructed breaths, percentage of decreased airflow, and degree of oxygen desaturation are used to determine whether obstructive apnea or hypopnea is present. Obstructive apnea is defined as >90% decrease in airflow despite respiratory effort. Obstructive hypopnea is defined as >50% decrease in airflow despite respiratory effort and a >3% decrease in oxygen saturation. The apnea-hypopnea index determines the severity of OSA. Severe OSA is defined as an apnea-hypopnea index score >10 and oxygen desaturation nadir <80%. In the absence of a polysomnography study, the parent's description of the symptoms or home sleep video is used to determine the need for AT.

**BOX 65-1 Congenital Conditions Associated with Obstructive Sleep Apnea**

- Acromegaly
- Apert syndrome
- Crouzon syndrome
- Goldenhar syndrome
- Hurler syndrome
- Hunter syndrome
- Pierre Robin sequence
- Treacher Collins syndrome
- Trisomy 21

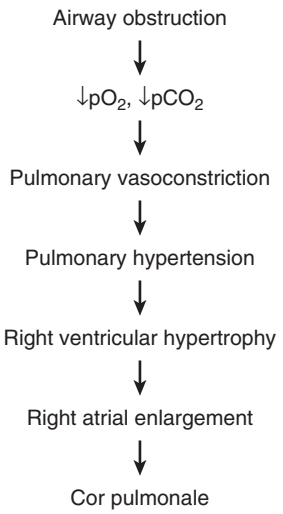


**FIGURE 65-1** ■ Pathophysiology of OSA.

### 3. What should be included in the preoperative evaluation for adenotonsillectomy?

The preoperative evaluation should be directed at assessment of the airway, cardiopulmonary system, and bleeding history (Box 65-2). Tonsillar hypertrophy is classified according to the percentage of pharyngeal airway it occupies, as follows:

+1 = <25%
+2 = 25–50%
+3 = 50–75%
+4 = >75%

A classification of 3 or 4 correlates with an increased risk of airway obstruction during induction of general anesthesia. The presence of a craniofacial abnormality contributes to difficulty with mask ventilation and intubation. Alternative airway management devices may be necessary.

A cardiopulmonary evaluation should be performed in a patient with severe OSA. The following examinations may be considered:

- Chest x-ray—cardiomegaly
- ECG—right atrial enlargement, right ventricular hypertrophy
- Echocardiogram—pulmonary hypertension, cardiac function
- Arterial blood gas—carbon dioxide retention
- Hemoglobin and hematocrit—polycythemia

**BOX 65-2 Preoperative Evaluation of Patients with Severe Obstructive Sleep Apnea**

- Airway
  - Tonsillar size
  - Craniofacial abnormalities
- Pulmonary
  - Arterial blood gas
- Cardiac
  - Electrocardiogram
  - Echocardiogram
  - Chest x-ray
  - Cardiac consultation
- Hematology
  - Hemoglobin and hematocrit
- Bleeding history
  - Coagulation studies
  - Platelet count

A pediatric cardiac consultation is indicated if pulmonary hypertension or cor pulmonale is suspected.

A bleeding history should be obtained. Coagulation studies are unnecessary, unless the patient's history or family history is suggestive of an existing coagulopathy (e.g., excessive bleeding after cuts or tooth extraction, easy bruisability).

The presence or recent history (within 2 weeks) of an upper respiratory infection (URI) should be sought. URIs are common in pediatric patients, especially in patients undergoing AT. Complications associated with URIs are laryngospasm, bronchospasm, secretions clogging the endotracheal tube, postextubation stridor, and oxygen desaturation in the postanesthesia care unit. The factors associated with increased risk are productive cough, rhinorrhea, parent's impression that the child is ill, history of asthma, history of prematurity, passive smoking, and use of an endotracheal tube. If the patient's symptoms are suggestive of increased risk of complications under general anesthesia, consideration can be given to postponing surgery for 3–4 weeks. However, these patients may have recurring episodes of URIs, and it may not be possible to find that window of opportunity. Symptoms such as rhinorrhea or productive cough may be chronic, and postponing surgery would not lead to reduction of risk. If the decision is made to proceed with surgery, the risks of general anesthesia should be discussed with the parents and documented in the record. The reader is referred to a complete discussion of the risks of general anesthesia in a child with an URI and the approach to identifying the child who is at risk (Tait and Melviya 2005).

### 4. Is premedication recommended for this child?

Premedication should be administered with caution, if at all, in patients with OSA. Significant airway obstruction may develop because patients with OSA are particularly sensitive to the effects of sedatives. If premedication is administered, pulse oximetry may be beneficial, and emergency airway equipment should be immediately available.

## 5. Describe the intraoperative management for adenotonsillectomy.

Induction of general anesthesia can be accomplished with either inhalation or intravenous agents. Airway obstruction commonly occurs during induction of general anesthesia and is frequently overcome by placement of an oral airway when the patient reaches an adequate depth of anesthesia, application of continuous positive airway pressure (CPAP) in a spontaneously breathing patient, or positive pressure ventilation in an apneic patient. In a patient with severe OSA, insertion of an intravenous line before induction may be beneficial to allow for the administration of emergency medications if necessary.

Endotracheal intubation with a preformed endotracheal tube is the most common method for securing the airway during AT. The preformed endotracheal tube easily fits into the mouth retractor the surgeon places for surgical exposure and does not obstruct the surgeon's view. A standard endotracheal tube may become kinked after placement of the mouth retractor in an attempt to push the tube away from the surgeon's view. A cuffed endotracheal tube is preferred because it provides additional protection against aspiration of blood in the airway. During placement of the mouth retractor and during the procedure, kinking or dislodgment of the endotracheal tube may occur either distally into the right main stem bronchus or out into the pharynx or esophagus. Monitoring of breath sounds and capnography is important for the detection of these events. Monitoring of peak airway pressures also alerts the anesthesiologist to possible kinking of the endotracheal tube.

An alternative to endotracheal intubation is the use of a supraglottic device. Problems with supraglottic devices include dislodgment or obstruction during placement of the mouth retractor.

No one method is superior for maintenance of general anesthesia. However, opioids should be administered judiciously because these patients are sensitive to their effects, and return of spontaneous ventilation and extubation at the end of the procedure may be delayed. Maintenance of spontaneous ventilation throughout the procedure provides the added advantage of titrating opioids to the patient's respiratory rate. This would ensure that the patient does not receive an excessive amount of opioids and allows for extubation at the end of surgery. Muscle relaxants may be used but are not necessary for surgical exposure.

Medications administered intraoperatively for postoperative analgesia include nonsteroidal antiinflammatory drugs (NSAIDs) such as ketorolac and acetaminophen. The administration of NSAIDs for AT is controversial because of the concern of a possible increased incidence of post-AT bleeding. Although there are studies showing that ketorolac does not result in an increased incidence of bleeding postoperatively, many surgeons still prefer to avoid NSAIDs. Acetaminophen can be administered either rectally (40 mg/kg) or intravenously (15 mg/kg).

Postoperative nausea and vomiting (PONV) occurs commonly after AT. PONV may be secondary to opioid administration, blood swallowed during the procedure, or inflammation of the airway. Antiemetic prophylaxis is warranted. Dexamethasone (0.5–1.0 mg/kg), which is usually given for airway edema, also provides antiemetic prophylaxis. Because AT is associated with a high risk of PONV, ondansetron (0.1–0.15 mg/kg) may be administered intraoperatively as well. Alternatively, ondansetron can be ordered as a rescue medication in the postanesthesia care unit (PACU).

At the end of the procedure, the surgeon passes an orogastric tube to suction any blood that has entered the stomach. When the child is awake and has demonstrated adequate spontaneous ventilation, the endotracheal tube can be removed. Meticulous attention should be paid to ensuring a patent airway because laryngospasm occurs frequently on extubation. Deep extubation is an acceptable alternative; however, some anesthesiologists take full stomach precautions with these patients because of the presence of swallowed blood in the stomach. Airway obstruction and laryngospasm may occur after deep extubation.

Postobstructive pulmonary edema occurs occasionally after AT. The mechanism for development of postobstructive pulmonary edema after sudden relief of a chronically obstructed airway is different than when acute airway obstruction occurs (e.g., laryngospasm). In chronic airway obstruction (e.g., tonsillar hypertrophy), an intrinsic positive end expiratory pressure develops that results in an increased intrathoracic pressure compensating for the low intrathoracic pressures generated by inspiring against an obstruction. Placement of an endotracheal tube relieves the obstruction, decreasing the intrathoracic pressure, which results in an increase in venous return and pulmonary blood volume. The increase in pulmonary blood volume may lead to transudation of fluid into the lung; this becomes evident after removal of the endotracheal tube at the end of the procedure. Treatment consists of oxygen, diuretics, and reintubation if needed to provide CPAP or positive end expiratory pressure.

Patients should be placed in the tonsillar position (lateral decubitus with head down) and supplemental oxygen should be provided during transport to the PACU.

## 6. What are the anticipated postoperative problems?

Analgesia should be provided with judicious administration of opioids. If acetaminophen is not administered in the operating room, it should be ordered postoperatively. Surgeons commonly prescribe codeine (in combination with acetaminophen) for postoperative analgesia. However, the analgesic effect of codeine is variable because it is dependent on cytochrome P450 debrisoquine-4-hydroxylase (CYP2D6) for conversion to the active metabolite. Genetic variations result in either gene duplication (greater fraction of active metabolite) or inactive genes (decreased active metabolite). Deaths have been reported in patients who are rapid metabolizers of codeine.

Because PONV and pain on swallowing occur frequently in these patients, they are required to drink without vomiting before discharge from the PACU. Antiemetic medication may be helpful. Bleeding may occur after AT and is discussed subsequently.

### 7. Which patients should be admitted postoperatively?

Patients at increased risk for postoperative respiratory complications are frequently admitted overnight for apnea monitoring, including the following:

- <3 years old
- Craniofacial abnormalities
- Neuromuscular abnormalities

Depending on your institution, apnea monitoring may require admission to an intensive care unit. Patients who do not meet PACU discharge criteria must be admitted as well; these include the following:

- Continued need for supplemental oxygen
- Poor oral intake
- Continued vomiting
- Exhibit airway obstruction in the PACU

### 8. How is a patient with postadenotonsillectomy bleeding managed?

Bleeding after AT occurs either in the first 24 hours or, more commonly, 5–10 days postoperatively when the eschar falls off. The preoperative evaluation of these patients should be directed at assessment of the airway and volume status (Box 65-3). A complete assessment of the airway may be impossible in an agitated child, but visual inspection of the external airway and details of airway management during the previous AT are helpful.

Assessment of the volume status and fluid resuscitation must be performed expeditiously. The amount of blood loss may not be evident because much of the blood may have been swallowed. Heart rate and blood pressure help guide fluid management. If intravenous access cannot be accomplished rapidly, intraosseous access should be obtained. If shock is present, a bolus of non–glucose-containing isotonic fluid (20 mL/kg) is administered over 5–10 minutes and repeated as needed if hypotension persists. Blood is drawn for hemoglobin, type and cross, platelet count, and coagulation studies. Emergent surgery cannot be delayed waiting for the results because the bleeding will not stop until surgical control is obtained.

**BOX 65-3 Preoperative Evaluation for Postadenotonsillectomy Bleeding**

- Airway assessment
  - Anatomy—visual inspection
  - Previous anesthetic
- Volume status
  - Heart rate and blood pressure
  - Intravenous or intraosseous access
  - Non–glucose-containing isotonic fluid
  - Blood transfusion (based on hemoglobin and hematocrit)

In the operating room, the following items should be prepared:

- Multiple laryngoscope blades
- Styletted endotracheal tubes
- Two large-bore suctions
- Alternative airway devices
- Tracheostomy equipment

Induction of general anesthesia should not proceed without an attending surgeon present and ready to perform a surgical airway, if necessary. Full stomach precautions are taken with these patients (i.e., rapid sequence induction with cricoid pressure). An awake fiberoptic intubation for an identified difficult airway may be impossible in an agitated child or if there is blood in the airway. A mask inhalation induction may be performed if there is concern about the airway. The patient is placed in the right lateral decubitus position with the head down. This position may decrease the risk of aspiration because blood pools in the oral pharynx.

The choice of induction agent depends on the hemodynamic stability and volume status of the patient. Administering a 20-mL/kg bolus of isotonic fluid before induction may prevent hypotension. Etomidate or ketamine in reduced doses may be administered if volume status is still a concern. Alternatively, propofol may be used in a decreased dose. Either succinylcholine or rocuronium may be administered. However, if the procedure is short, the duration of action of rocuronium exceeds the surgical time. Succinylcholine, with its short duration of action, may be preferable if a difficult airway is anticipated.

Hemoglobin and hematocrit levels should guide blood transfusions. Coagulation factors are replaced if a coagulopathy is detected by laboratory testing or is suspected.

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CASE 66

# Foreign Body Aspiration

Michael Chietero, MD

## QUESTIONS

1. What is foreign body aspiration, and how does it occur?
2. How does a patient with foreign body aspiration typically present?
3. What are the preoperative concerns in a patient with foreign body aspiration?
4. How is a patient with foreign body aspiration managed intraoperatively?
5. What are the postoperative concerns in a patient who has aspirated a foreign body?

An 18-month-old boy was brought to the pediatric emergency department by his parents. Two hours previously, he had gagged and choked while eating dinner. Since then, he has been agitated and coughing intermittently.

### 1. What is foreign body aspiration, and how does it occur?

Foreign body aspiration, the lodging of a substance in the trachea or bronchus, is a very serious condition and can be a life-threatening emergency because there is a potential for complete airway obstruction. Foreign body aspiration occurs most commonly in children 1–3 years old because they often put foreign substances in their mouths, lack molars to chew their food adequately, and often run or play with objects in their mouths. Peanuts, seeds, and other food particles are the most common foreign bodies aspirated (Figure 66-1). Less frequently, other objects such as plastic game pieces and small batteries are aspirated. In addition, certain aspirated objects may cause intense irritation and edema (e.g., peanuts from the oil component) or corrosion and necrosis (e.g., batteries) to the airway mucosa.

Foreign bodies can also be ingested into the hypopharynx, esophagus, and stomach. Although often not as urgent or life-threatening, these cases can still present a significant challenge. These children are typically older (1–6 years old), and the foreign bodies are usually coins, bones, or plastic game pieces.

### 2. How does a patient with foreign body aspiration typically present?

There is often a history of choking, gagging, coughing, or wheezing occurring when the child is eating or when playing with small objects. A period of cyanosis may be noted by the parents. A foreign body large enough to obstruct the trachea completely requires immediate treatment with back blows and chest compressions in infants or abdominal thrusts in children. More often, airway obstruction is incomplete, and these patients typically present to the emergency department.

On physical examination, the child may appear agitated. Agitation could be due to hypoxemia. Tachypnea and tachycardia are often present. Coughing, unilateral decreased breath sounds, and wheezing are the classic signs. There should be a high suspicion for foreign body aspiration in any child in this age range who presents to the emergency department with new-onset wheezing, especially if unilateral. If the child shows significant respiratory compromise, rapid transport to the operating room is indicated. In stable children with a questionable diagnosis, chest x-rays may be helpful. Although most foreign bodies are not radiopaque, indirect findings such as hyperinflation of the obstructed lung secondary to air trapping or atelectasis secondary to decreased ventilation may be suggestive of the diagnosis. Hyperinflation is best visualized in an expiratory film but may be difficult to obtain in younger age groups.

The presentation of a patient with foreign body ingestion is slightly different. Coughing and choking can occur initially because of laryngeal irritation, followed by refusal to feed, increased salivation, discomfort with swallowing, and vomiting. In contrast to airway foreign bodies, these foreign bodies are often radiopaque, and a chest x-ray is frequently helpful to confirm the diagnosis, revealing type and location. These cases are typically not as urgent, with the exception of ingestion of potentially toxic objects, such as batteries, or potentially traumatic objects, such as open safety pins (Figure 66-2).

### 3. What are the preoperative concerns in a patient with foreign body aspiration?

Patients should be thoroughly evaluated before coming to the operating room, especially noting their preoperative respiratory status and oxygen saturation. The type of foreign body aspirated (i.e., food particle or inanimate object),

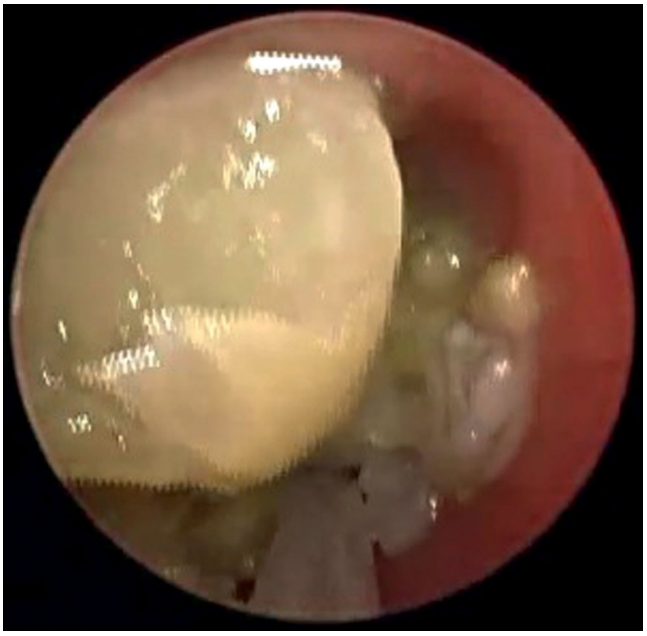

**FIGURE 66-1** ■ A piece of broccoli in the bronchus. Note erythema and edema of the mucosa.

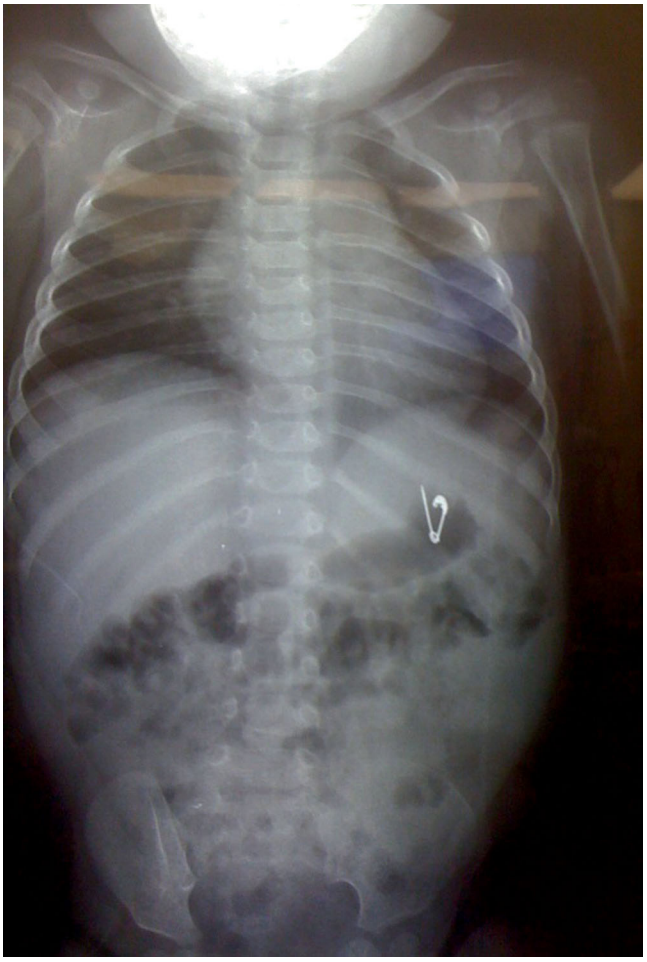

**FIGURE 66-2** ■ Ingestion of an open safety pin.

its potential location, and the potential for complete airway obstruction should be ascertained. Aspiration risk secondary to the presence of a full stomach needs to be assessed, and a decision needs to be made in conjunction with the surgeon whether or not the procedure can be safely delayed until the child is NPO (nil per os ["nothing by mouth"]) for an appropriate amount of time.

Close communication, planning, and cooperation with the pediatric otolaryngologist or surgeon are critical to the success of this procedure. A management plan should be discussed and decided on before starting the case.

## 4. How is a patient with foreign body aspiration managed intraoperatively?

Before the induction of anesthesia, standard American Society of Anesthesiologists monitors should be applied, and an intravenous catheter should be placed, if one is not present already. Either an intravenous or inhalation induction of anesthesia can be performed. Inhalation anesthesia should be performed with 100% oxygen and sevoflurane. Nitrous oxide should be avoided, especially if air trapping is noted on the preoperative chest x-ray. In addition, a corticosteroid, such as dexamethasone (0.5–1 mg/kg), is often administered to treat potential airway edema.

The operative management of a patient with a foreign body aspiration involves rigid bronchoscopy that precludes the use of an endotracheal tube. The choice between maintaining spontaneous ventilation or instituting positive pressure controlled ventilation rests with the anesthesiologist and surgeon and is often based on personal preference. Positive pressure ventilation carries the theoretical concern of forcing the foreign body deeper into the airway, so many anesthesiologists opt for spontaneous ventilation to avoid this possibility. However, it is often difficult to maintain adequate depth of anesthesia with spontaneous ventilation, and the patient may move or cough during the procedure. There are many advantages and disadvantages of both spontaneous and controlled ventilation during rigid bronchoscopy (Table 66-1).

The rigid bronchoscope has a ventilating sidearm where the anesthesia circuit can be attached; however, contamination of the operating room with anesthetic gases may be an issue. Alternatively, total intravenous anesthesia (TIVA) allows for a deep level of anesthesia without polluting the operating room, while providing the surgeon with a quiet field to visualize the tracheobronchial tree. Topical spray of the larynx and vocal cords with 4% lidocaine (maximum of 4 mg/kg) often is beneficial because it decreases the incidence of coughing and laryngospasm.

When the child is adequately anesthetized, the surgeon takes over the airway and intubates the trachea with the rigid bronchoscope. When the foreign body has been identified, the surgeon attempts to remove it with forceps. The aspirated object is often too big to be removed through the bronchoscope, so the forceps and bronchoscope are removed from the trachea as a single unit. It is important to maintain a quiet field during this time because patient movement or coughing risks losing

TABLE 66-1 **Spontaneous versus Controlled Ventilation during Rigid Bronchoscopy**

| *Spontaneous Ventilation* | | *Controlled Ventilation* | |
|---|---|---|---|
| **Advantages** | **Disadvantages** | **Advantages** | **Disadvantages** |
| Avoids theoretical risk of forcing foreign body deeper into airway<br>Allows for continuous ventilation during removal of foreign body<br>Allows for immediate assessment of airway adequacy after foreign body removal | Difficult to maintain adequate depth of anesthesia, risking patient movement and coughing during procedure | Ensures adequate depth of anesthesia, preventing patient movement, especially with neuromuscular blockade<br>Ensures adequate oxygenation and ventilation and may decrease atelectasis | During periods of apnea, risk of oxygen desaturation<br>Theoretical concern that positive pressure ventilation may move foreign body more distally, making removal more difficult |

the foreign body into the trachea. The result could be complete airway obstruction or relocation into the contralateral, unaffected main stem bronchus. Organic food particles (especially peanuts) often fragment when grasped with the forceps, and multiple passes must be performed to remove it completely. After the foreign body is removed, the surgeon takes another look to evacuate any viscous secretions and to assess whether any residual components remain and the degree of resultant edema. This inspection helps guide postoperative management. If significant airway edema is present, a decision may be made to keep the patient's trachea intubated and admit the patient to the intensive care unit (ICU) postoperatively.

Foreign body ingestion in the gastrointestinal tract is removed via esophagogastroduodenoscopy with a flexible fiberoptic endoscope, usually performed by a gastroenterologist. The concern with an ingested foreign body is obstruction, trauma, or perforation of the gastrointestinal tract. General inhalation anesthesia or TIVA with endotracheal intubation is required because there is a risk of complete airway obstruction if the foreign body is lost into the trachea or hypopharynx during removal. If the patient has recently eaten, the procedure should be delayed for an appropriate amount of time. If the child is dyspneic and the procedure cannot be delayed, a rapid-sequence induction should be performed to decrease the risk of pulmonary aspiration. Cricoid pressure should be used cautiously, if at all, for foreign bodies in the hypopharynx because it may irritate the upper airway, dislodge the foreign body into the trachea, or cause trauma to the esophagus. Complications resulting from the removal of an ingested foreign body include trauma or perforation of the gastrointestinal tract (Box 66-1).

**BOX 66-1 Intraoperative Concerns**

**Foreign Body Aspiration**

- Spontaneous or controlled ventilation, at discretion of anesthesiologist and surgeon
- Sharing of airway with surgeon without endotracheal tube in place
- Corticosteroids to reduce airway edema
- Avoid nitrous oxide
- Deep inhalation anesthesia or TIVA, especially during foreign body removal
- Potential for complete airway obstruction
- Potential for airway compromise even after foreign body removed

**Foreign Body Ingestion**

- Aspiration risk
- Cautious cricoid pressure, if necessary
- Intubation to protect airway
- Risk of trauma to gastrointestinal tract

### 5. What are the postoperative concerns in a patient who has aspirated a foreign body?

Because residual mucosal edema and viscous secretions often persist after foreign body removal from the airway, respiratory status must be carefully monitored in the postoperative period. Wheezing and stridor as well as hypoxia may continue to be present. Humidified oxygen may be beneficial. If airway trauma and edema are severe, the patient can remain intubated and sent to an ICU.

Complications after foreign body aspiration are rare, but they do occur. Complications include laryngeal, tracheal, or bronchial trauma; pneumothorax; and pneumonia. Failure to remove the foreign body by bronchoscopy occurs in a small percentage of cases, necessitating either repeat rigid bronchoscopy or rarely mediastinoscopy or thoracotomy.

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CASE 67

# MRI and the Down Syndrome Child

**Cheryl K. Gooden, MD, FAAP**

## QUESTIONS

1. What is magnetic resonance imaging?
2. What are the magnetic field problems associated with the magnetic resonance imaging?
3. What are the specific problems encountered with physiologic monitors and equipment in the magnetic resonance imaging suite?
4. What are the possible patient problems encountered in the magnetic resonance imaging scanner?
5. What are the clinical manifestations of Down syndrome?
6. Describe the preanesthetic evaluation of children with Down syndrome.
7. What anesthetic alternatives are available for children with Down syndrome undergoing magnetic resonance imaging?
8. What are the postanesthetic concerns for children with Down syndrome after magnetic resonance imaging?

A 4-year-old boy with an intracranial mass presented for magnetic resonance imaging (MRI) of the brain. Past medical history was significant for Down syndrome (trisomy 21) and seizure disorder. Surgical history included tonsillectomy and adenoidectomy under general anesthesia at age 2 years without complications.

### 1. What is magnetic resonance imaging?

MRI incorporates the use of static and gradient magnetic fields with radiofrequency (RF) pulses to produce images of the body. Magnetic field strengths range from 0.15–3.0 tesla (T). The tesla is a measure of magnetic field strength (1 T = 10,000 gauss). Image quality depends on the strength of the magnetic field.

Hydrogen is the element most commonly used in MRI because it is the most abundant element in human tissue and it can be magnetized. Atoms, such as hydrogen, with an unpaired number of protons or neutrons respond to and align themselves within the magnetic field of the MRI scanner.

After placement of the patient within the cylindrical bore of the magnet, a steady state is established in which hydrogen atoms are in alignment. RF pulses are introduced and deflect the orientation of the atoms. When the RF pulses are eliminated, the hydrogen atoms return to their original position of alignment. As these atoms establish a resting state, the energy emitted is used to produce a resulting image.

### 2. What are the magnetic field problems associated with the magnetic resonance imaging?

MRI magnets exert a substantial pull on ferromagnetic objects. The major concern is that the magnet could convert ferromagnetic objects into missiles that can lead to injury or lethal outcomes to patients or personnel. Care must be taken to avoid the use of or to have in one's possession objects such as pens, scissors, clamps, stethoscopes, nonlithium batteries, ferromagnetic compressed gas cylinders, and other objects that are ferromagnetic. Before bringing any piece of equipment into the MRI suite, it should be checked to ensure that it is MRI-compatible.

Patients with implanted ferromagnetic devices or objects, which include pacemakers, tissue expanders with metallic ports, implantable cardioverter defibrillators, implantable infusion pumps, cochlear implants, and certain types of intracranial aneurysm clips, are generally excluded from MRI studies. The magnetic fields of MRI scanners can potentially affect the function and safety of these devices. Newer aneurysm clips contain nonferrous material and are not considered to be problematic. However, a thorough investigation of the type of aneurysm clip is required before proceeding with an MRI study. Metallic-based substances such as eye makeup or tattoos can produce local skin irritation during MRI scanning (Box 67-1). Metals that are known to be safe include stainless steel, titanium, alloys, and nickel. Plastic equipment is preferred for use in proximity to MRI magnets.

### 3. What are the specific problems encountered with physiologic monitors and equipment in the magnetic resonance imaging suite?

The use of conventional electrocardiogram (ECG) monitors in the MRI suite can distort the image because wire leads act as antennas. Additionally, ECG monitors may be unable to distinguish myocardial electrical potentials from background static magnetic field and RF pulses.

**BOX 67-1 Devices and Objects Considered Unsafe for Magnetic Resonance Imaging**

- Pacemakers
- Implantable cardioverter defibrillators
- Tissue expanders with metallic ports
- Implantable infusion pumps
- Cochlear implants
- Intracranial aneurysm clips (certain types)

Voltage induced in the wire leads can cause electrical shock hazards and burns to the patient.

Magnetic fields produced by MRI scanners can cause interference with and possibly inactivation of conventional operating room pulse oximeters. Either nonferrous or fiberoptic cabled pulse oximeters should be used. The pulse oximeter probe is best positioned on a distal extremity, as far from the site to be scanned as possible. In this way, interference and possible scan artifact can be minimized.

The oscillometric method is optimal for noninvasive blood pressure monitoring in the MRI suite because it is not affected by magnetic fields. Fiberoptic systems in conjunction with invasive blood pressure monitoring have been used successfully. In addition, central venous pressure can be monitored if necessary. There are several transducers that lack ferrous components and can be used in the MRI suite.

The use of side-stream capnography with a long sampling line allows for monitoring ventilation, anesthetic gas concentrations, and circuit disconnection during MRI scanning. However, the long sampling line may create a greater lag time between the actual event and the time of detection.

Several MRI-compatible anesthesia machines are available commercially. Only oxygen, air, and nitrous oxide cylinders made of aluminum can be used in the MRI suite. Ferromagnetic compressed gas cylinders are attracted by the magnet and have resulted in injury and death to patients and personnel. Infusion pumps should be checked for MRI compatibility as well.

## 4. What are the possible patient problems encountered in the magnetic resonance imaging scanner?

The MRI environment creates an unavoidable distance between patients and anesthesiologists. The patient's inaccessibility after placement in the MRI scanner can be problematic when immediate access is required. Visibility is limited when the patient is placed within the scanner gantry. Some MRI systems are equipped with a closed-circuit camera which allows for continuous visualization of the patient.

Noise is produced by the MRI scanner as a result of the vibration of wire loops producing gradient current in the presence of RF pulses. This noise can be loud at times and may average approximately 95 dB. Auditory protection, such as earplugs, should be provided to all patients undergoing a scan.

The risk of burns during MRI is another possible patient problem. The monitoring systems that may be associated with burns in the MRI scanner have been discussed previously.

Gadopentetate dimeglumine (gadolinium) is a commonly used MRI contrast agent that is eliminated by the kidneys. It is a low-osmolar ionic medium, with a slower clearance in neonates and infants compared with adults. Reported adverse effects include thrombophlebitis, hypotension, headache, nausea, and vomiting. A more serious complication, first reported in 2006, is nephrogenic systemic fibrosis, which involves progressive and severe fibrosis of the skin and other systemic organs. This is seen in patients with acute or chronic kidney insufficiency (glomerular filtration rate $<30$ mL/minute/1.73 $m^2$), end-stage renal disease, and hepatorenal syndrome, and in patients in the perioperative liver transplantation period. Patients on hemodialysis should undergo dialysis soon after receiving gadolinium, although it is unknown whether this prevents the development of nephrogenic systemic fibrosis.

Finally, anxiety and claustrophobia are possible problems encountered by awake patients (Box 67-2).

## 5. What are the clinical manifestations of Down syndrome?

Down syndrome (trisomy 21) is the most common autosomal chromosomal abnormality causing mental retardation. It occurs in approximately 1 in 800 live births. Children with Down syndrome can have associated congenital defects and other medical problems requiring surgical intervention. Anesthetic management of these patients can present many challenges.

Clinical manifestations of Down syndrome that are of particular concern to the anesthesiologist include macroglossia, micrognathia, obstructive sleep apnea, small subglottic area, and recurrent pulmonary infections. Other considerations for the anesthesiologist include hypotonia, atlantoaxial instability, seizure disorders, high arched palate, and varying degrees of mental retardation. Congenital heart defects occur in 30–50% of children with Down syndrome. These lesions include endocardial cushion defects, ventricular septal defect, atrial septal defect, patent ductus arteriosus, and tetralogy of Fallot. Pulmonary hypertension may also be present. Table 67-1 provides a review of systems specific to patients with Down syndrome.

**BOX 67-2 Patient-Related Considerations for Magnetic Resonance Imaging**

- Patient inaccessibility
- Lack of patient visibility
- Noise
- Burns
- Gadolinium related
  - Side effects: thrombophlebitis, hypotension, headache, nausea and vomiting
  - Complications: nephrogenic systemic fibrosis
- Anxiety, claustrophobia (may be encountered in awake patient)

TABLE 67-1 **Review of Systems: Child with Down Syndrome**

| System | Clinical Features |
|---|---|
| Airway | Macroglossia<br>Small mouth<br>High arched palate<br>Small nasopharynx<br>Micrognathia<br>Small subglottic area<br>Short, broad neck<br>Tonsillar and adenoidal hypertrophy |
| Cardiac | Endocardial cushion defect<br>Patent ductus arteriosus<br>Ventricular septal defect<br>Atrial septal defect<br>Tetralogy of Fallot |
| Pulmonary | Recurrent respiratory tract infections<br>Pulmonary hypertension (associated with congenital heart disease)<br>Obstructive sleep apnea<br>Increased risk for postoperative pulmonary complications |
| Musculoskeletal | Hypotonia<br>Temporomandibular joint laxity (and laxity of other joints)<br>Atlantoaxial instability<br>Cervical spondylosis |
| Neurologic | Seizure disorder<br>Mental retardation |
| Gastrointestinal | Duodenal atresia<br>Increased incidence of Hirschsprung disease |
| Immune and hematologic | Altered immune response<br>Increased incidence of lymphocytic and myeloid leukemia<br>Frequent infections (particularly respiratory)<br>Polycythemia (neonatal period) |

### 6. Describe the preanesthetic evaluation of children with Down syndrome.

The preanesthetic evaluation of children with Down syndrome should include a complete history and physical examination. The anesthetic assessment focuses particularly on the organ systems most commonly involved in Down syndrome. A detailed systematic approach is necessary to prepare for potential intraoperative events. Further evaluation of these patients depends on the extent of organ system involvement.

Atlantoaxial instability is present in 10–20% of children with Down syndrome and is a major source of concern in the perianesthetic period. Several neurologic deficits may be associated with atlantoaxial instability (Box 67-3). Screening for atlantoaxial instability includes lateral cervical spine radiographs in the flexed, extended, and neutral positions. The atlas-dens interval is often used to quantify movement of the atlantoaxial joint. The atlas-dens interval is measured from the posterior margin of the anterior arch of the first cervical spine to the anterior margin of the dens. The normal atlas-dens interval for children is ≤4.5 mm.

**BOX 67-3 Neurologic Deficits Associated with Atlantoaxial Instability**

- Gait abnormalities
- Neck pain
- Torticollis
- Mild extremity weakness
- Hyperreflexia
- Spasticity

The current recommendation is that screening for atlantoaxial instability should be performed at 3–5 years of age. Follow-up cervical radiographs at 3-year intervals are no longer recommended. Obtaining a good history and neurologic assessment are key factors. When a child with Down syndrome presents for general anesthesia, all precautions must be taken to maintain the cervical spine in neutral position.

### 7. What anesthetic alternatives are available for children with Down syndrome undergoing magnetic resonance imaging?

Premedication for a child with Down syndrome may be necessary to facilitate induction of anesthesia. Oral or intranasal midazolam may be considered for premedication. Intramuscular ketamine has also been used successfully. However, ketamine is relatively contraindicated for the patient in this case because of his seizure disorder. Parental presence during induction of anesthesia is quite helpful. However, parental presence should not be viewed as a substitute for premedication.

If the airway examination appears normal, either an inhalation or intravenous induction can be performed. An endotracheal tube and laryngeal mask airway used with general anesthesia are good options. Sedation with a propofol or dexmedetomidine infusion may also be considered. The choice of anesthetic technique for a child with Down syndrome involves similar decision making as with any patient.

### 8. What are the postanesthetic concerns for children with Down syndrome after magnetic resonance imaging?

Postanesthetic concerns after MRI are the same as after an anesthetic in the operating room. The child with Down syndrome should be observed in either a postanesthesia care unit or a recovery area at the MRI location equipped with appropriate monitors and nursing personnel. The child can be discharged as soon as criteria defined by the facility have been met. Because many MRI examinations are performed on an outpatient basis, parents should be informed about what to expect and observe in their children after discharge from the facility. In addition, instructions must be given to parents to contact the facility immediately if they observe any untoward reaction in their children.

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SECTION 12

# PAIN

CASE 68

# Acute Postoperative Pain

**Stelian I. Serban, MD**

## QUESTIONS

1. Is this an appropriate analgesic regimen before surgery?
2. What is the difference between tolerance, physical dependence, addiction, and pseudoaddiction?
3. What is preemptive analgesia; could it be considered for this patient?
4. What are the clinical implications of inadequate postoperative analgesia?
5. How is pain classified, and what is central sensitization?
6. Which agents could be used intraoperatively to diminish postoperative opioid use?
7. What are the advantages of neuraxial versus parenteral opioid analgesia for this patient?
8. What is patient-controlled analgesia?
9. What are the differences between major opioids used for neuraxial analgesia; what is the main mechanism by which opioids produce analgesia in the epidural space?
10. Compare the different local anesthetics used in the neuraxial space, and identify the main mechanism of action.
11. What are the alternative postoperative analgesic modalities for this patient?
12. What are the short-term and long-term goals of analgesia for this patient?

A 28-year-old woman with osteosarcoma presented for excision of a mediastinal mass under general anesthesia. She underwent left hemipelvectomy approximately 2 years ago. There was no other significant medical history. Her symptoms consisted of allodynia over her left lower extremity with radicular symptoms in an $S_1$ distribution and somatic pain in the left pelvis and hip area. Her current medications included methadone, 10 mg orally every 4 hours, and hydromorphone, 8 mg every 2–3 hours for breakthrough pain. Additionally, she stated she "needed" to take hydromorphone and oxycodone, which she obtained from her sister, who had back pain.

### 1. Is this an appropriate analgesic regimen before surgery?

Using long-acting and short-acting opioids for breakthrough cancer pain has been the mainstay of therapy for chronic malignant pain for >4 decades. This concept began with the World Health Organization "analgesic ladder" for treating moderate-to-severe pain associated with malignancies. Methadone pharmacokinetics allows for two or three times daily dosing to provide analgesia; however, its metabolic half-life is 72–96 hours with a bioavailability of almost 98%, and this has to be taken into account when dosing methadone more than three or four times daily. Dosing methadone every 4 hours, as in this patient, not only predisposes to toxic effects such as respiratory depression but also has the potential for rapid development of tolerance and hyperalgesia. More recent guidelines published in the *Annals of Internal Medicine* recommend a baseline electrocardiogram for all patients started on methadone treatment and ongoing cardiac evaluation, especially for patients with multiple comorbidities or who are treated with drug classes known to prolong Q–T intervals. Numerous case reports exist of life-threatening arrhythmias associated with the use of methadone.

Breakthrough cancer pain can be treated with any short-acting opioid such as hydromorphone or oxycodone depending on the individual genetic profile of opioid receptors and CYP450 metabolism. One of the biggest challenges in treating cancer breakthrough pain is the ability to ensure fast and effective analgesia. Most opioids, such as morphine and hydromorphone, achieve an onset of action within 15–20 minutes when administered orally. Almost complete plasma metabolism occurs within 3 hours. In cases where a more rapid onset of analgesia is sought, administration of faster lipophilic agents, such as fentanyl via the buccal or transmucosal route, should be considered.

### 2. What is the difference between tolerance, physical dependence, addiction, and pseudoaddiction?

Tolerance is a clinical and biomolecular phenomenon characterized by diminished clinical effect after repeated exposure to a medication. Rapid escalation of doses could represent an indication of drug-aberrant behavior. Tolerance to analgesic effects of specific doses can occur later in treatment, but tolerance to side effects of opioids

occurs much sooner (e.g., nausea, vomiting, sedation, constipation). Cross-tolerance refers to tolerance resulting from use of another opioid with similar pharmacologic action. Use of long-term opioids can also induce a central sensitization syndrome characterized by hyperalgesia.

Physical dependence can occur after long-term analgesia with opioids. Abrupt cessation produces a withdrawal syndrome characterized by hypertension, tachycardia, insomnia, dysphoria, hallucinations, and a subjective "craving for drug."

In contrast, addiction is a psychobiologic syndrome associated with impaired control over substances (i.e., compulsive use despite harm or craving). Addiction appears to be influenced by genetic, social, and environmental factors and is sometimes difficult to distinguish from other forms of abuse, such as self-medication to alleviate stress, to alleviate depression, or to facilitate sleep.

A common entity, which is present in this clinical scenario, is pseudoaddiction, the "need" to increase the doses of opioids for adequate analgesia without any particular linkage to a clear addictive behavior. However, an addictive personality trait cannot be excluded.

## 3. What is preemptive analgesia; could it be considered for this patient?

The concept of preemptive analgesia was developed, although never entirely proved, approximately 20 years ago. Administration of certain medications that reduce peripheral or central nociception was associated with markedly reduced use of postoperative opioids. These medications included gabapentinoids (e.g., gabapentin, pregabalin), cyclooxygenase-2 inhibitors (e.g., celecoxib, rofecoxib), and nonsteroidal antiinflammatory drugs (NSAIDs) (e.g., ibuprofen, ketorolac).

Inhibition of prostaglandins and inflammatory cytokines in the periphery was the proposed mechanism of preemptive analgesia by NSAIDs and cyclooxygenase-2 inhibitors. Inhibition of presynaptic glutamate secretion in the substantia gelatinosa via inhibition of $Ca^{++}$-gated channels was the proposed mechanism of gabapentinoids.

This patient would benefit from a single dose of gabapentin (600–1200 mg) given before incision and oral or intravenous (650–1000 mg) acetaminophen. Ketorolac or celecoxib used before surgical procedures with anticipated high blood volume loss poses certain challenges, such as increased intraoperative blood loss and acute kidney injury. They should be used as a last alternative after discussion with the surgeon.

## 4. What are the clinical implications of inadequate postoperative analgesia?

Inadequate postoperative analgesia can predispose patients to various complications, some with potentially ominous consequences (Table 68-1). Pain increases secretion of adrenergic mediators (e.g., epinephrine, norepinephrine) from the medullo-suprarenal gland and presynaptic sympathetic afferents. Adrenergic responses cause intense vasoconstriction and sustained tachycardia, which can result in increased myocardial oxygen consumption; this may lead to cardiac dysrhythmias, coronary vasoconstriction, and poor peripheral and central perfusion. Liberation of catecholamines produces enhanced cortisol levels followed by a decreased inflammatory response through elevated cytokine and prostaglandin levels. Additionally, there is an increase in basal glucose levels with decreased pancreatic insulin secretion that ultimately leads to poor wound healing. Stress associated with inadequately treated acute pain can produce hypercoagulability and impaired activity of both innate and adaptive immunity. Consequences of these complications may include venous thromboembolic disease and increased risk of postoperative infections. Unmanaged, acute postoperative pain can

TABLE 68-1 **Clinical Implications of Inadequate Postoperative Analgesia**

| Physiologic Change | Effect | Result |
|---|---|---|
| Increased adrenergic mediators | Tachycardia<br>Vasoconstriction<br><br>Increased cortisol levels<br>Increased serum glucose | Increased myocardial oxygen consumption<br>Cardiac dysrhythmias<br>Myocardial ischemia<br>Decreased inflammatory response<br>Poor wound healing |
| Hypercoagulability | Deep vein thrombosis | Risk of pulmonary embolus |
| Decreased immunity | | Postoperative infections |
| Delayed mobility | Deep vein thrombosis<br>Joint stiffness | Risk of pulmonary embolus<br>Delayed rehabilitation<br>Prolonged hospitalization |
| Respiratory splinting<br>Pulmonary vasoconstriction | Decreased tidal volume<br>Increased dead space | Atelectasis<br>Pneumonia<br>Hypoxia |
| Decreased gastrointestinal motility | Increased transit time | Ileus<br>Delayed oral intake |
| Increase urinary sphincter tone | Urinary retention | Urinary tract infection |
| Increased stress and anxiety | | Poor patient satisfaction |

delay mobilization, which can also increase the risk of venous thromboembolic disease, produce joint stiffness, delay rehabilitation, and prolong hospitalization.

Decreased inspiratory efforts secondary to "splinting" of the intercostal and abdominal muscles leads to a decrease in tidal volume and inspiratory reserve capacity. Pulmonary vasoconstriction results in an increase in the total pulmonary dead space. The end result is atelectasis and increased bronchial secretions predisposing these patients to tracheobronchial and pulmonary infections.

Decreased motility of the gastrointestinal tract leads to increased transit time (ileus), and the adrenergic response may lead to mucosal ischemia. Urinary retention and sphincter constriction results in inability to void, which promotes urinary tract infections.

Aside from negative impacts on various organ systems, inadequate postoperative pain control increases stress and anxiety levels in patients and families. The increased stress and anxiety levels result in overall negative experiences, which are reflected in poorer outcomes and lower pain satisfaction scores.

## 5. How is pain classified, and what is central sensitization?

Nociception is a complex process. It involves multiple mechanisms of transduction and translation of chemical reactions that occur in the periphery after injury. From there, impulses are transmitted through various channels via specific fibers and ultimately integrated at central levels (thalamus and cortex). After injury, various mediators, such as prostaglandins, cytokines, and interleukins, are liberated from activated mast cells and platelets. This group of substances, commonly known as "inflammatory soup," generates chemical transmissions via neuronal sodium influx in dorsal root ganglia afferent fibers, comprising mostly A-delta and C fibers.

Pain is classified as either somatic, the most common cause of acute postoperative pain syndromes, or visceral, depending on its source (Table 68-2). Both types of pain can be subdivided further into either neuropathic, often described as "shooting" (e.g., intercostal neuritis after thoracotomy), or nonneuropathic, which is sympathetic-mediated or non–sympathetic-mediated. Sympathetic-mediated pain can be discerned easily among other syndromes by the presence of allodynia (i.e., pain secondary to nonnoxious stimuli), hyperesthesia (i.e., increased sensitivity to nonnoxious stimuli), and hyperalgesia (i.e., increased pain secondary to noxious stimuli). This type of pain does not follow a dermatomal pattern of transmission but is intimately associated with chronic persistent postoperative pain syndrome.

Although mechanisms are complex, they involve *N*-methyl-D-aspartate (NMDA) receptors that regulate the amount of mediators secreted and open channels in postsynaptic membranes. This particular receptor is believed to be mainly responsible for the "central sensitization" mechanism, and it could explain why serially maintained impulses from the periphery keep the postsynaptic channels open for long periods. This theory is consistent with the observation that NMDA antagonists, such as methadone and ketamine, reduce postoperative pain, especially in patients who have tolerance of or are dependent on high doses of preoperative opioids.

## 6. Which agents could be used intraoperatively to diminish postoperative opioid use?

In a patient who has tolerance to or is addicted to opioids, a multimodal analgesic approach can be accomplished with various agents. Analgesia can begin preoperatively or intraoperatively. Agents used include primarily anti-inflammatory and NMDA antagonists. Intravenous acetaminophen, in doses of 650–1000 mg, has been shown to decrease opioid use during major orthopedic surgery. Although there are no reports showing that intravenous acetaminophen poses a risk to increasing liver transaminases, caution should be exercised in patients with previous liver injury or transplantation. Ketorolac, a direct prostaglandin inhibitor, has been studied in thoracoabdominal surgery. Ketorolac, in therapeutic doses of 30 mg, is the analgesic equivalent of 10 mg of morphine administered intravenously. However, this dose can result in inhibition of platelet aggregation and potentially acute tubular necrosis leading to renal failure. Most thoracic surgeons do not use it until 24 hours after incision. It has never been proved that reducing the ketorolac dose to 15 mg reduces the risk for these complications. Doses exceeding 45 mg or 60 mg do not offer better analgesic outcomes compared with other major opioids.

Ketamine and methadone, both NMDA receptor antagonists, have been extensively studied for the treatment of chronic malignant and nonmalignant pain, including sympathetically mediated pain syndromes. Although believed to be useful for addicted individuals, methadone has emerged more recently as a long-acting opioid used for intraoperative analgesia in doses of 5 mg or 10 mg administered intravenously. Owing to its unique pharmacokinetics, with a bioavailability of >95%, methadone achieves an analgesic level comparable with 10 mg of

TABLE 68-2 **Pain Classification**

| Type | Origin | Character | Origin |
|---|---|---|---|
| Somatic | Superficial anatomic structures (e.g., skin, muscles, ligaments) | Stabbing, achy<br>Follows a specific dermatome level | A-delta fibers |
| Visceral | Deeper structures such as hollow organs (e.g., stomach, intestines) | Poorly defined<br>Not associated with specific dermatome | C fibers to dorsal horn |

morphine within the first 60 minutes. Its NMDA activity coupled with long-standing mu receptor agonism secondary to its beta-elimination half-life probably creates diminished glutamate excitatory activity in the dorsal horn that is responsible for less opioid use. Methadone can easily be continued throughout the postoperative period in total doses of 5 mg or 10 mg daily, divided into two doses (e.g., 2.5 mg or 5 mg twice a day). Because of its "unpredictable" half-life, methadone is rarely prescribed more often than two or three times daily.

Ketamine, mainly used as an anesthetic induction agent, has been popular among anesthesiologists for a long time. Several more recent studies employed ketamine as an induction agent, maintenance agent, or both for both spine and thoracoabdominal surgery. Ketamine, when infused during surgery in doses of 0.3–0.5 mg/kg per hour and continued throughout the first 24–48 hours postoperatively, was clearly associated with less opioid use. However, these patients need to be monitored postoperatively in an intermediate monitored care unit for side effects such as tachycardia, hypertension, dysphoria, and hallucinations. Ketamine may be contraindicated for patients with cardiovascular disease because of tachycardia and hypertension. Dysphoria and hallucinations can be prevented by administration of benzodiazepines (e.g., diazepam or lorazepam) in divided doses.

## 7. What are the advantages of neuraxial versus parenteral opioid analgesia for this patient?

Some studies show that analgesia achieved by neuraxial opioids is not superior to analgesia produced by parenteral opioids in the postoperative period. However, most studies show that neuraxial opioids (Table 68-3) decrease the total amount of opioids administered, resulting in decreased pain scores, respiratory depression, nausea, pruritus, and constipation. For example, the dose of morphine used in the epidural and intrathecal space is approximately one tenth to one hundredth of the dose administered via the parenteral route. Another advantage of the neuraxial route is the ability to administer intermediate-acting or long-acting local anesthetics (e.g., bupivacaine or ropivacaine) in addition to opioids. Inclusion of local anesthetics has been shown to enhance the analgesia achieved and decrease the use of opioids via both the neuraxial route and the parenteral route. One of the main side effects of neuraxial local anesthetics is reduced preload, which predisposes to hypotension. This side effect is generally corrected by administration of fluids or vasoconstrictive agents or both. Additionally, for certain patient groups, clonidine, a direct $\alpha_2$-adrenergic receptor agonist, can be added to the epidural infusion in doses of 0.5–1 μg/mL. Addition of clonidine decreases the amount of postoperative opioids required but increases sedation and vasodilation. The advantages of neuraxial techniques are listed in Box 68-1.

Although parenteral analgesia remains a feasible mode of treatment, opioid doses for tolerant patients would be much higher with a very narrow therapeutic window; this creates a situation where adverse effects, such as decreased sensorium and respiratory depression, are more likely to occur. Patients with opioid tolerance or pseudoaddiction who receive only parenteral opioids very often require benzodiazepines to decrease their anxiety levels and muscle relaxants to counteract "tense" thoracic and abdominal walls that can exacerbate postoperative pain. These agents have the propensity to increase and "tip over" the overall respiratory depressant effects of parenteral opioids.

Despite the many advantages of neuraxial analgesia, there are also associated risks, such as hematoma and infection. In some published studies, the incidence of neuraxial hematoma in the epidural space was reported as 1:150,000 compared with 1:220,000 in the intrathecal space. Guidelines for the performance of neuraxial techniques in patients receiving anticoagulation must be strictly followed (see Chapter 51 for full details). Finally, placing these catheters in various anatomic locations require specialized expertise.

## 8. What is patient-controlled analgesia?

Patient-controlled analgesia (PCA) involves administration of opioids via a pump that the patient controls. A continuous basal rate may or may not be set in addition to a bolus, of which the dose and timing frequency (usually 6–10 minutes) are determined by clinicians.

TABLE 68-3 **Advantages of Neuraxial versus Parenteral Opioids**

| Neuraxial | Parenteral |
|---|---|
| Less total opioid consumption | No special techniques needed |
| Use of local anesthetics and clonidine with opioid-sparing effect | Easy titration |
| Decreases infection rates | Lack of neuraxial hematoma and infections |
| Decreases opioid-induced side effects | No effects on anastomoses (vagal output) |
| Improved satisfaction rates (?) | Cost-effective |
| | Similar satisfaction scores (?) |

**BOX 68-1 Advantages of Neuraxial Analgesia**

- Efficacious levels of analgesia
  - Decreased "splinting" improving overall respiratory effort
  - Decreased incidence of atelectasis and infection
- Vasodilation by local anesthetics
  - Afterload reduction
    - Decreased myocardial workload decreasing risk for adverse cardiac events
- Increased unopposed vagal output to gastrointestinal muscular layer
  - Promotes gastric emptying time
  - Increased intestinal transit
  - Intestinal mucosa vasodilation
- Decreased opioid use
  - Bladder emptying time decreases
  - Promotes proper micturition
  - Decreased bladder urinary retention
  - Decreased urinary tract infections
- Enhancement of fibrinolytic-to-coagulation ratio
  - Decreased incidence of thromboembolic events

Patients control analgesia by pressing a button that delivers a preset dose. The risk of overdosing is limited by predetermined dose and timing frequency. Before initiating PCA, it is advisable to attain a plasma concentration commensurate with the desired analgesic level.

The most commonly used opioids and suggested dosing schedules employed in clinical practice for postoperative pain are listed in Table 68-4. The choice of opioid is determined by pharmacokinetics (e.g., lipophilic profile), side effects, practitioner's familiarity, availability, and cost. For example, owing to its histamine release, morphine might not be the first choice in patients with obstructive lung disease (e.g., asthma, emphysema). Hydromorphone may be the first choice in patients with tolerance to other opioids because it exhibits a stronger affinity to spinal and supraspinal mu opioid receptors with potentially less side effects such as nausea and vomiting.

Whether patients benefit from instituting a basal rate in the immediate postoperative period is still debated. Initial studies documented decreased pain scores and diminished opioid use when minimal basal rates were used postoperatively. However, subsequent research showed a threefold increase in the incidence of somnolence, respiratory depression, nausea, and vomiting when basal rates were provided; this can be attributed to the waxing and waning character of surgical pain in the first 24 hours. Common medications, such as benzodiazepines and antihistamines, may contribute to the higher incidence of somnolence and respiratory depression. This situation is of particular concern in a patient with obstructive sleep apnea, who has a greater susceptibility to respiratory depression from opioids, especially when combined with other sedatives. There are many patients in whom the diagnosis of obstructive sleep apnea is unknown, which makes using a basal rate even more problematic. If a basal rate is used, additional monitoring for the first 24 hours is warranted.

## 9. What are the differences between major opioids used for neuraxial analgesia; what is the main mechanism by which opioids produce analgesia in the epidural space?

Neuraxial opioids activate mu receptors in the substantia gelatinosa of the spinal cord dorsal horn. Epidural opioids have to transfer through the dura mater, the rate of which depends on its lipophilicity. The onset of analgesia is directly related to the lipophilicity and dose of opioid administered. Fentanyl and sufentanil, with higher lipid solubility, cross the dura mater much faster than less lipid-soluble opioids, such as morphine or hydromorphone. Because of their higher lipid solubility, a greater proportion of fentanyl and sufentanil transfers into epidural vessels. Studies have shown that the higher the gradient of fentanyl across the dural layer, the quicker the onset, and less opioid can achieve initial high plasma concentrations.

In contrast to highly lipid-soluble molecules, the less soluble ones, such as morphine or hydromorphone, have the tendency to "linger" in the epidural space before crossing the dura mater. This "lingering" accounts for their delayed mu receptor agonism in the substantia gelatinosa (i.e., the onset of morphine's analgesic effect is 30–60 minutes after administration). The rate of intravascular absorption is also delayed and is primarily dependent on the opioid dose and the complexity of the epidural vasculature. Another important mechanism of action for these drugs is cephalad migration in the epidural and intrathecal spaces. The consequence is "delayed" supraspinal analgesia and delayed onset of adverse effects, in particular, respiratory depression. For morphine, the response to this migration can occur 12–18 hours after administration. As a result, these patients should be monitored for respiratory depression for at least 24 hours with continuous pulse oximetry. Hydromorphone has similar pharmacokinetic properties to morphine, and monitoring requirements are similar.

Intrathecal opioids behave similarly to epidural opioids but with much smaller doses. For example, the dose of morphine in the intrathecal space is 10 times smaller than via the epidural route (1:10), whereas for hydromorphone, the ratio decreases to 1:5. For lipid-soluble drugs, the ratio is 1:4 for fentanyl and 1:5 for sufentanil.

For opioid-tolerant patients, hydromorphone, for its strong mu receptor agonism, or fentanyl, for its quick onset of action, may be the best option for epidural administration. Usually, solutions administered via the epidural route have either 10–15 μg/mL of hydromorphone or 2–5 μg/mL of fentanyl. Local anesthetics and other adjuncts (e.g., clonidine) are commonly added to opioid infusions, not to attain a superior analgesic effect but rather to decrease the dose of opioid needed. Bupivacaine 0.0625%–0.125%, with or without clonidine 0.5–1 μg/mL, is the most commonly used adjuvant.

TABLE 68-4 **Routine Adult Patient-Controlled Analgesia Opioid Dosing**

| Drug | Basal Rate (mg/hour) | Bolus Dose (mg) | Lock-Out (minutes) |
|---|---|---|---|
| Fentanyl | 0.01–0.015 | 0.01–0.02 | 6–10 |
| Hydromorphone | 0.1–0.2 | 0.1–0.3 | 6–10 |
| Morphine | 1 | 0.4–1.8 | 6–10 |

## 10. Compare the different local anesthetics used in the neuraxial space, and identify the main mechanism of action.

Local anesthetics are usually added to epidural opioid infusions to achieve a higher dermatomal level of analgesia and anesthesia and to decrease the opioid dose, while achieving similar analgesia. Local anesthetics are categorized into short-acting, intermediate-acting, and long-acting. Their principle mechanism of action involves direct inhibition of $Na^+$-gated channels along the neurilemma layer and decreased signal output to the central nervous system by increasing the threshold for membrane depolarization. The action is more intense as the concentration of local anesthetic increases and depends on the amount of myelin present on the outer

membrane of nerve fibers. Small myelinated A-delta and unmyelinated C fibers, which are primarily responsible for nociception, are inhibited before the large myelinated A fibers.

Effects of local anesthetics are related to their p$K_a$ (i.e., the physiologic pH at which 50% of molecules are in a nonionized state) and lipid solubility. Because only the nonionized molecules can cross the neuronal membrane, inhibition of $Na^+$ channels depends on the amount of nonionized form available at a given pH. The p$K_a$ of all local anesthetics is higher than physiologic pH to varying degrees. At physiologic pH (7.4), a greater proportion of the local anesthetic molecules exists in the ionized form that cannot penetrate the neuronal membrane. When comparing the time to onset of action of various local anesthetics, agents with a lower p$K_a$ (i.e., closer to physiologic pH) have a greater proportion of nonionized molecules and a shorter time to onset of action. By adding sodium bicarbonate to the local anesthetic solution, increasing pH, the time to onset of action can be shortened further (Table 68-5). Bupivacaine and ropivacaine have the same p$K_a$ but different onset times and durations of action. The variance in lipophilicity helps to explain these variations.

Lipid solubility determines the speed of onset of local anesthetics in a similar fashion to opioid-induced analgesia. The greater the lipid solubility, the faster the molecules inhibit depolarization in the primary afferents and efferents in the dorsal horn.

Reuptake of local anesthetics by the epidural and subdural vessels contributes to the rate of removal and ultimate metabolism. Local anesthetics are metabolized either by liver cytochrome microenzymes (e.g., bupivacaine, ropivacaine, lidocaine) or by plasma esterases (e.g., chloroprocaine, procaine, cocaine).

TABLE 68-5 **Physicochemical Properties of Local Anesthetics**

| Anesthetics | p$K_a$ | Onset (hours) | Half-Life (hours) |
|---|---|---|---|
| **Amides** | | | |
| Bupivacaine | 8.1 | 0.3–0.5 | 3.5 |
| Etidocaine | 7.7 | 0.3–0.5 | 2.6 |
| Lidocaine | 7.9 | 0.1–0.3 | 1.6 |
| Mepivacaine | 7.6 | 0.1–0.3 | 1.9 |
| Ropivacaine | 8.1 | 0.1–0.3 | 1.9 |
| **Esters** | | | |
| Chlorprocaine* | 8.7 | 0.01–0.1 | 0.11 |
| Procaine* | 8.9 | 0.1–0.3 | 0.14 |

*Chlorprocaine and procaine have a p$K_a$ >8 but a short onset time and duration of action. This would seem to be unexpected. Chlorprocaine and procaine are used in much higher concentrations than most other local anesthetics. Consequently, the number of molecules of local anesthetic is much higher in these solutions compared with other commonly used drugs such as bupivacaine.

## 11. What are the alternative postoperative analgesic modalities for this patient?

Patients, such as the patient in this case, who are already on high-dose opioids preoperatively, are ideal candidates for multimodal analgesia in the postoperative period. Gabapentinoids (e.g., gabapentin, pregabalin) and NSAIDs (e.g., ketorolac) reduce the amount of opioids required. The starting dose for gabapentin is 300 mg three times a day. In older patients or patients with renal impairment, the dose should be decreased to 100 mg two or three times a day. Doses can be increased every 48–72 hours up to 600–800 mg three times a day. For pregabalin, a starting total dose of 50 mg per day divided into two doses might prove efficacious. For routine postoperative care, gabapentin should not exceed 1200 mg in divided doses, and pregabalin should not exceed 150 mg in divided doses. These medications should not be stopped abruptly because of the risk for seizures. When severe surgical pain has abated, these medications should be weaned over the course of 2 weeks.

NSAIDs provide analgesia through peripheral and potentially central prostaglandin inhibition. Doses of 15–30 mg of ketorolac every 6 hours have the ability to maintain adequate analgesia with minimum effects on renal parenchyma or gastric mucosa. Doses >30 mg have not been shown to be more efficacious and have the propensity of inducing acute tubular necrosis in the renal medulla. Because of the potential risk of hematoma, most thoracic and colorectal surgeons would agree to start ketorolac no sooner than 24 hours after surgical incision.

Intravenous acetaminophen, a centrally mediated anti-inflammatory medication, has captured the interest of clinicians involved in spine and colorectal surgeries. Although its mechanism of action remains largely unknown, it has shown promise when used in conjunction with smaller doses of opioids in the immediate perioperative period. In patients > 50 kg, the dose of intravenous acetaminophen is either 650 mg every four hours or 1000 mg every 6 hours. These doses are efficacious in decreasing postoperative pain scores while also decreasing opioid use. The main concern with the use of intravenous acetaminophen is the risk of liver toxicity. When appropriate dosing, as approved by the U.S. Food and Drug Administration (FDA), was followed, liver toxicity was not clinically significant. The cost of intravenous acetaminophen is greater than the cost saving in reduced opioid dosing. However, the greater cost may be offset by the reduced rate of adverse events, particularly respiratory depression, which occurs with greater opioid use.

## 12. What are the short-term and long-term goals of analgesia for this patient?

Short-term goals are aimed at providing optimal perioperative analgesia in addition to proper and routine postoperative care. For complicated patients such as this one, consultation with a pain management specialist is indicated. A multimodal analgesic regimen might include the following agents:

- Methadone in doses of 2.5 mg three times a day
- Hydromorphone or morphine via PCA pump
- Gabapentin 300 mg three times a day

- Nortriptyline 10 mg at night
- Intravenous acetaminophen 1000 mg every 6 hours
- Ketorolac 30 mg every 6 hours

Long-term goals should take into consideration risks of tolerance and addiction. An open dialogue among clinicians, the patient, and family members regarding long-term treatment plans should be ongoing. Pain management specialists in conjunction with a counselor or psychologist may be needed to address this patient's analgesic issues.

After the acute pain phase is over, interventional options, such as neurolytic blocks with alcohol or phenol and radiofrequency ablation of somatic or sympathetic nerve fibers, should be considered. A new modality of treatment involving neuromodulation, via spinal cord stimulation or intrathecal therapy, has been used for these patients, especially for palliative purposes. Considering that the dosage of opioid used in the intrathecal space is significantly smaller than the dosage via the parenteral route, this modality would facilitate decreasing the total daily amount of opioid usage, minimizing side effects. An additional benefit of this method is the ability to add a local anesthetic, such as bupivacaine or ropivacaine, along with other adjuvants, such as clonidine. A more recently added breakthrough bolus device as part of the intrathecal pump allows the patient to administer additional boluses during breakthrough pain. This added feature makes this modality an ideal tool for palliative treatment when all other analgesic regimens have been futile.

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CASE 69

# Low Back Pain

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QUESTIONS



A 42-year-old man presented to a pain management specialist with low back and leg pain that began after lifting a heavy object. The pain started in the middle of his lower back and radiated down the back of his right leg into the sole of his right foot. The pain was not relieved with acetaminophen and bed rest. Magnetic resonance imaging (MRI) of the lumbar spine showed a herniated disk at the L5-S1 level with impingement of the S1 nerve root. The patient was otherwise in excellent health.

## 1. What is the incidence of low back pain?

Low back pain with or without radiculopathy (pain or abnormal neurologic function caused by pressure on or irritation of a spinal nerve) is the second most common reason patients visit a physician and accounts for 3% of all hospital discharges. During their lifetime, 80% of the U.S. population experience low back pain, and it has been estimated that at any time approximately 15% of Americans have low back pain. Back pain affects patients of all ages; elderly adults have more severe pain and pain of longer duration.

## 2. What is the differential diagnosis of low back pain?

Low back pain can be caused by a multitude of pathologic processes. Although most cases of low back pain are of muscular or spinal origin, many intraabdominal and lower thoracic pathologies can refer pain to the low back. Examples include pancreatic cancer, lower lobe pneumonia, and aortic aneurysms.

For a structure in the spine to cause pain, it must be innervated, subject to possible injury or irritation, and in theory, the pain should be reversible with local anesthetic blockade of the structure. The most common cause of low back pain is believed to be myofascial pain, or muscular in origin. Other common causes of low back pain include internal disk disruption (IDD), sacroiliac (SI) joint pain, and pain from facet joint arthropathy. Lumbar stenosis, which causes narrowing of the spinal canal, is a common cause of low back pain, especially in elderly patients, as is lumbar degenerative disk disease and spondylosis. Less frequent skeletal causes include metabolic (osteoporosis), neoplastic (primary or metastatic), infectious (osteomyelitis, epidural abscess), traumatic (fractures), and congenital (scoliosis) conditions. Rheumatoid and other types of inflammatory arthritis can also cause low back pain.

A herniated disk (herniated nucleus pulposus) usually causes pain or other neurologic dysfunction down the leg. Back pain and leg pain of neurologic origin may also originate from irritation of nerves by spinal osteophytes; tumors in the pelvis or near the spinal column; or diseases of the neuraxis, such as inflammation (herpes zoster) or neoplasms (intradural or epidural tumors).

Because of the large differential diagnosis, a thorough investigation and evaluation is necessary to determine the cause of lower back pain. Although it is easy to rule out many factors that may cause pain, the exact etiology of pain often is difficult to determine, especially when dealing with nonradicular pain.

## 3. Discuss the evaluation of a patient with low back pain.

Low back pain must be evaluated and managed the same way as any other presenting complaint. Although most

cases of low back pain resolve with conservative treatment, back pain lasting >1 month requires a complete clinical evaluation, consisting of a full history, physical examination, and interpretation of laboratory data. The history should concentrate on the characteristics and location of the pain and a review of modifying factors. Associated factors, such as leg weakness or changes in bladder or bowel function, need to be elicited. A full medical and surgical history and complete review of systems are required. While performing a physical examination that concentrates on the lower back and lower extremities, a differential diagnosis of the cause of pain should be obtained. Before any intervention on the spine, lumbosacral MRI or computed tomography (CT) scan should be obtained to rule in a diagnosis and to rule out rarer sources of pain, such as a malignancy or epidural abscess.

### 4. What is the classic presentation of a patient with a herniated nucleus pulposus?

The average age of patients presenting with a herniated disk is 30–50 years. Although pain from a herniated nucleus pulposus (herniated disk) may start after trauma, such as lifting a heavy object, it also can occur without any obvious inciting event. Depending on the nerve root involved, the dermatomal distribution of pain may be in the back of the leg (lower lumbar disks) or in the groin or anterior thigh (upper lumbar to midlumbar disks). The pain and occasionally accompanying neurologic dysfunction may be caused by mechanical compression of nerve roots or more likely by chemical inflammation from substances released from degenerating intervertebral disks (e.g., phospholipase A, bradykinin, histamine). The pain is usually aggravated by bending, coughing, or sneezing and is improved with resting and lying down. Rarely, bowel or bladder dysfunction can occur. CT scan or MRI is invaluable in confirming the diagnosis. However, imaging must be correlated with clinical symptoms, because positive findings on imaging may not be related to the present symptoms. Approximately 30% of asymptomatic adults have abnormalities on lumbar MRI.

Physical examination demonstrates increased pain when tension is applied to the lumbosacral plexus. Tests such as the bowstring sign (radicular pain elicited by popliteal pressure with the hip flexed and knee extended) and the Lasègue test (radicular pain secondary to foot dorsiflexion with the leg extended) are indicative of nerve irritation.

Sensory deficits may manifest over the dermatomal distribution of the involved nerve. Reflex testing of L4 radiculopathy may show a decreased response to the knee reflex, whereas S1 radiculopathy may show a decrease in the Achilles reflex. Motor deficits over the respective nerve root may also occur; for example, L5 radiculopathy may cause weakness of dorsiflexion of the foot.

### 5. Differentiate the clinical presentation of a patient with a herniated nucleus pulposus from a patient with spinal stenosis.

Spinal stenosis, which is primarily seen in older patients, is caused by narrowing of the central spinal canal or the lateral neuroforamen by a combination of enlarging posterior facet joints, osteophytes from osteoarthritis, hypertrophy of the ligamentum flavum, and bulging of the disk anulus. These structures may impinge on nerve roots or the cauda equina and produce typical radicular pain, although patients with spinal stenosis may also present with nonradicular low back pain. Patients with spinal stenosis may experience neurogenic claudication, which is leg pain while walking that is relieved by sitting and resting. Neurogenic claudication differs from vascular claudication in that the sitting position relieves the pain in the former condition, and cessation of walking relieves the pain in the latter condition.

Pain from spinal stenosis differs from the pain of a herniated disk in that flexion of the lumbar spine relieves spinal stenosis pain. Disk disease pain is typically relieved by reclining and may be increased with flexion of the lumbar spine. Another difference between spinal stenosis and disk disease is that pain and neurologic deficits can extend over several dermatomes with spinal stenosis because of the diffuse nature of the disease. A herniated nucleus pulposus usually manifests as a localized disease of a limited dermatomal distribution. Spinal stenosis is characterized by chronic, mild discomfort that progresses over time. Conversely, the hallmark of disk disease is the acute and severe onset of radicular pain (Table 69-1).

CT scan or MRI ultimately makes the definitive diagnosis. As noted under Question 4, it is important that the findings on these scans are correlated with clinical symptoms.

### 6. What are the pathogenesis and treatment of myofascial syndrome (trigger points)?

Myofascial trigger points can be found in >50% of the population. Acute muscle strain or chronic repetitive motion leads to tissue damage and the release of calcium from the sarcoplasmic reticulum, causing a localized, sustained contracture of the muscle fibers. Myofascial syndrome manifests as discrete, well-localized, point pain and tenderness over these areas. A taut muscular band is often palpated causing a painful reaction (jump sign) when pressure is applied.

Multiple treatment modalities exist. More common treatments include spray and stretch technique (with ethyl chloride), trigger point injections with local anesthetic (with or without steroids), massage therapy, transcutaneous electrical nerve stimulation, and acupuncture.

TABLE 69-1 **Spinal Stenosis versus Herniated Disk**

| Spinal Stenosis | Herniated Nucleus Pulposus |
|---|---|
| Pain relieved with flexion of spine | Pain relieved by reclining |
| | Pain increased with flexion |
| Pain and neurologic deficits over several dermatomes | Limited dermatome distribution |
| Chronic mild discomfort progressing with time | Acute and severe onset |

Although used by some practitioners, the efficacy of botulinum toxin for the treatment of myofascial pain has not been firmly established in clinical trials.

### 7. What are the signs and symptoms of sacroiliac disease, and how is it treated?

The SI joint may be responsible for almost 20% of cases of chronic, nonradicular back pain. The SI joint is a synovial joint bordered by multiple strong ligaments. Strain and degeneration cause pain and restricted motion. Pain from the SI joint is concentrated over the joint but may radiate into the ipsilateral buttock and posterior thigh. Tenderness to palpation may be elicited over the joint, although this is not universal. A positive Faber test (unilateral low back pain with a combination of flexion, abduction, and external rotation of the hip) is suggestive of SI joint pain.

SI disease is treated by fluoroscopy-guided steroid injections into and around the joint. Although the relief from this treatment may be long-lasting, it is often transient. The exact innervation of the SI joint is debatable and not completely understood, and long-lasting relief from techniques such as radiofrequency lesioning has been variable. Physiotherapy and appropriate use of medications may help with the pain.

### 8. What are the facet joints, and how does pathology of facet joints manifest?

Facet joint arthropathy is a common cause of back pain in younger and older patients. Facet joints are paired joints at each vertebral level and are true synovial joints. Synovitis and articular degeneration cause local tenderness over the involved joint with referred pain into the buttock and posterolateral leg, which usually, but not always, worsens with extension of the spine.

Painful manifestations of facet disease, sacroiliitis, and lumbosacral radiculopathy often mimic each other. A diagnosis of facet joint disease may be made by history, physical examination, and interpretation of radiographs. However, the only way to confirm the diagnosis is with blockade of medial branch nerves, which innervate the joint. When a diagnosis is confirmed, radiofrequency lesioning of the nerves is considered the best treatment for long-lasting relief. Injecting local anesthetic and steroids directly into the facet joint may provide long-lasting relief.

### 9. What is the mechanism of action of epidural steroid injections?

Radicular pain is caused by nerve inflammation from chemical irritation and less commonly from direct impingement of the nerve. Steroids injected into the epidural space produce antiinflammatory effects on the nerve roots of a more concentrated nature compared with oral steroids. A series of epidural steroid injections (ESIs) may be performed depending on the patient's response; the traditional "cookbook" formula of up to three injections performed every 2 weeks is no longer standard practice. A typical ESI contains 80 mg of methylprednisolone, 12–18 mg of betamethasone, or 40–80 mg of triamcinolone. If the patient has significant but incomplete pain relief, the injection can be repeated in 3–4 weeks. If no relief is obtained, another route of epidural steroid administration should be considered. The three most commonly performed approaches to the epidural space are transforaminal, caudal, and interlaminar. Standard of practice dictates that no matter what approach is chosen, it should be performed under fluoroscopic guidance with the use of contrast dye. Contrast-enhanced fluoroscopy ensures proper needle placement and that the injectant reaches the proper target and greatly eliminates the risk of intravascular injection.

More recent studies of the efficacy of ESIs have shown benefits of transforaminal ESIs in the treatment of radicular pain, including decreased pain, increased function, and decreased need for surgery. Caudal ESIs have shown efficacy in the treatment of both radicular and nonradicular pain from lumbar stenosis and degenerative disk disease. Older studies looking at the efficacy of interlaminar ESIs produced variable conclusions; however, many of these studies had design flaws.

Better response to ESIs generally is shown in younger patients and patients with pain of <6 months' duration. Large series have supported the relative safety of this procedure. Recognized but rare complications of ESIs include dural puncture, salt and water retention, congestive heart failure, hyperglycemia, epidural abscess, and hemorrhage. Transforaminal approaches risk radicular artery injection of a particulate steroid compound, which could produce anterior spinal artery infarction and paralysis.

### 10. What are the pathogenesis, diagnosis, and treatment of internal disk disruption?

IDD is a common cause of axial (nonradicular) low back pain. IDD may begin as a vertebral end plate fracture caused by chronic repetitive motion or acute strain leading to annular tears of varying degrees. Nerve endings may grow into the inner annulus (which is normally noninnervated) and can become sensitized by chemicals leaking from the nucleus pulposus via the tears. Clinically, IDD manifests as bandlike axial back pain. Lumbosacral MRI may be helpful in making the diagnosis, but a provocative diskogram correlating radiologic and clinical findings may be more specific and sensitive.

Oral analgesics and physical therapy are first-line treatments for IDD. The role of interventional therapy for IDD is questionable, and there is no widely accepted therapy for it. ESIs have been used, but there is little evidence showing efficacy. Intradiscal electrothermocoagulation (IDET) has been championed by many interventional pain specialists, but its efficacy has not been proved in large-scale studies. In IDET, a flexible probe is percutaneously introduced into the disk annulus, and heating occurs. Several theories have been proposed regarding the mechanism of action of IDET. It may interrupt the nerve supply to the disk, denature the chemical mediators of sensitization, coagulate the collagen in the disk to close the tear, or coagulate the nociceptors. Alternative techniques that produce a radiofrequency lesion, instead of a heat lesion, to the annulus are available. If instability is present along with IDD, spinal fusion may be necessary.

## 11. What oral medications are prescribed for low back pain?

Oral analgesics and physical therapy should be the cornerstone of treatment in most cases of low back pain. Nonsteroidal antiinflammatory drugs (NSAIDs) are frequently used to relieve low back pain. They serve a dual purpose, acting as both an antiinflammatory agent and an analgesic. Prostaglandins sensitize nociceptors to painful stimuli and potentiate the algesic effect of bradykinins. By inhibiting the enzyme cyclooxygenase, NSAIDs inhibit prostaglandin synthesis, reduce inflammation, and provide analgesia. Side effects of NSAIDs include gastric irritation, renal dysfunction, platelet inhibition, hypertension, increased risk of myocardial infarction, hepatic dysfunction, and tinnitus. Commonly used NSAIDs include diclofenac, 75 mg twice daily; meloxicam, 7.5 mg twice daily; and etodolac, 200–400 mg three times a day (maximum 1000 mg/day). Cyclooxygenase-2 specific inhibitors (celecoxib, 200 mg daily) provide analgesia and antiinflammatory actions and decrease the detrimental side effects of NSAIDs such as gastric ulceration and bleeding.

In recent years, anticonvulsant agents (gabapentin, pregabalin) have been used in the treatment of low back pain when there is a neuropathic component to the pain. The exact mechanism of the analgesic property of this class of drugs has not been specifically determined, although decreased calcium influx leading to decreased neurotransmitter release has been postulated. A useful side effect of this class of medications is sedation, so a larger dose is often administered at night to help patients sleep. These medications are started at a low dose (e.g., gabapentin, 100–300 mg three times daily, or pregabalin, 25 mg three times daily) and are titrated to effect. Side effects include sedation, dizziness, and weight gain, especially at higher doses.

Less frequently, tricyclic antidepressants (TCAs) are used as analgesic agents. TCAs, such as amitriptyline and nortriptyline, decrease the reuptake of serotonin and norepinephrine, which are neurotransmitters in the descending inhibitory spinal cord pain nerve pathways. TCAs have analgesic properties independent of their antidepressant activity. Other effects of TCAs that can be used in pain management include sedation (fostering a good night's sleep), potentiation of opioid analgesia, and mood elevation.

Muscle relaxants (e.g., cyclobenzaprine, 5–10 mg; metaxalone, 800 mg; or tizanidine, 2–4 mg, all administered three to four times daily) can be used short-term when there is a component of pain from muscle spasm. The most common side effect of this class of medications is sedation. An extended-release formulation of cyclobenzaprine is now available and can be administered in doses of 15–30 mg at bedtime to decrease the pain from muscle spasm and to promote a good night's sleep (Table 69-2).

Although opioids are often used and are considered acceptable by most practitioners for short-term therapy of acute back pain, the use of long-acting opioid agents for chronic pain is very controversial. Some studies point out their safety and benefits, including analgesia and improved functioning, whereas other studies point out the various side effects associated with opioid use, such as nausea and constipation, tolerance with the need for escalating doses, addiction, respiratory depression, pruritus, hyperalgesia, and euphoria or dysphoria. In addition, deficiency in immune and endocrine function may occur with prolonged use of opioids. The individual practitioner must decide about the use of long-term opioids in each patient. If opioids are used, guidelines for their use, such as those published by the American Society of Interventional Pain Physicians, should be followed.

## 12. What is failed back syndrome, and how is it managed?

Failed back syndrome (FBS) is a syndrome in which pain persists, usually with decreased functioning, after lumbar surgery. The incidence of FBS is 15%–30%. The etiology of FBS includes complications (scarring) from the surgery, performing the "wrong surgery" (i.e., incorrect

TABLE 69-2 **Treatment Options for Low Back Pain**

| Type | Medication | Typical Dose (Oral) | Side Effects |
|---|---|---|---|
| NSAIDs | Diclofenac | 75 mg bid | Gastric irritation |
| | Meloxicam | 7.5 mg bid | Platelet inhibition |
| | Etodolac | 200-400 mg tid (maximum 1000 mg/day) | Renal dysfunction |
| | Celecoxib | 200 mg qd | Hepatic dysfunction<br>Increased risk of MI<br>Tinnitus |
| Anticonvulsants | Gabapentin | 100–300 mg tid* | Sedation |
| | Pregabalin | 25 mg tid* | Dizziness<br>Weight gain |
| Muscle relaxants | Cyclobenzaprine | 5–10 mg tid or qid | Sedation |
| | Metaxalone | 15–30 mg hs (extended release)† | |
| | Tizanidine | 800 mg tid or qid | |
| | | 2–4 mg tid or qid | |

*bid,* Twice a day; *hs,* at bedtime; *MI,* myocardial infarction; *NSAIDs,* nonsteroidal antiinflammatory drugs; *qd,* once a day; *qid,* four times a day; *tid,* three times a day.
*Start at low dose and titrate up to desired effect.
†Given before bedtime to help decrease pain from muscle spasm and improve sleep.

original diagnosis), not performing extensive enough surgery, or new pathology.

Because of the multiple causes of FBS, treatment is varied and is focused on the probable cause of pain, although this is often hard to identify. Pain management techniques that have been used for FBS include selective nerve root blocks with local anesthetic and steroid; caudal or interlaminar ESIs below or above the surgical scar; epidurolysis, a technique that breaks up adhesions in the epidural space; and epiduroscopy, which allows for lysis of adhesions and specific steroid injections under direct visualization. Spinal cord stimulation is becoming an important tool in the treatment of refractory FBS. With this technique, a set of electrodes is placed into the posterior epidural space, which provide analgesia when electrically stimulated. The electrodes and battery/generator are surgically placed under the skin, to allow an active lifestyle. Before placing the permanent leads, a trial with percutaneously placed leads must be performed, with documentation of at least 50% pain relief and a decrease in analgesic medication consumption.

Long-term analgesic regimens are frequently prescribed for patients with FBS in conjunction with the above-noted invasive techniques. Physical therapy and promotion of an active lifestyle are necessary.

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CASE 70

# Postherpetic Neuralgia

Yury Khelemsky, MD

## QUESTIONS



An 82-year-old woman presented to the pain management office with severe right chest wall pain. The pain started 5 months ago, before an outbreak of vesicular rashes in the same distribution; however, the pain persisted after the lesions resolved. The pain radiated from the posterior to anterior thorax and was stabbing and burning in nature.

### 1. What is postherpetic neuralgia?

Postherpetic neuralgia (PHN) is a chronic pain syndrome that develops after an acute outbreak of varicella-zoster virus, also known as shingles. In acute herpes zoster, reactivation of dormant virus in a cranial or dorsal root ganglion leads to pain and a characteristic rash in the distribution of one or more dermatomes. Typically, the pain associated with acute herpes zoster resolves after approximately 1 month; however, approximately 10% of patients develop persistent pain, which if present after 4 months from rash onset is classified as PHN.

### 2. What is the pathophysiology of postherpetic neuralgia?

Pain during the acute episode of herpetic neuralgia is likely secondary to inflammation produced as viral particles move along nerves and damage affected neural structures. Sustained activity of primary afferent neurons supplying the dorsal horn may induce long-term potentiation of stimuli, known as central sensitization. Central sensitization along with neuronal degeneration is a likely pathophysiologic mechanism of PHN. Ongoing viral replication does not appear to be responsible for PHN.

### 3. What are the clinical manifestations of postherpetic neuralgia?

Patients with PHN typically present with sharp or burning pain over the distribution of thoracic, cervical, or trigeminal nerves, in the area of the resolved rash. Rarely, patients may experience radicular pain without a preceding rash. Allodynia, defined as pain resulting from a normally nonpainful stimulus, such as light touch, is nearly universal in patients with PHN. Areas of diminished or absent sensation to pain, touch, temperature, and vibration may also be present. PHN is associated with significant psychosocial dysfunction and decreased quality of life, especially in elderly patients.

### 4. What are the risk factors for development of postherpetic neuralgia?

Advanced age, greater rash severity, intensity of acute pain, deep pain at initial presentation, female gender, ophthalmic location, anxiety and depression, and allodynia have been described as predictors for the development of PHN.

### 5. Can postherpetic neuralgia be prevented?

Several strategies have been employed to prevent PHN, including vaccination, antiviral agents, tricyclic antidepressants, gabapentinoids, neuraxial blockade, and peripheral nerve blocks. Shingles cannot be transmitted between individuals. However, varicella-zoster virus can be spread from a person with active shingles (blisters) to a person who has never had chickenpox, resulting in the development of chickenpox but not shingles. Vaccination is the most effective preventive intervention, decreasing the incidence of PHN by 66.5%. Initiation of antiviral medications, all of which have similar efficacy, within 72 hours of rash onset can decrease the severity of acute pain and the duration of PHN. Administration of amitriptyline, a tricyclic antidepressant, within 48 hours of the onset of rash and continuing for 2 months can decrease the incidence of PHN. In an uncontrolled study, gabapentin was found to be effective in preventing PHN when used in conjunction with an antiviral agent. It is unclear if epidural or intrathecal injection of local anesthetic or glucocorticoid or both, prevents PHN because studies on this topic have had

**BOX 70-1 Prevention of Postherpetic Neuralgia**

- Vaccination
- Antiviral agents
- Tricyclic antidepressants (e.g., amitriptyline)
- Epidural steroid injection
- Gabapentin
- Stellate ganglion block
- Paravertebral blocks

mixed results. Stellate ganglion and paravertebral blocks have shown some promise in preventing PHN (Box 70-1).

### 6. Which medications can be used to treat postherpetic neuralgia?

PHN may be treated with opioids, gabapentinoids, tricyclic antidepressants, lidocaine patches, tramadol, capsaicin, and divalproex sodium. Although it is thought that combinations of two or more therapies with different mechanisms of action may provide more effective analgesia, the evidence for any particular medication or combination of medications is weak. Current guidelines suggest that tricyclic antidepressants, gabapentinoids, and topical lidocaine 5% patches should be considered as first-line therapy, with topical capsaicin and opioids reserved as second-line treatments.

Tricyclic antidepressants are efficacious in the treatment of PHN. However, these medications are associated with significant anticholinergic adverse events. Nortriptyline and desipramine may be better tolerated than amitriptyline. The gabapentinoids, pregabalin and gabapentin, have similar effectiveness. Dizziness and somnolence are the most common side effects. Tramadol is less effective than opioid analgesics but has fewer side effects.

Lidocaine 5% patches offer a topical treatment option without risking systemic side effects. Other topical therapies, such as capsaicin 0.075% cream and 8% patch, may be employed; however, a high frequency of application site reactions relegates these options to the category of second-line therapy. To prevent application site burning, the 8% capsaicin patch (Qutenza) must be applied after topical anesthesia is established. If appropriately applied, a single treatment can provide analgesia for 12 weeks (Box 70-2).

**BOX 70-2 Pharmacologic Treatments**

- Opioids
- Gabapentinoids
- Tricyclic antidepressants
- Lidocaine patch
- Tramadol
- Capsaicin patch
- Divalproex sodium

**BOX 70-3 Interventional Treatments**

- Intrathecal steroids
- Spinal cord stimulation
- Peripheral nerve stimulation
- Intrathecal alcohol

### 7. Which interventional modalities may be used to treat postherpetic neuralgia?

Intrathecal steroid injections may be effective in PHN; however, the use of this modality is limited. Successful spinal cord stimulation and peripheral nerve field stimulation have been reported in patients with acute herpes zoster and PHN, but randomized controlled studies are lacking. Intrathecal alcohol should be considered as a last resort for patients with intractable disease (Box 70-3).

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CASE 71

# Complex Regional Pain Syndrome

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## QUESTIONS

1. Define complex regional pain syndrome type 1 and type 2.
2. What are the pathophysiologic theories regarding the etiology of complex regional pain syndrome?
3. Delineate the different stages of complex regional pain syndrome.
4. What are the signs and symptoms of complex regional pain syndrome?
5. How is complex regional pain syndrome diagnosed?
6. What nerve blocks can be used for diagnosis and treatment of complex regional pain syndrome?
7. What other modalities can be used to treat complex regional pain syndrome?

A 39-year-old secretary was healthy until 1 year ago when she tripped and fell onto her right arm while at work. She awoke 10 days later with severe burning pain from the palm to the midforearm. The arm began to swell and intermittently turned pale and red. When the patient presented, the arm was exquisitely tender to touch and the patient was unable to wear long-sleeved shirts. She was unable to use the arm and had become depressed.

### 1. Define complex regional pain syndrome type 1 and type 2.

Complex regional pain syndrome (CRPS) is a disease process that consists of continuous pain, often burning in nature, usually consequent to an injury or a noxious stimulus. CRPS usually manifests with varying degrees of autonomic and trophic changes along with sensory and motor dysfunction.

CRPS type 1 was previously known as reflex sympathetic dystrophy, and CRPS type 2 was previously known as causalgia. The nomenclature has been changed to dispel some of the old theories regarding the possible etiologies for these diseases.

CRPS types 1 and 2 have similar signs and symptoms. In CRPS type 2, a history is commonly elicited describing a macroscopic nerve injury, such as a traumatic amputation, whereas with CRPS type 1, the inciting event may be a minor injury or may never be determined.

### 2. What are the pathophysiologic theories regarding the etiology of complex regional pain syndrome?

Understanding of CRPS has increased substantially over the past decade. Three major pathophysiologic pathways have been identified: aberrant inflammatory mechanisms, vasomotor dysfunction, and maladaptive neuroplasticity. The clinical heterogeneity of CRPS is indicative of patient-to-patient variability in the activation of these pathways after noxious stimuli.

Even minor tissue trauma can be sufficient to amplify signaling in traumatized tissue and result in long-term peripheral sensitization. However, the way in which the immune system and nervous system interact, particularly in bones, muscle, and connective tissue, is not fully understood.

Vasomotor dysfunction is common in CRPS. The affected limb is usually warmer than the healthy limb early on and cooler than the healthy limb later on. This shift in temperature suggests that the activity in vasoconstrictor neurons changes over time in CRPS.

The central nervous system undergoes functional and structural changes in people with persistent pain, and these changes are thought to be especially important in people with CRPS. A potentially important mechanism is hyperalgesic priming. According to this theory, a transient insult triggers long-lasting changes in primary afferent nociceptors that cause them to become hyperresponsive to future mild insults that would not normally provoke pain.

Other theories include the existence of ephapses, or neurologic short circuits between the somatic and sympathetic nervous systems, possibly caused by trauma. It is unclear whether these connections are actual structural connections or "chemical" connections caused by the release of neurotransmitters. These ephapses could explain the clinical findings in CRPS. Stimuli that are usually mediated by the autonomic nervous system, such as responses to emotion, temperature, and weather, are rerouted through the somatic nervous system and cause pain. Stimuli that are usually mediated by the somatic nervous system, such as light touch, are rerouted through the autonomic nervous system and cause an uncoordinated sympathetic response.

### 3. Delineate the different stages of complex regional pain syndrome.

CRPS is usually described in three different stages (Table 71-1).

#### *Stage 1: Acute or Hyperemic Stage*

Stage 1 occurs within days to weeks of the initial injury and is characterized by a predominance of severe burning or lancinating pain. It is notable for signs of sympathetic blockade; the area affected is red, warm, and dry. Hyperesthesia—an exaggerated response to stimuli—and allodynia—a painful response to nonpainful stimuli—are prominent symptoms of this stage. Treatments instituted in stage 1 have the best prognosis for a cure.

#### *Stage 2: Dystrophic Stage*

Stage 2 occurs weeks to months after the initial insult. The signs and symptoms of this stage are consistent with sympathetic hyperexcitability. The area involved is pale or cyanotic and cool. Burning pain associated with hyperesthesia and allodynia is very common. Although treatments in this stage can be successful, the longer the duration of the symptoms, the poorer the prognosis.

#### *Stage 3: Atrophic Stage*

Stage 3 occurs months to years after the initial injury. Atrophy of the tissues in the involved area occurs because of prolonged vasoconstriction caused by increased sympathetic discharge over time. Burning and hyperesthesia become less prominent, and trophic changes predominate. The skin in the area becomes smooth and glassy, and the hair begins to fall out. The nails become brittle, and muscles become atrophic. The bones in the area show a classic patchy demineralization on radiography known as Sudek atrophy of the bone. The prognosis for pain relief and functionality is very poor at this point.

Frequently, patients do not experience all three stages of the syndrome. Stages may be skipped, or the progression may be halted with appropriate therapy.

### 4. What are the signs and symptoms of complex regional pain syndrome?

Patients with CRPS type 1 usually present with a history of very minor trauma, or patients may have no recollection of an injury. In contrast, the initial history for CRPS type 2 consists of a major injury with macroscopic nerve damage. Rarely, cerebrovascular accidents or myocardial infarctions may be complicated by CRPS. The most common symptom of CRPS is burning pain. Although CRPS usually occurs in an extremity, it can occur anywhere in the body, including the face or major joints, such as the knee or shoulder. Because of its atypical presentation, the diagnosis of CRPS in a joint is very difficult, and the clinician must have a high degree of suspicion when other pathologies have been ruled out. Because this syndrome derives from sympathetic innervation, affected areas can encompass nondermatomal distributions. Neurologic abnormalities such as allodynia and hyperesthesia are common with CRPS but can occur with somatic neuropathies as well. Depending on the stage of the disease, varying degrees of color, temperature, sweating, and trophic changes may be present. Less common manifestations include motor and sensory dysfunction.

### 5. How is complex regional pain syndrome diagnosed?

The diagnosis of CRPS is a clinical one, made by history and physical examination. Diagnosis of CRPS is based either on the Orlando criteria, endorsed by the International Association for the Study of Pain, or on a modified version called the Budapest criteria, summarized as follows:

a. Continuing pain, disproportionate to any inciting event
b. Must report at least one symptom in three of the categories in "d" below
c. Must report one sign in two or more of the categories in "d" below
d. No other diagnostic criteria can explain the signs and symptoms better
    i. Sensory: hyperesthesia or allodynia
    ii. Vasomotor: temperature asymmetry, skin color changes, or skin color asymmetry

TABLE 71-1 **Stages of Complex Regional Pain Syndrome**

| Stage | Name | Time | Findings |
|---|---|---|---|
| 1 | Acute or hyperemic | Days to weeks | Severe burning or lancinating pain<br>Skin is red, warm, and dry<br>Hyperesthesia<br>Allodynia |
| 2 | Dystrophic | Weeks to months | Skin is pale, cyanotic, and cool<br>Hyperesthesia<br>Allodynia |
| 3 | Atrophic | Months to years | Smooth glassy skin<br>Loss of hair<br>Brittle nails<br>Muscle atrophy<br>Demineralized bone (Sudek atrophy) |

iii. Sudomotor or edema: edema, sweating changes, or sweating asymmetry
iv. Motor or trophic: decreased range of motion, motor dysfunction (weakness, tremor, or dystonia), or trophic changes (hair, nails, or skin)

The most commonly used diagnostic test involves blocking the sympathetic innervation to the affected area and noting any improvement in the clinical symptoms.

## 6. What nerve blocks can be used for diagnosis and treatment of complex regional pain syndrome?

The two most common sympathetic nerve blocks used for both diagnosis and treatment of CRPS are stellate ganglion and lumbar sympathetic blocks. The stellate ganglion is created by a fusion of the inferior cervical sympathetic ganglion and the first thoracic sympathetic ganglion. Anatomically, it is located near the transverse process of C7 or T1 and has axons that arise from sympathetic cell bodies from the T1 through T5 spinal cord levels. Axons that pass through the stellate ganglion supply sympathetic innervation to the head, neck, and upper extremities.

Although the ganglion sits at C7 to T1, traditionally, a stellate ganglion block is performed at the level of the transverse process of C6, where Chaissagnac tubercle is located. Benefits of performing the injection at this level include a lower risk of pneumothorax and a decreased incidence of intravascular injection. The vertebral artery lies anterior to transverse process at C7 and dives posteriorly at C6 in most patients. Although for years the procedure was performed using only anatomic landmarks, at the present time, most are performed under fluoroscopic guidance at either the C6 or the C7 level. Fluoroscopic guidance and the use of contrast dye have allowed the procedure to be performed with greater safety at C7, increasing the likelihood of a successful block. A good indication of a successful sympathetic block to the head and neck region is the development of Horner sign (ptosis, miosis, and anhydrosis). A good indicator of a successful sympathetic block to the upper extremity is either vasodilation or increased temperature in the arm. Complications of a stellate ganglion block include hoarseness, intravascular (vertebral artery) injection causing seizures, pneumothorax, bradycardia, diaphragmatic paralysis, intrathecal or epidural injection, arm weakness, bleeding, and infection.

Lumbar sympathetic blocks are indicated for CRPS involving the lower extremities. These blocks should be performed under fluoroscopic guidance with contrast dye to confirm proper needle placement. The needle is placed anterolateral to the body of the lumbar vertebra at the L2, L3, or L4 level, most commonly at the L3 level. A good indicator of a successful sympathetic block to the lower extremity is either vasodilation or increased temperature in the leg. Complications that can occur include inguinal neuralgia, a selective nerve root block, intravascular injection, spinal or epidural anesthesia, renal trauma, and intradiscal injection.

## 7. What other modalities can be used to treat complex regional pain syndrome?

Physical therapy to prevent trophic changes associated with CRPS is of the utmost importance in conjunction with other treatment modalities. The key to successful therapy seems to be predominately dependent on treating the syndrome as early as possible. Psychotherapy is sometimes a productive adjunct to treatment.

The purposes of medications used to treat CRPS are to provide patient comfort to facilitate physical therapy, reduce pain, and decrease neuronal discharge. As a result of the continued poor understanding of the etiology of CRPS, medication management has proved to be challenging. However, medications should be selected with the goals of decreasing inflammation, ectopic firing of nerves, and sympathetic outflow. Pharmacologic therapies with calcitonin, bisphosphonates, free radical scavengers, steroids, and gabapentin have been studied with only bisphosphonate treatment showing improvement. Oral sympatholytics, such as beta blockers, decrease the effects of sympathetic discharge but can cause systemic side effects, especially related to the cardiovascular system. Tricyclic antidepressants and antiarrhythmic agents have also been described as therapies for CRPS. The use of opioids in the treatment of CRPS is controversial because of the risk of addiction and abuse.

Intravenous regional blocks can be performed along with or in lieu of sympathetic nerve blocks. Seven randomized controlled trials comparing intravenous regional blocks with placebo are available at the present. Mixed somatic and sympathetic blocks such as epidurals or spinals can be used but lack diagnostic specificity. Spinal cord stimulation has shown statistically better results for refractory CRPS at 2 years; however, there were no statistical differences in any measured variables over 5 years.

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CASE 72

# Cancer Pain Management

**Gordon M. Freedman, MD • Joel M. Kreitzer, MD • Vinoo Thomas, MD**

## QUESTIONS

1. What is the incidence of cancer pain?
2. What is the prevalence of cancer pain by organ system?
3. What are the different causes of pain in patients with cancer?
4. What is the WHO ladder?
5. What guidelines can be followed in devising a long-term analgesic regimen for treating cancer pain?
6. What are the advantages of set-dose extended-release opioid management?
7. What is breakthrough pain, and how is it treated?
8. Describe the anatomy of the celiac plexus.
9. What are the indications for performing a celiac plexus block?
10. How is a celiac plexus block performed, and what complications can occur?
11. What are the differences between alcohol and phenol neurolysis?
12. When would one use intrathecal versus epidural analgesia for cancer pain management?

A 57-year-old man presented to the pain management specialist complaining of epigastric pain radiating to the back. His sclerae were mildly icteric. Magnetic resonance imaging (MRI) showed a mass at the head of the pancreas.

### 1. What is the incidence of cancer pain?

The number of new cases of cancer in the United States is almost 2 million per year. Of these, approximately 50% of patients with intermediate-stage cancers and 75% of patients with advanced-stage cancers have pain. The incidence of cancer pain is approximately 1 million cases per year.

### 2. What is the prevalence of cancer pain by organ system?

Different organ systems are variably associated with cancer pain. Pancreatic cancer is the most common type of cancer associated with pain. Bone cancer is the second most common malignancy producing pain. Both cancers cause pain in >80% of cases. Breast, lung, and colon cancers are associated with pain in >70% of cases. Lymphomas and leukemias produce pain in about 60% of patients.

### 3. What are the different causes of pain in patients with cancer?

There are multiple causes of cancer pain. In approximately 65% of cases, pain is caused by direct invasion, involvement of nerves or the neuraxis, obstruction of a viscus, or metastasis to distant tissues. Anticancer treatments are responsible for 25% of cancer pain. Treatment-related pain is due to surgery, diagnostic procedures, chemotherapy side effects, and radiation complications. Syndromes unrelated to cancer cause 10% of pain in oncology patients. Patients with cancer may also have common non–cancer-related pain syndromes, such as lower back pain and headaches.

### 4. What is the WHO ladder?

The World Health Organization (WHO) devised a protocol (Box 72-1) for treating pain using a tiered approach. This protocol allows for the use of less potent medications initially (first tier), followed by increasingly more potent medications (second and third tiers) which are added in a stepwise approach until the patient is comfortable. According to the WHO, about 85% of cancer patients can be kept comfortable using this protocol.

In the WHO ladder, first-tier medications include nonopioid analgesics such as nonsteroidal antiinflammatory drugs (NSAIDs), antidepressants, and anticonvulsants. Second-tier medications include "weak opioids," which have ceiling dosages owing to their combination with acetaminophen or NSAIDs. Third-tier analgesics include all sole opioid preparations, both short-acting and extended-release preparations. Despite the addition of large doses of opioids in the third tier, the nonopioid medications from tier 1 should be continued, taking advantage of their different mechanism of action in treating pain. A good knowledge of opioid equipotency conversions is necessary to be able to change from one opioid to another.

The WHO ladder can be further extrapolated clinically to include invasive techniques. Oral analgesics are tried first, followed by intravenous opioids, analgesia via tunneled epidural catheters, implantable analgesic devices (e.g., intrathecal infusion pumps), and finally neuroablative procedures.

**BOX 72-1 Sequence for Management of Cancer Pain**

- WHO ladder
  - Tier 1—nonopioid analgesics
  - Tier 2—"weak opioids" (in combination with acetaminophen or NSAIDs)
  - Tier 3—pure opioids
- Tunneled epidural catheters
- Implantable analgesic devices
- Neuroablative procedures

## 5. What guidelines can be followed in devising a long-term analgesic regimen for treating cancer pain?

Guidelines frequently followed when treating cancer pain use a combination of different classes of analgesics to minimize the side effects of any one medication. The combination should use drugs that work on pain pathways at different levels to take advantage of their additive and synergistic effects, as follows:

- Opioids with a set dose and extended-release mechanism (Table 72-1) act on opioid receptors in the brain and the spinal cord.
- NSAIDs act primarily by inhibiting prostaglandin synthesis causing desensitization of peripheral pain receptors.
- Antidepressants act by inhibiting the reuptake of serotonin and norepinephrine, which results in stimulation of the descending inhibitory pain tracts in the spinal cord.
- Anticonvulsants (optional) act on the neuropathic components of pain.
- Fast-onset, short-duration analgesics given on an as-needed ("prn") basis address episodic, breakthrough pain.

## 6. What are the advantages of set-dose extended-release opioid management?

Set-dose extended-release opioids maintain analgesic blood concentrations within the therapeutic window more consistently over time compared with short-acting analgesics. The therapeutic window is the range of blood levels at which the desired clinical effect, in this case analgesia, is achieved. With blood levels above the therapeutic window, the patient begins to experience side effects. Drug blood levels below the therapeutic window would be ineffective and result in the patient experiencing pain. In contrast, as-needed ("prn") dosing of medications maintain analgesic blood concentrations within the therapeutic window for approximately one third of the time. Set-dose extended-release medications provide better analgesia with fewer overall side effects. New formulations of extended-release opioids have the advantage of decreasing the risk of abuse.

TABLE 72-1 **Common Extended-Duration Opioids**

| Name | Dosing Interval (hours) | Equipotent Dose (Equivalent to Morphine 10 mg IV) |
|---|---|---|
| Extended-release dilaudid (Exalgo; Mallinckrodt Pharmaceuticals, Hazelwood, MO) | 24 | 8 mg po |
| Extended-release oral morphine (MS Contin; Purdue Pharma LP, Stamford, CT) | 8–12 | 30 mg po |
| Extended-release morphine (Avinza; Pfizer Inc. New York, NY) | 24 | 30 mg po |
| Extended-release oral morphine (Kadian; Actavis U.S., Parsippany, NJ) | 12–24 | 30 mg po |
| Extended-release oral oxycodone (OxyContin; Purdue Pharma LP, Stamford, CT) | 8–12 | 20 mg po |
| Extended-release oral oxymorphone (Opana ER; Endo Health Solutions, Inc., Malvern, PA) | 12 | 10 mg po |
| Extended-release tapentadol (Nucynta ER; Janssen Pharmaceuticals, Titusville, NJ) | 12 | 100 mg po |
| Levorphanol | 6–8 | 4 mg po/2 mg IV |
| Methadone | 6 | 20 mg po/10 mg IV |
| **Patches** | | |
| Continuous-release fentanyl patch (Duragesic; Janssen Pharmaceuticals, Titusville, NJ) | 72 | 100 μg/hour = morphine 3 mg/hour IV |
| Buprenorphine transdermal patch (Butrans; Purdue Pharma LP, Stamford, CT) | 1 week | 5 μg/hour = morphine 30 mg/day po |

*IV,* Intravenously; *po,* orally.

TABLE 72-2 **Rapid-Onset Opioids (Fentanyl)**

| | Site of Absorption | Dosing Formulation |
|---|---|---|
| Abstral (ProStrakan, Inc., Galashiels, UK) | Sublingual | Tablet |
| Actiq (Teva Pharmaceuticals, Petach Tikva, Israel) | Buccal | Lozenge |
| Fentora (Teva Pharmaceuticals, Petach Tikva, Israel) | Buccal | Tablet |
| Lazanda (Archimedes Pharma U.S., Inc., San Francisco, CA) | Intranasal | Spray |
| Onsolis (Meda Pharmaceuticals, Somerset, NJ) | Buccal | Strip |
| Subsys (Insys Therapeutics, Inc., Chandler, AZ) | Sublingual | Spray |

## 7. What is breakthrough pain, and how is it treated?

Breakthrough pain is a transient exacerbation of pain on the background of stable pain in a patient receiving long-term opioid therapy. Breakthrough pain occurs in about 64% of patients with cancer with a median of four pain episodes per day with an onset of <3 minutes and a duration of about 30 minutes. The breakthrough pain can be due to end of dosing intervals of long-term pain medications, incident pain, nonvolitional precipitants (coughing, sneezing, flatulence), or can be idiopathic.

Breakthrough pain is mainly treated with fast-onset, short-duration analgesics. A new class of breakthrough analgesics is available (Table 72-2) for acute cancer pain known as rapid-onset opioids. Fentanyl (high lipophilicity) is the analgesic of choice for these medications. Their onset time is approximately 5–15 minutes, and the pharmacokinetic profile mirrors the time frame associated with acute pain. Risk Evaluation and Mitigation Strategies (REMS) are now required to be implemented by manufacturers of rapid-onset opioids. The purpose of the REMS is to try to decrease the risk of misuse and abuse of these rapid-onset opioids. The strategies emphasize the distribution of educational tools regarding the proper clinical use of the rapid-onset opioids to practitioners, pharmacists, and patients. Knowledge of the risks versus benefits must be documented by all of these parties to be able to be involved with the prescribing of this class of medications.

## 8. Describe the anatomy of the celiac plexus.

The celiac plexus is part of the sympathetic nervous system and is made up of the celiac, superior mesenteric, and aorticorenal ganglia. Nerve fibers that traverse the celiac plexus arise from cell bodies from T5 through T12 and leave the spinal cord without synapsing in the paravertebral ganglia. These sympathetic fibers form the greater, lesser, and least splanchnic nerves and coalesce around the celiac artery at approximately the L1 level. Here they synapse with postganglionic fibers that supply the intraabdominal organs below the diaphragm up to the splenic flexure of the large intestine. These include the stomach, small and large intestines, pancreas, hepatobiliary system, kidneys, adrenals, spleen, and omentum. The celiac plexus contains visceral afferent and efferent fibers and some parasympathetic fibers.

## 9. What are the indications for performing a celiac plexus block?

There are three main indications for blockade of the celiac plexus:

- To treat pain from intraabdominal organs (innervated by the celiac plexus), especially secondary to malignancy, which is the most common reason for performing celiac plexus blocks (this block can also be used for nonmalignant pain)
- To increase blood flow to the splanchnic vessels in abdominal angina
- To increase peristalsis in the gastrointestinal tract in dysmotility syndromes, such as with diabetes mellitus or scleroderma

## 10. How is a celiac plexus block performed, and what complications can occur?

Celiac plexus blocks are performed with either fluoroscopy or computed tomography (CT) scan. The patient is placed in the prone position unless he or she cannot tolerate it because of ascites or other intraabdominal processes. The plexus lies anterior to the aorta and posterior to the vena cava. Needles are placed from each side of the body to lie anterior to the body of L1 bilaterally. Dye injection confirms needle placement in the retroperitoneum. A maximum of 40 mL of either local anesthetic for diagnostic blocks (usually 0.25% bupivacaine) or neurolytic agent (see Question 11) for therapeutic blocks is injected.

Complications that can occur with celiac plexus blockade include hypotension; injury to adjacent viscera (e.g., kidneys, pancreas, pleura, lungs, aorta, intestines); lower extremity dysesthesias or motor dysfunction; intravascular injections; retroperitoneal hematomas; and intrathecal, epidural, intrapsoas, or intraosseous injections (Box 72-2).

**BOX 72-2 Complications of Celiac Plexus Block**

- Hypotension
- Trauma to kidneys, pancreas, pleura, lungs, aorta, intestines
- Lower extremity dysesthesias or motor dysfunction
- Intravascular injection
- Retroperitoneal hematoma
- Epidural, intrathecal, intradiscal, intraosseous, intrapsoas injection

TABLE 72-3 **Differences between Alcohol and Phenol for Neurolytic Blocks**

| | Alcohol | Phenol |
|---|---|---|
| Mechanism of action | Extraction of neuronal cholesterol, phospholipids, and cerebrosides<br>Precipitation of lipoprotein and mucoproteins | Coagulation of neuronal proteins |
| Injection | Painful | Local anesthetic effect (?) |
| Subarachnoid | Hypobaric | Hyperbaric |
| Potency | Greater (?) | Less (?) |
| Duration | Longer acting | Shorter acting |
| Perivascular injection | Safe | May cause blood vessel wall necrosis |

As is the case with any invasive procedure, sterile technique is imperative to avoid infection, especially in a patient with cancer who may be immunosuppressed.

## 11. What are the differences between alcohol and phenol neurolysis?

Neurolysis can be accomplished with several modalities including alcohol or phenol (Table 72-3). Alcohol for neurolysis is usually used in concentrations of 50%–70%. It produces neurolysis by extracting cholesterol, phospholipids, and cerebrosides and causing precipitation of lipoproteins and mucoproteins; this results in damage to both the Schwann cell and the axon. Clinically, alcohol is painful on injection and is hypobaric if used for intrathecal neurolysis. Relative to phenol, alcohol may be more potent with a longer duration of action.

The primary neurolytic effect of phenol is via coagulation of proteins. It also causes nonselective damage to neural tissue. Phenol might have a secondary local anesthetic effect. Intrathecally, phenol is hyperbaric. Phenol has a great affinity for vascular tissue, and injury to adjacent blood vessels must be considered when it is used. For this reason, many pain specialists prefer alcohol to phenol for celiac plexus blocks. Radiofrequency lesioning, cryoablation, and glycerol are other modalities used for neurolysis.

## 12. When would one use intrathecal versus epidural analgesia for cancer pain management?

Both epidural and intrathecal analgesia systems allow for the delivery of a wide variety of opioids, local anesthetics, and adjuvants (e.g., clonidine, baclofen) directly into the central nervous system. Epidural and intrathecal analgesia systems allow for smaller dosing compared with oral and intravenous administration and potentially fewer side effects. In particular, the use of local anesthetics enables denser analgesia and a possible opioid-sparing effect.

Permanent intrathecal analgesia reservoirs are more expensive to place than externalized epidural infusion systems but are less expensive to maintain in the long-term. If the patient's life expectancy is >3–4 months, the intrathecal analgesia system with an internal pump is financially preferable.

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SECTION 13

# AMBULATORY ANESTHESIA

CASE 73

# Ambulatory Surgery

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## QUESTIONS

1. Are there advantages to performing surgery on an ambulatory basis?
2. Which patients are considered acceptable candidates for ambulatory surgery?
3. Are there patients who should never have surgery on an ambulatory basis?
4. Are diabetic patients suitable candidates for ambulatory surgery?
5. What types of surgical procedures are appropriate for ambulatory surgery?
6. What is the appropriate fasting time before ambulatory surgery that necessitates an anesthetic?
7. Should drugs be administered to empty the stomach or change gastric acidity or volume before administering an anesthetic?
8. How are patients evaluated before an ambulatory anesthetic?
9. Which preoperative laboratory studies should be obtained before surgery?
10. Should an internist evaluate each patient before ambulatory surgery?
11. Is an anxiolytic premedication advisable before ambulatory surgery, and what agents are appropriate?
12. What are the reasons for last-minute cancellation or postponement of surgery?
13. What is the ideal anesthetic for an ambulatory surgical procedure?
14. What are the relative or absolute contraindications to general anesthesia in the ambulatory setting?
15. What are the advantages and disadvantages of performing regional anesthesia in ambulatory surgery patients?
16. What are the advantages and disadvantages of nerve block techniques for ambulatory surgery patients?
17. Describe the intravenous regional anesthetic technique (Bier block) for surgery on the extremities.
18. What sedatives can be administered to supplement a regional anesthetic?
19. What complications of nerve block anesthesia are of special concern to ambulatory surgery patients?
20. Do all ambulatory surgery patients require tracheal intubation?
21. What is the role of propofol in ambulatory surgery?
22. What is total intravenous anesthesia, and what are its advantages and disadvantages?
23. Define the term "moderate sedation"; when is it used, and what advantages does it offer over general anesthesia?
24. Can succinylcholine myalgias be avoided?
25. Can a relative overdose of benzodiazepine be safely treated with an antagonist?
26. Do newer volatile agents offer advantages over older agents?
27. What are the etiologies of nausea and vomiting, and what measures can be taken to decrease the incidence and severity of nausea and vomiting?
28. How is postoperative pain best controlled in ambulatory surgery patients?
29. What discharge criteria must be met before a patient may leave the ambulatory surgery center?
30. What are the causes of unexpected hospitalization after ambulatory surgery?
31. When may patients operate a motor vehicle after receiving general anesthesia?
32. What is the role of aftercare centers for ambulatory surgery patients?
33. Are quality assurance and continuous quality improvement possible for ambulatory surgery?

A 38-year-old woman is scheduled for diagnostic pelvic laparoscopy at 3 o'clock in the afternoon as an ambulatory procedure. She arrives at the ambulatory surgery center (ASC) 1 hour before scheduled surgery, accompanied by her 11-year-old son, and appears to be extremely apprehensive. Prior medical history is significant for asymptomatic gastroesophageal reflux disease; long-standing stable asthma that has been successfully treated with inhaled sympathomimetics and steroids; and type 1 diabetes mellitus, currently controlled with 25 units of neutral protamine Hagedorn (NPH) and 6 units of regular insulin every morning and 10 units of NPH and 3 units of regular insulin every night.

### 1. Are there advantages to performing surgery on an ambulatory basis?

There are multiple advantages to performing surgery on an ambulatory basis. First, patients return more quickly to the familiar home environment; this can be very

important for both pediatric and geriatric surgical patients. A reduction in nosocomial infections has also been noted. Medication errors related to faulty prescribing or dispensing of drugs is decreased in ambulatory surgery.

Overall costs for ambulatory procedures are usually reduced. Cost savings are due to decreased laboratory testing, fewer medical consultations, and reduced numbers of pharmaceuticals dispensed. The significant expense of both the inpatient hospitalization and the hospital facility fee is avoided.

Other, less tangible advantages include ease of scheduling procedures and an improved sense of patient privacy because most ASCs are staffed by a small consistent group of personnel.

## 2. Which patients are considered acceptable candidates for ambulatory surgery?

Acceptable candidates for ambulatory surgery generally have relatively stable medical conditions. However, many centers now accept American Society of Anesthesiologists (ASA) physical statuses III and IV patients for selected, relatively noninvasive surgical procedures and diagnostic studies. Generally, less invasive surgery is performed on patients who are less healthy, whereas more invasive surgery is performed on ASA physical status I or II patients. Patients with cardiovascular disease have an increased risk of perioperative complications and may not be suitable candidates for invasive ambulatory procedures. Patients with severe physical or mental handicaps are often excluded from consideration as candidates for ambulatory surgery. Patients or caregivers must be able to comprehend and comply with postoperative instructions for successful ambulatory surgery.

Ambulatory surgery is well suited for pediatric patients. Generally, ambulatory surgical procedures performed on children are shorter in duration, less extensive, and less invasive than most procedures performed on adults. Additional benefits to pediatric patients include less disruption of the child's normal feeding schedule and decreased separation time from parents. Exposure to the unfamiliar and frightening hospital milieu can be reduced to the bare minimum. Additionally, because recovery times are short for procedures such as myringotomy and tubes, circumcision, and inguinal herniorrhaphy, early discharge from the facility is feasible.

Preoperative communication and collaboration between anesthesiologists and surgeons are essential in the event of a questionable or problem patient. The surgeon who is to perform the procedure, the patient, and the family must be agreeable to the concept of ambulatory surgery. However, reimbursement schedules created by insurance carriers often convince the occasional skeptic because costs associated with hospitalization for procedures that can be readily performed on an ambulatory basis usually are not covered. Overwhelming and incontrovertible evidence of medical necessity for inpatient care must be presented to obtain authorization for postoperative hospitalization.

## 3. Are there patients who should never have surgery on an ambulatory basis?

Ex-preterm infants who are <55–60 weeks postconceptual age should not have ambulatory surgery. These infants are at risk for postoperative apnea and bradycardia for the next 12 hours (and may last up to 48 hours) after sedation and general anesthesia. In-hospital monitoring of ex-preterm infants is recommended postoperatively. For similar reasons, term infants <44 weeks postconceptual age should have surgery performed as inpatients. Postoperative respiratory monitoring is mandatory for at least 12–18 hours. If possible, surgery and diagnostic procedures requiring sedation or general anesthesia should be postponed until the child passes the unsafe period.

## 4. Are diabetic patients suitable candidates for ambulatory surgery?

Diabetic patients may present a major challenge for the anesthesiologist when scheduled for ambulatory surgery. Because of the critical nature of glucose homeostasis, it may be advisable to handle exceptionally brittle diabetics on an inpatient basis. Preoperatively, diabetic patients must be carefully assessed for the presence of end-organ damage. Cardiovascular disease, autonomic and renal insufficiency, and gastroparesis may lead to potential problems in the perioperative period.

It is preferable to schedule surgery for patients with type 1 diabetes as the first or second case of the day. The major concerns are to avoid the extremes of plasma glucose, both hypoglycemia and hyperglycemia, and acidosis. Delays in insulin administration may lead to ketoacidosis despite the fasting state. For this reason, it is recommended that patients receive insulin along with a continuous infusion of dextrose on arrival at the ASC. Insulin may be administered by either the subcutaneous or the intravenous route. The advantage of administering a continuous infusion of regular insulin versus one third to one half of the usual long-acting insulin dose subcutaneously has not been demonstrated. Another option for early-morning surgical procedures is to administer the usual long-acting insulin dose subcutaneously immediately after surgery and shift the time of all meals and future insulin injections by the same offset.

Patients receiving oral hypoglycemic agents must be carefully monitored in the perioperative period by fingerstick or blood glucose determinations. The half-life of some oral agents (e.g., chlorpropamide) may be 60 hours. Patients with type 2 diabetes mellitus rarely develop ketoacidosis. However, these patients can experience hyperosmolar, nonketotic coma when significant hyperglycemia and dehydration occur.

Before discharge, it is critical that diabetic patients are capable of eating. They also should be relatively free of nausea that might lead to emesis and inability to maintain adequate caloric intake.

## 5. What types of surgical procedures are appropriate for ambulatory surgery?

Initially, ambulatory surgery procedures were limited to 1½ hours. The concern was for lengthy postanesthesia

recovery time that would extend beyond the facility's hours of operation. However, newer anesthetic agents allow for safe discharges on a timely basis even after long procedures performed with general anesthesia.

The types of surgical procedures that may be performed on an ambulatory basis depend on whether an ASC is truly a freestanding unit (i.e., geographically detached from a hospital) or is located within a hospital or directly contiguous to an inpatient facility. Hospital-based units often accept patients with a greater severity of baseline illness and may perform more complex surgical procedures for many reasons. In the event of unexpected massive surgical hemorrhage, availability of immediate blood bank support is crucial and available in hospitals. However, when the need for blood may be anticipated preoperatively, freestanding ASCs can arrange for blood products to be available, and transfusions may be administered if the need arises. Patients may also be asked to donate one or more units of autologous blood, which may be kept available for intraoperative or postoperative use. Procedures in which blood might be administered include extensive liposuction or reduction mammoplasty. Radiology services, subspecialty consultative services, and the relative ease of hospital transfer for overnight admission allow performance of more involved and invasive procedures in hospital-based ASCs.

Ideal procedures for ambulatory surgery result in relatively minor postoperative physiologic changes including fluid shifts and blood loss. Commonly performed surgeries include procedures from all surgical disciplines and subspecialties. A few examples include cataract extraction; breast surgery; plastic surgery; gynecologic procedures such as dilation and curettage, hysteroscopy, termination of pregnancy, and laparoscopy; arthroscopy; and inguinal and umbilical herniorrhaphies. The common denominator of all these procedures is that they are associated with only mild to moderate degrees of postoperative pain, which may be readily controlled by oral analgesic agents.

In the early days of ambulatory surgery, a tonsillectomy was an example of a procedure that was considered to require overnight in-hospital observation. Today, tonsillectomy is being performed on an ambulatory basis in many centers, although the period of postoperative observation is increased compared with other ambulatory surgeries. After tonsillectomy, nausea and vomiting are the most common complications causing morbidity. Early bleeding, if it occurs, usually becomes evident within the first 6 hours. It is acceptable to discharge individuals to home who are otherwise in good health, reside within a reasonable distance from the facility, are accompanied by a responsible adult, and have successfully tolerated oral intake without nausea and vomiting. It is especially important that adequate fluid repletion is accomplished before discharge because early attempts at fluid intake by mouth after tonsillectomy may be unsuccessful as a result of pharyngeal pain.

## 6. What is the appropriate fasting time before ambulatory surgery that necessitates an anesthetic?

The preoperative fasting period prescribed for patient who will receive anesthesia is identical for inpatients and outpatients. The ASA fasting guidelines recommend 8 hours for solids, 6 hours for light meals (i.e., toast and tea), 4 hours for breast milk, and 2 hours for clear liquids. Ingestion of 8 oz. of orange juice without pulp or coffee without milk has not been shown to increase gastric volume. Both resting gastric volume and acidity may be reduced, which may decrease further the incidence and potentially devastating sequelae of intraoperative aspiration.

Other benefits result from decreasing the fasting time in patients preoperatively. Patients allowed to drink clear fluids are more content while waiting for surgical procedures that either were delayed or were scheduled later in the day. Thirst is relieved, and hunger may be diminished. Ingestion of glucose-containing solutions may also prevent relative degrees of hypoglycemia. Medications required for the maintenance of homeostasis, such as blood pressure and cardiac drugs, can be taken orally up to 1 hour before surgery with 1 oz. of water.

Fasting guidelines should not be made on a case-by-case basis but rather should be reflected in facility-wide or institution-wide guidelines.

## 7. Should drugs be administered to empty the stomach or change gastric acidity or volume before administering an anesthetic?

Studies regarding differences in resting gastric volume between inpatients and ambulatory patients have yielded conflicting results. No evidence supports the notion that every patient must receive liquid nonparticulate antacids (0.3 molar sodium citrate, 30 mL) before induction of anesthesia. A soluble (nonparticulate) antacid is substituted for the conventional nonabsorbable antacid containing aluminum, magnesium, or calcium hydroxide to avoid severe chemical pneumonitis that may result from aspiration of these particulate substances. Other pharmacologic agents include $H_2$-receptor blockers (e.g., ranitidine, famotidine), which inhibit gastric acid production and decrease gastric volume. Mental confusion has been reported after intravenous administration of cimetidine in geriatric patients. Ranitidine is more potent and specific and has a longer duration of action than cimetidine. Metoclopramide increases tone in the lower esophageal sphincter and facilitates gastric emptying. However, it does not guarantee a stomach free of gastric contents. Metoclopramide, in conjunction with an $H_2$ receptor blocker, may be more efficacious than one drug by itself. However, routine use of these drugs in patients without specific risk factors is not currently recommended. Additionally, although nonparticulate antacids work immediately, these intravenous drugs take 30 minutes to several hours for full effect.

Diabetes mellitus with evidence of autonomic dysfunction or gastric atony (gastroparesis), documented symptomatic hiatal hernia, untreated gastroesophageal reflux, pregnancy in active labor, significant obesity, acute abdomen, and current opioid use or abuse are conditions that appear to increase the incidence of gastric regurgitation and aspiration during induction or emergence from general anesthesia or during heavy sedation. Prophylaxis in these situations is recommended. There

is no advantage to administration of triple prophylaxis with $H_2$-receptor antagonists, soluble antacids, and metoclopramide. If prophylaxis with an $H_2$ blocker is employed, it should be given the evening before as well as on the morning of surgery. Another effective regimen combines metoclopramide on the morning of surgery and a nonparticulate antacid immediately before surgery.

Despite administration of pharmacologic agents and imposition of fasting, significant amounts of acidic gastric contents may remain. Aspiration of gastric material is a relatively rare occurrence. If a patient is observed to aspirate and if symptoms of coughing, wheezing, or hypoxemia while breathing room air do not develop within 2 hours, significant respiratory sequelae are unlikely. Reliable and otherwise healthy ambulatory patients can probably be discharged after several hours of observation in the postanesthesia care unit (PACU). They must be instructed to contact their physician at the onset of symptoms.

## 8. How are patients evaluated before an ambulatory anesthetic?

Ideally, on the day before surgery, the patient would have a private conference with the anesthesiologist who will be caring for him or her. Rapport and trust could be established, a history could be obtained, and physical assessment could be conducted. Appropriate laboratory tests would be ordered, and additional consultations, if necessary, could be requested. Finally, information from old medical records could be obtained.

To avoid an additional trip for the patient and family, some facilities substitute a screening telephone interview for a personal interview conducted by either a nurse or an anesthesiologist several days before surgery. Pertinent medical history can be elicited, general and specific instructions can be given, and reassurance can be offered to the patient. In this scenario, laboratory studies and additional components of the medical record, including an electrocardiogram (ECG) and radiographs, if necessary, are performed immediately before surgery. Previously established criteria and patient comorbidities determine the tests that must be obtained. On the day of surgery, the anesthesiologist must review all information with the patient, conduct the appropriate examination, and obtain informed consent.

The surgeon must assume a large degree of responsibility for the patient's preoperative preparation. Surgeons are often the only physician to see patients before the day of surgery. Beside conducting a thorough history and physical examination, the surgeon may also request medical consultation when appropriate. To aid in the screening process, surgeons may selectively order laboratory and other examinations according to written guidelines established by the medical facility. However, a mechanism should be in place for free communication between the surgeon's office and the facility so that appropriate action may be taken when abnormal laboratory values or other reports are received.

The anesthesiologist's preoperative interview should be conducted in a relaxed, unhurried, and comprehensive manner both chronologically and geographically apart from the operating room. It is less than optimal to conduct a preanesthesia interview and examination with the patient stripped of clothing and strapped to the operating room table. Additionally, with the surgeon and nurses waiting and instrumentation prepared, the pressure on the anesthesiologist to proceed with anesthesia may be intense.

The anesthesiologist should not fail to question patients firmly regarding the use of illicit and nonprescription drugs. In one patient population, 25% of subjects tested positive for commonly abused substances in their urine. Depending on the drug involved, modifications in patient management, including cancellation of surgery, might be well advised. Additionally, users of illicit drugs may have diminished capability or interest in complying with postoperative instructions.

## 9. Which preoperative laboratory studies should be obtained before surgery?

For an ambulatory surgery unit that is affiliated with or attached to a hospital, clinical laboratory testing guidelines should be identical to the related institution. It has been well established that "shotgun," nonselective screening batteries of laboratory, radiographic, and other studies yield an extraordinarily low rate of abnormal findings, few of which may have a significant impact on patient management. Patients scheduled for surgery should have preoperative testing ordered selectively, based on the results of their history and physical examination. Indiscriminate testing can have potentially serious and deleterious consequences. To explain abnormal results, additional studies may be required. Some invasive studies have inherent dangers. Abnormalities often are simply ignored, creating a potential medicolegal liability. Indiscriminate screening often reveals abnormalities that are irrelevant to either the surgery or the choice of anesthetic agent or technique. Some centers use handheld computers to obtain patient histories. Branching lines of questioning dependent on previous answers allow extensive information gathering. At the conclusion of the interactive interview, computers can provide detailed printouts of significant findings and suggest indicated preoperative testing. Many facilities do not require preoperative testing in otherwise healthy men and women $<$40–50 years old who are undergoing superficial surgical procedures.

## 10. Should an internist evaluate each patient before ambulatory surgery?

The same rules and standards regarding preoperative evaluation of patients apply for surgery scheduled on both an inpatient and an ambulatory basis. An internist or medical subspecialist should be consulted whenever the stability of a patient's medical condition is questionable. Although the magnitude of physiologic perturbations associated with some ambulatory surgery procedures may be minor, there is nothing minor about the administration of an anesthetic. A complete written history and physical examination are required as part of the medical record before administration of anesthesia and commencement of surgery. This history and physical

examination may be performed by the surgeon if the patient has no comorbidities that would necessitate input from an internist or medical specialist.

### 11. Is an anxiolytic premedication advisable before ambulatory surgery, and what agents are appropriate?

Because the goal of anesthesia for ambulatory surgery is to permit early discharge to home, there was concern that the administration of short-acting anxiolytic or analgesic premedication might delay recovery from anesthesia and prolong time in the PACU with a resultant delay in patient discharge. Many patients experience anxiety in the immediate preoperative period, and pharmacologic management is quite acceptable. The administration of either diazepam, 5–10 mg orally, 1–2 hours before surgery or midazolam, 1–2 mg intravenously, after an intravenous catheter is placed before surgery can ameliorate distress if deemed desirable. The amnestic effect of intravenous midazolam is powerful, and patients may not remember having seen their surgeon if it is administered before meeting the surgeon. Midazolam can also be given orally, although much larger doses (0.5–1 mg/kg) are required because of first-pass hepatic degradation. Opioid premedication may contribute to the incidence of postoperative nausea and vomiting (PONV). Preoperative oral doses of clonidine, a centrally acting $\alpha_2$-adrenergic agonist, have been used to provide sedation, reduce anesthetic requirements, and decrease episodes of hypertension and tachycardia during intubation and maintenance of general anesthesia. Side effects include dry mouth, hypotension, and postoperative sedation.

Relaxation techniques can be taught preoperatively to patients and may aid in reduction of anxiety levels. Instruction of these techniques is time-consuming and requires substantial patient motivation. They are usually reserved for select patients with extreme phobias. The effects of longer acting anesthetics and the surgical procedure itself contribute more significantly to the recovery time and delayed discharge. Although time to discharge, a gross measurement, may remain unaffected, tasks that require fine coordination and speedy reaction times may still be deleteriously affected by the anesthetic (i.e., both premedication and intraoperative anesthetic techniques).

### 12. What are the reasons for last-minute cancellation or postponement of surgery?

The incidence of last-minute postponement or cancellation of ambulatory procedures often exceeds the cancellation rate for inpatient procedures. Multiple factors contribute to this problem. Repeat physical examination by the surgeon may reveal the disappearance of pathology. Patients may forget and ingest either solid food or liquids before arrival at the medical facility. Abnormal test results that were not available or not previously reviewed may be discovered. Communication between the surgeon and anesthesiologist regarding laboratory abnormalities helps to reduce the incidence of last-minute cancellation of surgery, consequences of which distress both the patient and the surgeon and make for inefficient use of available operating room time. Additional questioning may reveal either new symptoms or significant history that was not previously elicited. Physical findings apparent on a last-minute assessment by the anesthesiologist may preclude the safe administration of an anesthetic. Examples include an acute upper respiratory tract infection or an exacerbation of bronchospastic pulmonary disease. Finally, patients may arrive late to the facility or without a responsible escort to accompany them home.

### 13. What is the ideal anesthetic for an ambulatory surgical procedure?

No single anesthetic is ideal for every procedure. However, the goal of the anesthetic is to allow for patient discharge shortly after completion of the procedure. An ideal general anesthetic agent would have rapid onset, permit quick return to baseline levels of lucidity and equilibrium, and provide freedom from deleterious cardiovascular and respiratory effects. It would provide intraoperative amnesia, analgesia, and muscle relaxation and possess antiemetic properties. This ideal single agent does not exist at the present time (Table 73-1). In an attempt to avoid some of the unpleasant side effects associated with general anesthesia, regional anesthetic techniques, including field blocks, intravenous regional block (i.e., Bier block), various approaches to the brachial plexus, ankle block, and spinal and epidural anesthesia, have been offered to patients as an alternative to general anesthesia.

### 14. What are the relative or absolute contraindications to general anesthesia in the ambulatory setting?

Sometimes general anesthesia should be avoided, if possible. For example, patients with severe, poorly controlled asthma or documented bullous emphysema should not receive general anesthesia. In these cases, lesser concern should be given to the possibility of a postdural puncture headache (PDPH) if more serious sequelae are likely to result during or after administration of a general anesthetic. However, such cases are the exception rather than the rule, and in most instances, the final choice of anesthesia should remain with the patient, guided by the anesthesiologist. Additionally, when patients arrive for extremely minor surgery without an escort, a local anesthetic injection alone without sedation might suffice for anesthesia. This type of anesthesia might allow the patient to return home unaccompanied. It sometimes becomes necessary to supplement local anesthesia with intravenous sedation, and an escort would be mandatory under these circumstances.

### 15. What are the advantages and disadvantages of performing regional anesthesia in ambulatory surgery patients?

Regional anesthesia offers several advantages for patients undergoing ambulatory surgery. If little or no intraoperative sedation is required, little or none of the "hangover"

TABLE 73-1 **Drugs Used during Ambulatory Surgery**

| Drug | Class | Action | Intravenous Dose Range | Potential Side Effects |
|---|---|---|---|---|
| Midazolam | Benzodiazepine | Sedative-hypnotic | 1–4 mg/70 kg | Apnea and potentiation of hypotension in combination with opioids |
| Propofol | Diisopropylphenol | Induction sedative-hypnotic | 2.0–2.5 mg/kg; 0.1–0.2 mg/kg/minute infusion and 10–20 mg bolus as needed | Pain on injection; hypotension; respiratory depression; apnea |
| Fentanyl | Opioid | Analgesia | 1–3 μg/kg | Respiratory depression; apnea; nausea; vomiting; miosis; depression of cough; bradycardia; hypotension |
| Remifentanil | Opioid | Analgesia | Bolus 0.5-1 μg/kg, then infusion 0.02–0.3 μg/kg/minute | Respiratory depression; apnea; nausea; vomiting; miosis; depression of cough; bradycardia; hypotension |
| Ranitidine | $H_2$ blocker | Histamine receptor antagonist | 150 mg orally or 50 mg IV preoperatively | Headache; fatigue; drowsiness; dizziness; nausea; vomiting; abdominal pain; diarrhea; constipation |
| Naloxone | Opioid antagonist | Competitive antagonist | 20–40 μg bolus, titrate to effect | Precipitate withdrawal symptoms; hypertension; tachycardia; arrhythmias |
| Flumazenil | Imidazobenzodiazepine | Specific benzodiazepine antagonist | 0.2 mg every 1 minute up to total dose of 1.0 mg; may repeat every 20 minutes | Central nervous system excitation; seizures; nausea; vomiting; acute withdrawal |
| Droperidol | Butyrophenone | Antiemetic | 10–20 μg/kg; 0.625–1.25 mg/70 kg | Dysphoria; extrapyramidal signs; sedation; hypotension; la belle indifférence; catatonia; prolonged QT interval; torsades de pointes, FDA "black box" warning |
| Ondansetron | 5-$HT_3$ receptor | Antiemetic | 4 mg/70 kg over 2.5 minutes | Pain on injection; rash; headache |
| Dexamethasone | Steroid | Antiemetic, antiinflammatory | 4–10 mg | Perineal "burning"; hyperglycemia |
| Transderm scopolamine | Anticholinergic | Antiemetic, anti–motion sickness | 1.5 mg slow-release patch | Dry mouth; dysphoria; sedation |
| Labetalol | alpha 1- and beta-adrenergic blocker | Antihypertensive | 5–20 mg increments every 5 minutes up to total dose of 80 mg | Bronchospasm; conduction delays; bradycardia |
| Esmolol | Relative beta-1-selective adrenergic blocker | Antihypertensive, antiarrhythmic | 10-mg bolus; add increasing doses every 3 minutes as needed up to 300 mg total; then may administer 50–200 μg/kg/minute | Bradycardia; conduction delays; hypotension; bronchospasm; congestive heart failure |
| Desflurane | Ether | General anesthesia | Minimum alveolar concentration 6% inhaled | Myocardial depression; respiratory depression; airway irritation |

*FDA,* Food and Drug Administration; *IV,* intravenously; *5-$HT_3$,* 5-hydroxytryptamine 3.

effect will be present throughout the postoperative period. Patients who express fear about losing consciousness or the loss of control associated with general anesthesia may prefer regional techniques. Some patients have a strong desire to remain awake to view arthroscopic surgery as it is performed.

However, spinal or epidural anesthesia has potential disadvantages. There had been concern regarding the apparent increased incidence of PDPH in patients who ambulate postoperatively. Experience has shown that the incidence of PDPH is equal among patients who are nonambulatory and ambulatory, but that the onset may be delayed in patients who remain recumbent for a longer period of time. If spinal anesthesia is chosen, the use of conventional smaller gauge needles and newer designs (e.g., Greene, Sprotte, Whitacre) that include modifications at the tip appear to reduce markedly the incidence of PDPH. Pencil-point Greene, conical Sprotte, and side port Whitacre needles split rather than cut dural fibers, which may reduce cerebrospinal fluid leak and ameliorate PDPH. Reducing the incidence of PDPH to approximately 1%–2% or less would be an ideal goal. Technical failure rates of the various needles must also be figured into the overall equation.

Patients must be informed of the potential for PDPH because ambulatory patients expect to resume their normal activities shortly after surgery. Additional recommendations to reduce the incidence of headache include aligning the bevel edge of conventional needles parallel to the longitudinal axis of the body and the dural fibers. This represents an attempt to prevent cutting dural fibers and allows for separating them intact. Avoiding multiple dural punctures also is helpful. Maintenance of adequate hydration intraoperatively and postoperatively and avoidance of straining or lifting are recommended. Patients presenting with persistent PDPH may require an epidural blood patch for relief. It is especially important to follow up patients with a telephone call at 24–48 hours after surgery to inquire about the presence of any problems. Conservative treatment of PDPHs in ambulatory patients includes traditional mild analgesics, fluids, and bed rest. An epidural blood patch should be considered early if the headache is perceived by the patient to be extraordinarily severe or incapacitating or the patient must return to work immediately or care for children.

To avoid PDPH in younger patients, an epidural anesthetic may be offered if regional techniques are requested or medically indicated. Epidural anesthesia requires greater technical expertise and may be slightly more time-consuming to perform compared with spinal anesthesia. Insertion of a catheter into the epidural space allows additional incremental doses of anesthetic to be added if surgical time is unexpectedly lengthened. Additionally, shorter acting local anesthetics facilitate coordinating block recovery and procedure completion. However, the incidence of PDPH after unintended dural puncture with larger gauge epidural needles is significantly higher. The reported incidence of headache after general anesthesia in ambulatory patients exceeds the incidence of headache after regional anesthesia, although it is usually much less incapacitating and is self-limited. Postoperative headache is postulated to result from starvation and dehydration.

Spinal anesthesia provided by tetracaine and bupivacaine has been associated with PACU stays lasting 6–8 hours. This must be considered before performing regional anesthesia, especially if the procedure is performed later in the day. Another disadvantage of spinal anesthesia for ambulatory patients is the potential for persistent autonomic blockade lasting 1–2 hours after restoration of motor function. This autonomic blockade can result in inability to urinate and urinary bladder catheterization. Increasing duration of sympathetic blockade correlates with increased incidence of urinary retention.

### 16. What are the advantages and disadvantages of nerve block techniques for ambulatory surgery patients?

There are numerous advantages of nerve block techniques for surgery. They can provide profound analgesia into the postoperative period, which may allow early return home. However, rapid return to presurgical levels of mental alertness and acuity can be achieved only if judicious amounts of sedative drugs are administered during both performance of the block and surgery. Patients may experience a decreased incidence of nausea in the early postoperative period if smaller amounts of intravenous opioids are required or can be avoided entirely; this may also allow earlier alimentation and speedier return to normal functioning.

There are a few disadvantages to performing nerve blocks in patients undergoing ambulatory surgery. Preparation and performance of a block anesthetic may require more time than the induction of general anesthesia. In some instances, the performance of regional blocks and establishment of surgical anesthesia may take longer than the proposed operation. Brachial plexus and other nerve blocks have a known failure rate, and incomplete or inadequate anesthesia delays the onset of surgery further. Some patients cannot tolerate any sensation whatsoever and may require inordinately large amounts of sedative drugs throughout the procedure. Increased use of sedatives might easily negate some of the advantages of selecting a regional approach.

Patients who have not been seen by an anesthesiologist before the actual day of surgery and arrive with the expectation of receiving general anesthesia may be unprepared to accept another technique. The surgeon's preference also influences the receptiveness of patients to regional techniques. A surgeon who prefers the use of major conduction anesthesia or nerve blocks often informs patients of the benefits and availability of these techniques during preoperative discussions.

### 17. Describe the intravenous regional anesthetic technique (Bier block) for surgery on the extremities.

The intravenous regional anesthetic, Bier block, is an easily performed and extremely predictable method for providing anesthesia of the extremities. It is best reserved for procedures on the upper extremity below the elbow,

although it can provide anesthesia for surgery on the distal lower extremity as well. The technique of intravenous regional block requires little technical skill other than the placement of an additional intravenous catheter in the hand or foot of the extremity to be anesthetized. The block has a rapid onset, and the success rate approaches 100% in most hands. Only minor patient discomfort occurs during performance of the block. After the arm is exsanguinated by wrapping it in an Esmarch (elastic) bandage, a tourniquet is inflated to 100 mm Hg over systolic pressure, and the elastic bandage is then removed. Through the previously placed intravenous catheter, 50 mL of 0.5% preservative-free lidocaine is injected. Surgical anesthesia is achieved within approximately 10 minutes.

Because infused local anesthetic may enter the systemic circulation, anesthesiologists must remain vigilant for development of subtle central nervous system (CNS) changes. Frank seizures may occur if the tourniquet fails shortly after the drug is injected.

Usually, little or no intraoperative sedation or adjunctive analgesia is required. On release of the tourniquet, anesthesia rapidly dissipates. The Bier block is recommended when postoperative surgical pain is apt to be minimal. It is ideal for procedures such as ganglion cyst excision, trigger finger repair, removal of foreign bodies, and carpal tunnel release.

## 18. What sedatives can be administered to supplement a regional anesthetic?

The best anxiolytic may be a solid relationship between the anesthesiologist and patient. However, excellent rapport may be difficult to establish within the confines of a fast-paced ASC. It has been shown that a preoperative visit with the anesthesiologist immediately before surgery may serve as a powerful anxiolytic.

In the pharmacologic realm, intravenous midazolam provides excellent sedative and anxiolytic properties (Table 73-1). It is water-soluble, nonirritating to veins, painless on administration, provides superb amnesia with rapid onset, and well accepted by patients. Diazepam can cause significant discomfort on intravenous infusion as well as thrombophlebitis in a significant number of cases. Intravenous diazepam has been virtually eliminated from the practice of anesthesia. Midazolam has a much shorter elimination half-life of 1–4 hours compared with diazepam and provides a significantly shorter time to recovery. Midazolam is best titrated every 2 minutes in increments of 1–2 mg because its onset is rapid, and effects may be profound. Sedation after small to moderate intravenous doses usually lasts approximately 20–30 minutes. The profound amnestic properties may interfere with assimilating and following instructions. Some patients who receive midazolam become completely disoriented, uncooperative, or even combative. This situation may necessitate increasing the depth of sedation, pharmacologic reversal, or conversion to a general anesthetic.

Remifentanil is an excellent addition for a patient who requires a short-acting opioid either to provide analgesia during the performance of a painful block or to provide adjunctive analgesia during an inadequate block. It can be administered by intravenous bolus or by continuous infusion. Bolus doses of 0.5 μg/kg may be administered with repeat doses titrated to desired effect. For a continuous infusion, the dose ranges from 0.02–0.3 μg/kg/minute. Side effects common to all drugs in the opioid class include nausea, vomiting, and significant respiratory depression. Because remifentanil has no redistribution and is quickly eliminated by plasma esterases, it does not provide postoperative analgesia. Alternatively, fentanyl administered in intravenous bolus doses of 25–50 μg can be employed to provide adjunctive analgesia. In contrast to remifentanil, fentanyl provides postoperative analgesia because it is redistributed and has an elimination half-life of 180 minutes.

Propofol also can be used to provide sedation. It can be administered by either bolus dose (10–20 mg) or continuous infusion (0.05–0.1 mg/kg/minute) and titrated to the desired hypnotic effect. Inherent antinausea and antiemetic properties of propofol provide an advantage in the ambulatory setting.

## 19. What complications of nerve block anesthesia are of special concern to ambulatory surgery patients?

The potential for pneumothorax must be considered when performing supraclavicular, infraclavicular, and interscalene approaches to the brachial plexus. In this regard, the axillary approach is much safer. Pneumothorax may necessitate placement of a chest tube or prolonged observation. The occurrence of CNS toxicity ranging from tinnitus to frank seizures secondary to an intravascular injection during attempted block may lead to postponement or cancellation of the procedure. Intralipid solution should always be on hand to treat local anesthetic–induced cardiotoxicity.

## 20. Do all ambulatory surgery patients require tracheal intubation?

Whether ambulatory patients have increased gastric volumes compared with inpatients is questionable. The small incidence of documented aspiration among previously healthy individuals presenting for elective surgery does not indicate routine tracheal intubation for every patient. Tracheal intubation should be reserved for patients with known risk factors that predispose to aspiration. If the surgical procedure requires that the airway must be shared with the surgeon or if an airway cannot be easily or safely maintained using a supraglottic device, tracheal intubation should be performed.

The laryngeal mask airway (LMA), approved by the U.S. Food and Drug Administration (FDA) for use in 1991, has proved its value in both the inpatient and ambulatory surgery settings. It is presently manufactured in many sizes and is appropriate for adult patients as well as neonates. After induction of general anesthesia, the LMA is inserted blindly into the pharynx after the patient is placed into the sniffing position with extension of the head. Deep anesthesia is necessary for placement of the

device. After inflation of the cuff, formation of a low-pressure seal allows both positive pressure and spontaneous ventilation. After recovery of normal reflexes and when the patient is able to respond to commands and open the mouth, the device can be gently removed from the oral pharynx.

When properly placed, the LMA can free the anesthesiologist's hands for other tasks, including record keeping, monitoring adjustments, and other responsibilities. The incidence of sore throat after LMA use is less than that associated with tracheal intubation. Because muscle relaxants are not required for LMA insertion, postoperative myalgias associated with succinylcholine can be avoided. Additionally, ocular and oral trauma associated with conventional facemasks and oral airways may be avoided. Edentulous patients, characteristically more difficult to ventilate by facemask, can be managed well with this device. Because LMAs do not interfere with laryngeal function and glottic closure, an effective cough is possible with this airway in place.

Aspiration of gastric contents has been reported during LMA use. LMAs do not guarantee airway protection. Elective insertion of LMAs is contraindicated in patients who are at increased risk for aspiration. However, LMAs are indicated in urgent or emergent situations when airway management proves to be difficult. Contraindications include oral pathology, low pulmonary compliance, inadequate mouth opening, and increased risk of aspiration.

## 21. What is the role of propofol in ambulatory surgery?

Propofol may be used to provide sedation during regional anesthesia, to induce general anesthesia, and to maintain general anesthesia. Propofol is a water-insoluble, highly protein bound, lipophilic compound. It is rapidly redistributed, and hepatic and extrahepatic clearance (pulmonary) permit rapid recovery of cognitive function. It provides reduced postoperative sedation and drowsiness compared with traditionally employed ultrashort-acting barbiturates. Depressant effects on the CNS are dose dependent and range from mild sedation to unconsciousness. Neither retrograde nor antegrade amnesia is associated with this drug. For induction of anesthesia, propofol can be administered as a bolus dose (2–2.5 mg/kg slowly), and its effect can be maintained via continuous intravenous infusion (0.1–0.15 mg/kg/minute). Dosages are reduced in debilitated and elderly patients. For sedation during regional anesthesia, incremental doses of 10–20 mg (0.3 mg/kg) may be administered, or an infusion can be started. There is a known relationship between propofol serum drug levels and therapeutic effects. For propofol, the target concentration is 3–6 μg/mL to provide surgical anesthesia.

When administered as the sole agent, propofol may not provide amnesia 100% of the time, and intraoperative awareness has been reported. It is often used in conjunction with nitrous oxide, a volatile anesthetic, or midazolam. Propofol has no muscle relaxant or analgesic properties. For total intravenous anesthesia (TIVA), a continuous infusion of a short-acting opioid, such as remifentanil, can be administered along with an infusion of propofol. Additional bolus doses of propofol can be infused to deepen the level of anesthesia rapidly. Another major advantage of propofol appears to be a significantly diminished incidence of PONV. Propofol's inherent antiemetic properties allow earlier discharge of patients. When used for both induction and maintenance of anesthesia in cases lasting approximately 1 hour, faster recovery time is noted compared with a thiopental induction followed by maintenance with isoflurane and nitrous oxide. Patients anesthetized with propofol appear to awaken with a positive mood, and they regain equilibrium including the ability to ambulate early. The requirement for pain medication in the postoperative period appears to be reduced, which may be related to an overall feeling of well-being.

Two disadvantages of propofol include the lack of analgesic properties and pain on injection. Regarding the former, combining propofol with an opioid, such as remifentanil or fentanyl, provides analgesia. Discomfort associated with administration can be avoided by infusion into large veins and pretreatment with intravenous lidocaine. Injecting lidocaine, 10–25 mg intravenously, before administering propofol or adding lidocaine to the propofol solution ameliorates or eliminates the discomfort in most patients. Addition of lidocaine to propofol frequently produces clumping of the solution. There is concern that small clumps could act as pulmonary emboli.

Infectious hazards are associated with propofol use. Propofol is composed of soybean oil and egg lecithins, which serve as an excellent culture medium for bacterial growth. It is important to draw up the drug in an aseptic fashion shortly before it is administered. Additionally, it is imperative to discard the syringe after single patient use. Repeated use of the same syringe throughout the day for multiple patients has been associated with clusters of bacterial septicemia.

## 22. What is total intravenous anesthesia, and what are its advantages and disadvantages?

TIVA is a technique in which bolus doses or continuous infusions of intravenous anesthetic drugs are administered for induction and maintenance of anesthesia (Box 73-1). The various components of general anesthesia—hypnosis, amnesia, analgesia, muscle relaxation—can be provided individually and controlled by varying the rates of infusion, influencing serum concentrations. The depth of anesthesia can be controlled in a similar manner to dialing in desired concentrations on a vaporizer.

TIVA avoids the use of all gases with the exception of oxygen, compressed air, or helium. Contamination of the operating room suite that invariably occurs when using volatile agents, despite the use of scavenger systems, may be eliminated entirely. Because nonflammable gases may be employed, the technique is applicable to laser surgery. For procedures on the upper airway, TIVA is perfect for use with jet ventilation. Additionally, intravenous anesthesia does not depend on normal pulmonary function for wash-in or washout of active agents.

**BOX 73-1 Administration of Total Intravenous Anesthesia**

Infuse drugs into intravenous line as close to catheter as possible
No nitrous oxide or volatile anesthetic agents
Recommended continuous drug infusions
- Propofol alone
  - Induction dose: 2.0–2.5 mg/kg
  - Maintenance dose: 0.5–2.0 mg/kg/minute continuous infusion
    - In a 70-kg patient, the infusion rate is approximately the same as the percent isoflurane that would be used
  - As the sole agent does not provide reliable amnesia, and awareness is possible
- Propofol plus adjuvants
  - Propofol + tranquilizer (midazolam) + opioid (either remifentanil or fentanyl)
  - If patient movement during surgery is undesirable, addition of a muscle relaxant is indicated
  - For signs of light anesthesia (hypertension, tachycardia, sweating, tearing, or movement)
    - Increase infusion rate of propofol, not opioid *or*
    - Administer propofol bolus: 10–40 mg
  - If blood pressure or heart rate difficult to control within dosage guidelines
    - Addition of a β-adrenergic blocker (esmolol or labetalol) or vasodilator is recommended
    - Consider use of a depth of anesthesia monitor
- Turn off opioid infusion before anticipated end of procedure*

Turn off propofol before anticipated end of procedure*

*Cessation of infusions is based on context-sensitive half-time of each drug.

Refinement of computer-assisted infusion systems allows anesthesiologists to achieve therapeutic blood concentrations of various anesthetic and sedative drugs. Episodes of "light" anesthesia can be treated with bolus doses or increased infusion rates. Additional benefits include rapid awakening at the conclusion of surgery and reduced PONV in patients who receive propofol.

Because few facilities are equipped to measure blood concentration of intravenous anesthetics, a potential disadvantage of TIVA includes awareness during surgery. Alternatively, processed electroencephalography (EEG) is used to judge depth of CNS depression. The reliability of EEG is controversial. Each monitor uses a proprietary algorithm to analyze EEG data creating a linear score of 0–100. A score of 0 usually denotes complete EEG suppression, whereas a score of 100 usually correlates with the awake unsedated state. Each monitor has its own range of numbers that correlate with depth of anesthesia. These monitors are of questionable value.

Traditionally, when a patient became hypertensive or tachycardic intraoperatively, anesthesiologists would usually deepen the anesthetic. However, this change in vital signs can be attributed to several causes. The most common of these causes are "light" anesthesia, pain, and essential hypertension. Increased heart rate and elevated blood pressure that are concomitant with a higher CNS monitor score are most likely due to "light" anesthesia. The appropriate response would be to deepen the anesthesia with a bolus of propofol. If the monitor score remains within the range for general anesthesia, the response to increased heart rate and elevated blood pressure would be to give an opioid for pain. The choice of opioid would be either an ultra-short-acting opioid (e.g., remifentanil) for a short-lived painful stimulus (e.g., esophagoscopy) or a longer acting opioid (e.g., fentanyl) for a persistent painful stimulus (e.g., incision).

Whether or not it is cost-effective to use CNS monitors on all patients has been heatedly debated in the anesthesia community.

### 23. Define the term "moderate sedation"; when is it used, and what advantages does it offer over general anesthesia?

Moderate sedation, previously known as conscious sedation, is a state of decreased consciousness, airway patency, intact gag reflexes, and ability to respond to verbal instructions. When properly executed, moderate sedation provides anxiolysis, amnesia, safety, and comfort. Moderate sedation is a valuable adjunct to properly placed local anesthetic or regional anesthetic. Because interference with short-term memory occurs, the patient experiences a markedly distorted perception of time. The anesthesiologist can increase a patient's tolerance and acceptance of the discomforts associated with an ongoing procedure by providing encouragement and a sense of well-being and security. The goal is to allow the patient, anesthesiologist, and surgeon to communicate throughout the operative procedure.

Moderate sedation is achieved by titration of intravenous agents administered by intermittent bolus injection or continuous infusion. Because moderate sedation is part of a continuum, it is possible for moderate sedation to progress to deep sedation or even general anesthesia. Propofol, midazolam, and remifentanil have pharmacokinetic properties that achieve these goals. These characteristics include rapid onset, easy titration, and a relatively short duration of action, which allow for early recovery. Benzodiazepines and opioids are combined frequently. This combination predisposes to respiratory depression including apnea. Hypoxemia or apneic episodes have been demonstrated frequently when benzodiazepines and opioids are used together compared with either drug used alone. Supplemental oxygen should be provided via mask or nasal cannula, and respiration should be carefully monitored.

Present standards of care require monitoring heart rate, blood pressure, respirations (via end-tidal carbon dioxide), oxygen saturation, temperature, and ECG. Nasal cannulas are now available with a separate tube

that can be attached to the sampling probe from a capnograph, allowing for end-tidal carbon dioxide monitoring. This monitoring is particularly useful during procedures where the anesthesiologist may be physically separated from the airway.

Although a patient may appear awake and fully recovered at the end of surgery using this technique, vigilance for respiratory depression must be maintained throughout the postoperative period. In the PACU, hypercarbia or respiratory arrest may occur if the patient is left unstimulated.

### 24. Can succinylcholine myalgias be avoided?

Disadvantages of succinylcholine include postoperative myalgias and the potential for malignant hyperthermia. Myalgias, which occur five times more commonly after ambulatory surgery than after inpatient procedures, sometimes may far outlast the discomforts associated with surgery. Muscle pains may vary in intensity from mild to incapacitating and often develop on the first postoperative day. There is no guaranteed way to eliminate the succinylcholine myalgias. However, pretreatment with 1 mg of a nondepolarizing neuromuscular blocker, such as vecuronium, may ameliorate fasciculations and associated myalgias.

### 25. Can a relative overdose of benzodiazepine be safely treated with an antagonist?

Flumazenil is an intravenously administered competitive benzodiazepine receptor antagonist at specific benzodiazepine binding sites in the CNS. It can be titrated to obtain the desired degree of benzodiazepine antagonism as evidenced by patient arousal. Midazolam has varying effects at different dosages. At small doses, it is anxiolytic. Increasing the dose administered increases the amount of sedation encountered. Larger doses induce hypnosis (sleep). Careful titration of flumazenil may allow partial antagonism of excessive benzodiazepine effect.

When contemplating the use of any reversal agent in the setting of ambulatory surgery, it is important to remember that the duration of action of both flumazenil and naloxone (to reverse opioids) is short-lived. Additional patient observation before PACU discharge is required whenever these agents have been administered.

### 26. Do newer volatile agents offer advantages over older agents?

Two volatile anesthetic agents, desflurane and sevoflurane, both ethers, have been extensively used in clinical practice. Desflurane is a clear nonflammable liquid that is extremely insoluble and requires a specially designed, heated vaporizer for administration. The gas has an odor and is an airway irritant. It can produce coughing, breath-holding, and laryngospasm; its use as an inhalation induction agent is precluded. Its major advantage is low blood and tissue solubility, which allows for fast emergence compared with currently available volatile agents. Low solubility properties also allow rapid titration of anesthetic depth.

Although desflurane and isoflurane have similar muscle relaxing properties, higher levels of desflurane can be administered without concern about delayed emergence. Times to ambulation and discharge with desflurane are similar to propofol, although patients anesthetized with desflurane appear to be less sedated in the early postoperative period. However, nausea and vomiting were less frequent with propofol.

Sevoflurane is odorless. It does not predispose to coughing and breath-holding on rapid inhalation induction. Its solubility in blood approaches that of nitrous oxide. Fires have been reported when sevoflurane is used in the presence of desiccated soda lime. Both sevoflurane and desflurane can provide sufficient muscle relaxation to allow tracheal intubation. Both can trigger malignant hyperthermia.

### 27. What are the etiologies of nausea and vomiting, and what measures can be taken to decrease the incidence and severity of nausea and vomiting?

PONV remains a significant problem in patients who receive either general anesthesia or intravenous sedation. PONV is among the most commonly reported complications associated with ambulatory surgery, and hospitalization following an ambulatory procedure is often attributable to it. Persistent and severe retching or vomiting can disrupt surgical repairs and increase bleeding. PONV can lead to dehydration and electrolyte imbalances. Some degree of nausea or frank vomiting can be expected to occur in 10%–40% of patients who have not received antiemetic prophylaxis. The incidence of PONV depends on the type of surgical procedure performed and the anesthetic administered. It has been demonstrated that patients undergoing laparoscopy have a 35% incidence of nausea and vomiting; manipulation of abdominal viscera, retained intraperitoneal carbon dioxide, and use of electrocautery are potential causes. Symptoms occur regardless of whether a general anesthetic or epidural technique is employed. Arthroscopic surgical procedures are associated with a much lower incidence of symptoms than laparoscopic surgeries or ovum retrievals.

The cause of PONV is multifactorial (Box 73-2). Obesity, sudden movement or changes in patient position, history of motion sickness, postoperative hypotension, female gender, days 4 and 5 of the menstrual cycle, pain, opioid administration, anesthetic technique used, and site of surgery all contribute to these symptoms. They are often disquieting and sometimes incapacitating. Physical measures and pharmacologic agents have been employed in attempts to reduce the incidence of PONV. Examples include intraoperative gastric suctioning to remove stomach contents and limiting positive pressure during mask ventilation to reduce the potential for gastric dilation.

Multiple studies have both implicated and exonerated nitrous oxide. It is unlikely that this gas plays a major role in influencing the presence or absence of nausea in the postoperative period. However, induction agents do influence the incidence of postoperative symptoms. Etomidate and ketamine are associated with a much higher incidence of these symptoms compared with thiopental. General anesthesia

**BOX 73-2 Factors Associated with Postoperative Nausea and Vomiting**

**Associated Conditions**

- Obesity
- Pregnancy
- History of motion sickness
- History of previous postoperative vomiting
- Recent ingestion of food
- Anxiety
- Female gender
- Day 4–5 of menstrual cycle
- Diabetes mellitus
- Age (uncommon <3 years of age)

**Surgical Procedure**

- Strabismus correction
- Laparoscopy
- Dilation and curettage
- Orchiopexy
- Varicocelectomy
- Ear surgery

**Anesthesia-Related**

- Etomidate and ketamine > thiobarbiturates > propofol
- Opioid/$N_2O$/relaxant > than volatile anesthetic > propofol
- Intraoperative and postoperative opioids
- Positive-pressure mask ventilation forcing air into the gastrointestinal tract
- Anticholinesterases

**Miscellaneous**

- Blood entering gastrointestinal tract during surgery
- Uncontrolled pain
- Rapid changes in positioning or during rapid transport on stretcher
- Early ambulation and oral intake
- Systemic hypotension
- Vasovagal episode

$N_2O$, Nitrous oxide.

induced and maintained with propofol is associated with the least number of episodes of PONV.

Adequate hydration must be ensured during the operative period and maintained in the PACU. To avoid episodes of PONV, it is recommended to hydrate intraoperatively with at least 15–20 mL/kg of crystalloid solutions and to avoid pushing oral fluids and food postoperatively. Intravenous fluid repletion allows oral fluids to be offered sparingly. Solids should be withheld until the patient expresses hunger. In addition, postponing early ambulation may help to reduce symptoms.

Many drugs are helpful in the prevention of PONV (Table 73-2). Most authors recommend treating patients with a multimodal approach. This would require using different drugs from different pharmacologic groups. Popular drugs in the anesthesiologist's armamentarium against PONV are the serotonin receptor antagonists, ondansetron and granisetron. They do not appear to affect awakening from general anesthesia and have no extrapyramidal effects or sedative qualities. Ondansetron appears to offer improved control over nausea and vomiting. The effective dose is 2–4 mg intravenously and has a duration of action of up to 24 hours. The intravenous

TABLE 73-2 **Prophylaxis and Treatment of Postoperative Nausea and Vomiting**

| Class and Drug | Dosage and Route of Administration |
|---|---|
| Droperidol | 0.0625-0.125 mg IV |
| Phenothiazines<br>Prochlorperazine | 5–10 mg/70 kg IV/IM |
| Steroid<br>Dexamethasone | 4–10 mg IV in adults<br>150 μg/kg |
| Serotonin antagonists<br>Ondansetron | 1–4 mg/40–80 kg IV in adults;<br>0.1 mg/kg in children |
| Sympathomimetics<br>Ephedrine | 10–25 mg/70 kg IV/IM |
| Anticholinergics<br>Scopolamine patch | Releases 1.5 mg over<br>3 days transdermally |

*IM,* Intramuscularly; *IV,* intravenously.

form is approved by the FDA for prophylaxis and treatment of PONV associated with general anesthesia. An oral formulation is also available. It has been demonstrated that a combination of agents, perhaps in conjunction with propofol, may be most efficacious in the prophylaxis of PONV. Prophylactic administration of dexamethasone, 4–10 mg intravenously, at the beginning of the procedure in conjunction with ondansetron has also been shown to be efficacious in preventing PONV.

Droperidol has long been used as an antiemetic. Its use fell out of favor after a "black box" warning from the FDA was issued. Concern arose over the potential for arrhythmias in patients with prolonged QT intervals. However, it can still be used as long as continuous ECG monitoring is employed.

Transdermal scopolamine, proven earlier to prevent motion sickness, has been studied for the prevention of PONV. Although effective in reducing symptoms when applied before surgery, significant side effects, including dry mouth, sedation, dysphoria, and urinary retention, may occur. It is often reserved for preoperative use in patients who have a strong history of motion sickness. In pediatric patients, the incidence of visual disturbances and hallucinations after application of the patch is increased. Some clinicians have placed the patch before PACU discharge in patients whose nausea has not completely resolved. However, the patch should be avoided in elderly patients, pregnant patients, patients who are lactating, and patients with glaucoma.

Ephedrine has been used in the treatment of PONV in the PACU. Hypotension or documented postural hypotension in the postoperative period is often due to intravascular volume deficits and should be ruled out. Treatment consists of crystalloid infusion to correct hemodynamic instability. Ephedrine has been shown to be useful in patients whose symptoms are causally related to assuming the upright position. Ephedrine, 0.5 mg/kg given intramuscularly, has been used in patients undergoing laparoscopy with some success. Patients who received ephedrine also had lower sedation scores, and no

differences in mean arterial blood pressure were noted. It may be indicated in otherwise healthy patients who have a history of motion sickness or in patients who experience dizziness, nausea, or vomiting when attempting to ambulate in the postoperative period.

Many surgical centers have abandoned the routine administration of prophylactic antiemetics to every patient. However, the authors recommend antiemetics for specific surgical procedures, such as strabismus repair or laparoscopic surgery, that are associated with high incidences of PONV.

Sometimes simply relieving postoperative pain may alleviate nausea. The use of acupuncture has been reported in some studies to be effective, but its use is not widespread. A propofol-based anesthetic is associated with fewer emetic symptoms, earlier ability to tolerate oral alimentation, and shorter stays in the PACU compared with induction with a thiobarbiturate and maintenance with isoflurane. Despite careful anesthetic management including propofol and prophylactic medication, PONV still remains a problem.

## 28. How is postoperative pain best controlled in ambulatory surgery patients?

Management of postoperative pain in the PACU and after discharge is of major concern to the anesthesiologist. One important goal is to achieve adequate pain relief before discharge. Prevention of postoperative pain appears to be much easier to accomplish than treatment of pain that has been allowed to reach significant intensity. Inadequate postoperative analgesia remains a cause of unexpected overnight hospitalization.

For procedures that are expected to result in significant postoperative discomfort, addition of an opioid or a nonsteroidal antiinflammatory drug (NSAID), or both, as part of the anesthetic is helpful. Propofol does not provide postoperative analgesia. Intraoperative administration of long-acting local anesthetics, such as bupivacaine or ropivacaine, at the surgical site may provide hours of postoperative pain relief. This technique has proven to be most efficacious after inguinal and umbilical hernia repairs.

In the PACU, careful titration of small intravenous doses of opioids can safely provide satisfactory analgesia. Blood levels of opioids that provide analgesia are less than the levels that usually result in significant respiratory depression or marked oversedation. Fentanyl is the narcotic of choice for treating pain in the postoperative period. Its duration of action is modest, and intravenous doses of 25–50 μg may be repeated every 5 minutes until satisfactory pain relief has been achieved. Medicating patients with oral opioid preparations before discharge provides a more comfortable trip home because the intravenous drugs administered in the PACU have relatively short durations of action.

Home patient-controlled analgesia systems permit discharging patients who are expected to experience pain that may not be sufficiently controlled with oral agents. Experiments with patient-controlled analgesia in the home have found this modality to be both safe and effective. Oxycodone and codeine are suitable for amelioration of mild to moderate pain but are not strong enough to prevent hospitalization in a patient who experiences severe pain.

Ketorolac, a NSAID, has been administered orally, intramuscularly, and intravenously in an attempt to prevent and relieve pain and reduce opioid requirements. The drug itself is free of opioid-related side effects, including sedation, respiratory depression, and vomiting. Some clinicians are hesitant to employ this class of drugs because of their potential for bleeding. When administered orally, gastric irritation may be encountered. Cyclooxygenase-2 inhibitors minimize the potential for postoperative bleeding and the risk of gastrointestinal complications and are becoming popular as a nonopioid adjuvant for treating postoperative pain.

## 29. What discharge criteria must be met before a patient may leave the ambulatory surgery center?

Patients who have received a peripheral nerve block (e.g., ankle block, brachial plexus block) may be discharged despite the persistence of residual anesthesia or paresthesias. The effected limb should be protected from harm with either a sling, in the case of an upper extremity, or a bulky dressing, in the case of a lower extremity. The patient needs to be reminded that the block will dissipate in time, and discomfort will occur. For this reason, discharge instructions should include recommendations to take the prescribed oral analgesic medication at the first sign of discomfort because pain is most readily treated before it becomes excruciating.

Patients who received an epidural or spinal anesthetic can be discharged only when full motor, sensory, and sympathetic function has returned. Patients should demonstrate the ability to void because this provides evidence that residual sympathetic blockade has dissipated. Before attempting to ambulate, it is essential to ensure that all motor block has resolved.

Patients who have received general anesthesia may awaken either in the operating room or shortly after transfer to the PACU. Although the patient may appear to be lucid and oriented, numerous criteria must be satisfied before a patient may be considered ready for discharge from the facility (Box 73-3). Restoration of vital signs within 15%–20% of the preoperative baseline is ordinarily required. Patients should demonstrate an intact gag reflex and the ability to cough effectively and swallow liquids without difficulty. It is not necessary for patients to eat before discharge. Forcing patients to ingest unwanted food in the absence of hunger may serve to increase the incidence of PONV. Patients ordinarily are asked to demonstrate the ability to tolerate a small amount of liquid by mouth. If a patient experiences mild nausea and has been unable to ingest more than a few sips without vomiting or increased nausea, it is foolish to persist. Discharge can still be considered if there is continued inability to tolerate fluids, if written instructions are provided regarding steps to be taken (e.g., contact facility or surgeon). It is important to ensure that a normal state of hydration has been achieved before discharge; this is especially important after surgery in the oral cavity, where postoperative pain may preclude early oral intake.

Unless the patient was previously unable to walk or the procedure performed precludes ambulation, patients

**BOX 73-3 Guidelines for Safe Discharge after Same-Day Surgery**

Stable vital signs every 15 minutes × 4
Oriented to time, place, and person (or returned to preoperative status)
Capable of walking with minimal assistance (consider preoperative status)
Tolerable nausea and no active vomiting
Adequate pain control
Good hemostasis
Responsible adult present to accompany patient home
Able to tolerate oral fluids (optional)
Able to void
  After gynecologic, genitourinary, groin, and perineal procedures
  After epidural and spinal anesthetics

**BOX 73-4 Functions of the Escort in Ambulatory Surgery**

Provide translation when patient speaks a foreign language
Receive and comprehend postoperative instructions
Accompany patient during transport home
Serve as companion to patient during the first 24 hours after completion of surgery and assist in performing activities of daily living
Remain available to summon assistance in the event of a medical, surgical, or anesthetic complication

should be able to walk with assistance and without experiencing dizziness. If crutches are required, it should not be assumed that the patient received preoperative instruction and additional instruction should be offered. Hemostasis should be present at the surgical site, and control of pain should be satisfactory. The preoperative level of orientation should be achieved, although a mild degree of residual sedation is acceptable.

It is not essential for patients to urinate, unless genitourinary, gynecologic, or other surgery has been performed in the inguinal or perineal region. Patients and escorts should be instructed to contact either the ambulatory facility or the surgeon if the patient has not voided within 6 hours after PACU discharge.

Validated postanesthesia discharge scoring systems have been proposed and developed for the purpose of assessing when home readiness is achieved in the postoperative period. Criteria such as mental status, pain intensity, ability to ambulate, and stability of vital signs are given numeric values. A total score above a particular number may indicate a high likelihood of readiness for discharge. To be practical, a scoring system must be easily understood, simple to employ, and objective. Sophisticated pen-and-paper and neuropsychological tests to assess recovery from anesthesia are reserved solely for research purposes. After stability in vital signs is achieved, the ability to walk and urinate may be the best measures of a gross recovery from anesthesia and readiness for discharge. These activities indicate return of motor strength, CNS functioning, and restoration of sympathetic tone.

Patients and escorts should receive detailed, written discharge instructions regarding activity, medications, dressing care, and bathing restrictions. Instructions must be reviewed verbally with patients and escorts. Both must be advised to contact the facility in the event of untoward reactions or difficulties, such as bleeding, headache, severe pain, or unrelenting nausea and vomiting. Most postoperative complications occur after discharge. It is important to ensure comprehension of all information by the patient or designated escort (Box 73-4).

Most states mandate that patients who received other than a local anesthetic be discharged in the company of a responsible adult. Current definitions of "responsible adult" vary and may be broadened to include emancipated minors or responsible older children. Ideally, companions should remain with patients for at least 24 hours after surgery; this is especially important in the case of geriatric and debilitated patients. Problems may arise when impaired patients are discharged in the company of impaired escorts. Preferably, two adults should accompany pediatric patients home. After discharge, a child may suddenly experience nausea, vomiting, pain, fright, or disorientation. An escort who is driving a car cannot possibly pay attention to both child and traffic simultaneously.

A clear distinction is made between "home readiness" and "street fitness." "Home readiness" signals that the time has arrived to discharge the patient from the PACU. "Street fitness" is attained after approximately 24 hours have elapsed, when most of the more subtle and persistent CNS effects of general anesthesia have dissipated. Patients must be advised not to resume normal activities immediately on returning home.

Formal discharge criteria must be in place, and final evaluations should be conducted immediately before a patient's discharge from the PACU. All perturbations from normal, including vital signs and unusual symptoms, can be addressed.

Every attempt must be made to avoid premature discharge of the patient from the PACU. The consequences of such faulty judgments may include the necessity for emergency care elsewhere and possible readmission to another health care facility. When any element of doubt exists as to the stability or suitability of a patient for discharge, the better part of valor is to arrange for hospital admission for overnight observation.

### 30. What are the causes of unexpected hospitalization after ambulatory surgery?

Although a patient may be scheduled to return home after surgery, admission may be required for a host of reasons. Approximately one quarter of unexpected admissions after surgery are anesthesia related. The remainder result from either medical or surgical complicating factors (Box 73-5). Most ASCs experience an unexpected hospital admission rate ranging from <1% to approximately 4%. Unexpected hospitalization is greater after general anesthesia than after local

**BOX 73-5 Reasons for Hospitalization after Ambulatory Surgery**

**Surgical Causes**

- Improper designation as ambulatory surgery instead of day-of-admission surgery
- Surgery extended beyond anticipated procedure
- Surgical complication necessitating return to surgery or further observation
- Major intraoperative or postoperative hemorrhage
- Additional follow-up surgical or diagnostic procedure planned

**Medical Reasons**

- Poorly controlled concomitant medical condition
- Requirement for intravenous antibiotic therapy

**Anesthesia-Related**

- Unrelenting nausea or vomiting
- Aspiration pneumonitis
- Lethargy and lassitude
- Uncontrollable pain

**Miscellaneous Factors**

- Patient refuses to leave for home
- Surgeon requests overnight observation or additional tests
- No escort or suitable person to care for patient at home

or regional anesthesia. As might be anticipated, the addition of intravenous sedation to a local anesthetic increases the complication rate. Nausea, vomiting, dizziness, bronchospasm, and delayed emergence from anesthesia are common causes of anesthesia-related hospital admissions.

## 31. When may patients operate a motor vehicle after receiving general anesthesia?

Current recommendations are to refrain from operating heavy machinery including driving a car for approximately 24–48 hours after general anesthesia or intravenous sedation. Although a patient may feel completely recovered and appear that way to others, subtle psychomotor disturbances and cognitive deficiencies may persist postoperatively. Important decision making and activities requiring fine motor coordination should be postponed until after the first postoperative day. Despite admonitions to the contrary, surveys have revealed that some patients drive their automobiles within 24 hours after surgery, and some may even drive home from the facility.

As a result of CNS derangements or the surgery itself, patients may experience minor slips or even major falls after discharge. Some of these events could be related to confusion or subtle alterations in mental state. Others may be due to dizziness or pain. It is hoped that anesthetic agents of the future will be free of the prolonged and potentially hazardous CNS dysfunction seen with currently available drugs.

## 32. What is the role of aftercare centers for ambulatory surgery patients?

Patients may experience significant postoperative pain after some surgical procedures that cannot be readily controlled with oral opioids. Additionally, although they may require some skilled nursing observation or specialized care, these may be accomplished outside the setting of an acute care hospital both at lower cost and with greater comfort for the patient and family. With this in mind, the concept of a recovery care facility was born, creating a new category of inpatient postsurgical care. This health care model integrates ambulatory surgery with overnight or extended care outside of a hospital. Examples of applicable procedures include hysterectomy, cholecystectomy via laparotomy, shoulder repairs, and mastectomies. If this type of facility is unavailable, appropriate use of home care services including newer modalities of pain control may still allow patients to avoid inpatient postoperative care.

## 33. Are quality assurance and continuous quality improvement possible for ambulatory surgery?

To ensure quality as well as patient satisfaction, follow-up telephone calls by an anesthesia care team member should be made on the first postoperative day. Some facilities make two additional calls, one on the evening of surgery and another call 1 week after surgery. Postage-paid postcards may be sent to patients requesting information on the overall experience and specific areas of care. Space may be allocated for the patient to note side effects or adverse occurrences. Depending on surgeons to provide accurate feedback regarding complications is unreliable. A mechanism for follow-up must be in place to uncover and identify patterns that require remedial action.

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CASE 74

# Office-Based Anesthesia

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## QUESTIONS

1. What is office-based anesthesia?
2. What are the advantages and disadvantages of office-based anesthesia?
3. Discuss the important issues for consideration when setting up a safe office-based practice.
4. In what ways is morbid obesity a challenge to an office-based anesthesiologist?
5. What anesthetic techniques are appropriate to use in an office-based practice?

A 25-year-old woman presents for liposuction of the abdomen, thighs, hips, flanks, and back in the surgeon's office. She stands 62 inches (167 cm) tall and weighs 176 lb (80 kg). She denies any medical problems but reports snoring at night. Her only medication is an oral contraceptive, and she has not had any previous surgery. Anesthetic evaluation reveals an obese woman with a Mallampati class 3 airway.

### 1. What is office-based anesthesia?

Office-based anesthesia (OBA) is defined as the "provision of anesthesia services in an operatory or a procedure room that is specifically not licensed as an ambulatory surgery center (ASC) by the state in which it operates and which is integrated into the day to day operations of a doctor's office" (Koch et al. 2003). Historically, one of the earliest references to OBA dates back more than a century ago, when Long used ether to anesthetize his patient successfully to remove a neck tumor. Since then, the practice of OBA has changed dramatically. More recent advances in surgical technology and equipment, along with improved anesthetic techniques and drugs have made this venue appropriate for a very wide array of surgeries and procedures previously suitable only for hospitals or ASCs. It is estimated that 10 million procedures are performed in offices annually. Although many surgical specialties presently use this unique venue, cosmetic surgery in particular has seen a tremendous increase in volume. According to the American Society of Plastic Surgeons, 37% of cosmetic procedures and 28% of reconstructive procedures are performed in the office-based setting.

### 2. What are the advantages and disadvantages of office-based anesthesia?

OBA continues to increase in popularity for numerous reasons. Surgical and anesthesia techniques and available pharmaceuticals continue to improve. These advances have allowed for more complex and minimally invasive procedures to be performed safely and effectively in this setting.

There are unique advantages for surgeons and proceduralists and patients in this type of practice. Economically, it is advantageous because the cost is significantly less compared with the hospital setting. This difference in cost is mainly due to the high overhead costs associated with hospital facility fees, which include hospital maintenance, equipment, and staff, all of which constitutes a large component of the patient's overall procedure fee. In the office, this fee can be easily predicted and is often minimal compared with the hospital or an ASC. The cost savings can be passed on to the patient. In the interest of cost containment, insurance companies began offering incentives to surgeons to use their office locations. This venue also allows for greater surgeon and patient satisfaction. Scheduling is much easier in the office setting. For surgeons, an office-based practice can eliminate much of the unproductive time associated with long operating room turnovers, patient preparation, and driving between sites. Office-based surgery allows surgeons to perform nonsurgical duties such as patient consultations and follow-up examinations more easily.

For patients, office-based surgery is an attractive and convenient alternative to hospitals. It offers patients a more private and less stressful environment. There is better continuity of care because staffing in the office is more consistent. Exposure to nosocomial infections is also diminished.

However, there are numerous potential disadvantages to OBA. Office-based practices were once labeled as the "wild, wild, west of health care," with issues regarding standard of care and patient safety in the office-based practice not always being met. Most OBA practices have little or no oversight by local, state, or federal governments regarding certification and qualification of either surgeons or anesthesiologists, peer review, performance improvement, documentation, general policies and procedures, and reporting of adverse outcomes. At the present time, many states have placed regulations on office-based practices. However, these regulations vary

from state to state. Other states are steadily moving forward and have issued guidelines or policy statements. Because of anesthesiologists' role as patient safety advocates, it is incumbent on them to insist that the standard of care achieved in hospitals or ASCs is the same in every office in which surgery and anesthesia are performed. Health care providers who wish to practice in this setting should take advantage of the office-based surgery patient safety guidelines and recommendations published by a variety of professional societies and accrediting organizations. The American Society of Anesthesiologists (ASA) created "Guidelines for Office-Based Anesthesia," last affirmed on October 2009.

Another disadvantage of office-based practice is the limited resources available. Resources often taken for granted in the hospital, such as immediate availability of colleagues, other skilled nurses, laboratory services, and specialized equipment, are sparse or nonexistent. It is of utmost importance that we ensure that the standards of practice in the office, whether it is accredited or not, meet those of the hospital or ASC to provide patients with a safe office environment.

### 3. Discuss the important issues for consideration when setting up a safe office-based practice.

There is only one way to practice medicine, and that is the *safe* way. In office-based practice, where surgeries and procedures are performed in an elective manner, patient safety must never be compromised. Considerable consumer and physician pressures come into play in this setting. It is of utmost importance that anesthesiologists do not succumb to these pressures. We must always make sure that the standard of care in an office practice is no less than that of a hospital or ASC. Our level of vigilance should even be heightened in this venue because we are often alone, and resources we take for granted are limited.

There are many elements that need to be carefully considered for an office-based practice. Diligent and careful assessment of the physician or proceduralist, the physical office space, the patient's comorbidities, and the anticipated procedure is paramount. The ASA formulated "Guidelines for Non-Operating Room Anesthetizing Locations," "Guidelines for Office-Based Anesthesia," and "Considerations for the Anesthesiologist in the Office-Based Settings," which should be referred to by practitioners who are considering office-based practice for guidance.

#### *Physician*

The surgeon or proceduralist (e.g., gastroenterologist) must have the necessary and updated licensing and credentialing information, such as medical license, registration, and Drug Enforcement Agency certificate. The physician must be adequately trained, and board certification or eligibility by the American Board of Medical Specialties is preferable. The physician should have privileges to perform the proposed procedure in a hospital or have training and documented competency. The physician should participate in peer and quality review and continuing medical education. In addition, the physician must have admitting privileges and an emergency transfer agreement with a nearby hospital. The facility and the physician must also have adequate liability insurance.

#### *Office*

The office must be a safe location no matter where it is. As previously stated, the standard of care in the office should be no less than that of a hospital or ASC. The office must be appropriately stocked with age-appropriate and size-appropriate equipment and supplies. All equipment must be regularly serviced and calibrated with documentation according to manufacturers' suggestions. There must be a functioning waste gas scavenging system if inhaled agents or nitrous oxide are used. An adequate supply of compressed oxygen and backup supply for use in an emergency must be present. ASA standards for basic anesthetic monitoring must be implemented. These include electrocardiography, noninvasive blood pressure, pulse oximetry, end-tidal carbon dioxide monitoring, and temperature monitoring. Monitors must be routinely serviced and should have backup battery supply. All advanced cardiopulmonary life support emergency drugs should be available, including dantrolene if malignant hyperthermia triggering agents are used. A cardiac defibrillator with a battery backup must be immediately available, visible, and routinely checked. A source of suction, including a pharyngeal catheter, must be present.

Administrative issues, such as facility and personnel credentialing, development of policy and procedures manual, performance improvement, emergency and infection control protocols, and documentation, should be addressed as well.

#### *Patient*

Appropriate patient selection is a very important aspect of safe OBA. Patient selection is controversial among office-based practitioners because there are very few data to support the inclusion or exclusion of specific patient populations. The ASA "Guidelines for Office-Based Anesthesia" reads, "Patient who by reason of pre-existing medical or other conditions may be at undue risk for complications should be referred to an appropriate facility for performance of the procedure and the administration of anesthesia" (American Society of Anesthesiologists, www.asahq.org) This statement leaves much room for interpretation. The anesthesiologist must evaluate the patient's risk for OBA on an individual basis.

Determination of a patient's suitability for OBA begins with a thorough preoperative history and physical examination. Coexisting medical conditions that could potentially complicate the surgical procedure and anesthetic management must be identified. Whoever examines the patient preoperatively should be familiar with the ASA physical status classifications and implications. The American Society of Plastic Surgeons (ASPS) and ASA have made similar recommendations that patients who are assigned an ASA

physical status I or II are "reasonable candidates for the office-based surgery setting." The ASPS recommends that ASA physical status III patients "may also be reasonable candidates for office-based surgery facilities when local anesthesia, with or without sedation," is used. However, the ASA recommends that patients should be evaluated by the anesthesiologist before the day of surgery to determine their suitability for office-based surgery and anesthesia. It is imperative to consider all comorbidities when determining patient suitability. There must be clear communication between the surgeon and the anesthesia provider regarding this matter. The anesthesia provider must not succumb to physician and patient demands. The decision regarding the patient's clearance for anesthesia ultimately depends on the anesthesiologist. The ASA has also provided a list of specific patient factors that should be taken into consideration before performing OBA. These factors include the following:

- Known or suspected difficult airway
- Previous anesthetic or surgical problem
- Drug allergies that are of perioperative concern
- Substance abuse disorders including alcoholism
- Social situation that precludes having a responsible adult escort

Box 74-1 lists patients that may be excluded from OBA.

### *Procedure*

A wide array of surgeries and procedures are performed in the office-based setting. As newer surgical techniques and equipment have evolved, longer and more invasive operations are being performed successfully in the office. Suitable office-based surgeries range from simple incisional biopsies to minilaparoscopies (Box 74-2). The anesthesiologist should be medically comfortable and satisfied that the procedure to be performed is within the scope of the practice of the surgeon and the capabilities of the office.

As with patient selection, there is also very little, if any, conclusive scientific data to exclude specific procedures from this venue. Duration of procedure has long been correlated with the need for hospital admission. Longer procedures and longer anesthetic times are often associated with postoperative nausea and vomiting, pain, and bleeding, which warrant hospital admission. For these reasons, it is recommended that office-based procedures should be limited to 6 hours and should be completed by 3 p.m. to ensure adequate recovery time. Many surgeons circumvent this issue by giving their patients the option

**BOX 74-1 Patients Excluded from Office-Based Anesthesia**

ASA III and IV with poorly controlled:
- Diabetes
- Hypertension
- Coronary artery disease
- Chronic obstructive pulmonary disease

Obesity—BMI >35
Obstructive sleep apnea
Suspicion of difficult airway
Malignant hyperthermia susceptible
History of substance abuse
History of seizure disorder
No escort
Latex allergy?

**BOX 74-2 Commonly Performed Office-Based Procedures**

**Cosmetic**

Body
- Liposuction
- Breast augmentation, breast reduction, mastopexy
- Abdominoplasty
- Arm/leg lift

Face
- Facelift
- Blepharoplasty
- Rhinoplasty
- Meloplasty
- Mentoplasty
- Buccal fat extraction
- Brow lift
- Facial resurfacing (including laser)

**Gastrointestinal Endoscopy**

Upper/lower endoscopy (colonoscopy)

**Dentistry and Oral and Maxillofacial Surgery**

Tooth (especially wisdom) extraction
Pediatric dentistry

**Orthopedics and Podiatry**

Arthroscopy (knee, shoulder, and elbow)
Wrist, hand, and foot surgery

**Gynecology**

Dilation and curettage
Hysteroscopy
Mini-laparotomy
Endometrial ablation
Ovum retrieval

**Urology**

Vasectomy
Cystoscopy
Prostate biopsy
Laser resection
Lithotripsy/extracorporeal shock wave lithotripsy

**Ophthalmology**

Cataract extraction
Lacrimal duct probing
Ophthalmoplasty

**Otolaryngology**

Endoscopic sinus surgery
Turbinate resection
Septoplasty
Myringotomy

**Vascular**

Vein stripping

**Pain**

Injections
Radiofrequency ablation

to stay overnight in their office recovery room with a registered recovery room nurse. In addition, surgeries that involve or might result in excessive blood loss, significant fluid shifts, or hypothermia are not appropriate office-based surgeries. Ultimately, the patient's overall medical status and anticipated perioperative course is crucial in determining the appropriateness of a planned procedure in this setting. What is considered an appropriate office-based surgery for one patient may not be acceptable for another.

### 4. In what ways is morbid obesity a challenge to an office-based anesthesiologist?

Morbidly obese patients present unique challenges to anesthesiologists, and this is especially true in the office-based setting, where resources are limited. There is only one anesthesia provider. Anesthesia colleagues, residents, or certified registered nurse anesthetists are not available to assist in case of an airway emergency. Some emergency airway equipment (e.g., fiberoptic scope, videolaryngoscope) may be unavailable.

Morbidly obese patients have associated comorbidities that put them at risk during the perioperative period and that are of particular concern in the office-based setting. They are usually considered at increased risk for aspiration and require rapid-sequence induction for general anesthesia. Because of numerous physiologic parameters, these patients may be difficult to intubate or ventilate. An ominous situation is created where help is sparse and backup equipment is unavailable.

The option of providing monitored anesthesia care with moderate to deep sedation for morbidly obese patients is inadvisable because attempts at sedation may quickly convert to general anesthesia and result in loss of airway reflexes. These patients may have obstructive sleep apnea and are likely to have increased sensitivity to the effects of anesthesia and opioids. This increased sensitivity predisposes them to respiratory depression or apnea during the postoperative period. For all these reasons, it would be reasonable to avoid performing OBA on morbidly obese patients, especially patients with associated obstructive sleep apnea.

Another aspect of morbid obesity that predisposes these patients to perioperative complications is the risk of developing deep vein thrombosis (DVT) or pulmonary embolism. DVT with subsequent pulmonary embolism is a significant risk of abdominoplasty and liposuction, two very common office-based procedures as well as procedures morbidly obese patients are likely to undergo. Other patients who are at increased risk of developing DVT are elderly patients with malignancy, smokers, oral contraceptive users, patients on bed rest, patients with hypercoagulation disorders, and patients with a prior history of DVT.

### 5. What anesthetic techniques are appropriate to use in an office-based practice?

Most anesthetic drugs and techniques used in hospitals and ASCs can and have been safely and effectively applied in the office setting. The type of anesthesia should be appropriate to the patient's overall health status and surgical procedure. It should allow for rapid emergence and discharge, with minimal postoperative pain and nausea. Anesthetic techniques for office-based surgery range from local infiltration, with or without intravenous sedation (monitored anesthesia care) to regional and general anesthesia.

Monitored anesthesia care with intravenous sedation is the most common anesthetic technique used in the office setting. A combination of agents that provide rapid onset and fast recovery (e.g., propofol and remifentanil) with local anesthetic infiltration of the surgical site provides excellent intraoperative analgesia and reduces the need for postoperative opioid use. Other agents commonly employed are midazolam and ketamine. However, with this technique, the anesthesia provider must be able to deepen the level of anesthesia if necessary and still be able to rescue the patient from a deep level of sedation, if indicated. It is prudent to have all the necessary equipment and drugs to convert monitored anesthesia care anesthesia to general anesthesia at any given time.

As the complexity and duration of surgical procedures performed in the office setting continue to evolve, the use of general anesthesia has increased. With the advent of total intravenous anesthesia (TIVA) techniques, general anesthesia can be achieved without the need of an anesthesia machine and a waste gas scavenging system. TIVA also avoids the use of agents that trigger malignant hyperthermia. TIVA generally consists of a mixture of propofol and an opioid, with spontaneous or assisted ventilation either with or without a laryngeal mask airway or endotracheal tube. Another TIVA combination includes propofol and ketamine.

Regional anesthesia, such as central neuraxial blocks (e.g., spinal, epidural) and peripheral nerve blocks (e.g., brachial plexus, femoral, ankle) is a useful anesthetic technique for orthopedic and urologic office-based procedures. It provides excellent intraoperative and postoperative analgesia. It is not associated with significant postoperative sedation, even when used in conjunction with monitored anesthesia care. Nerve blocks without intravenous opioids offer a low incidence of postoperative nausea and vomiting. Regional anesthesia is associated with problems ambulating, post–dural puncture headache, prolonged autonomic blockade, and inability to urinate.

## SUGGESTED READINGS

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SECTION 14

# TRAUMA

CASE 75

# Thoracic Trauma

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## QUESTIONS

1. What are the consequences of thoracic trauma?
2. How are traumatic pneumothorax and hemothorax managed in patients undergoing laparotomy for splenic injury?
3. What are the mechanisms of morbidity and mortality from flail chest?
4. What are the management options for flail chest and pulmonary contusion?
5. What are the perioperative management options for traumatic hemopericardium?
6. What are the clinical implications of blunt cardiac trauma?
7. When should traumatic thoracic aortic injury be suspected, and how is it diagnosed?
8. How is surgery prioritized in patients with blunt trauma and multiple injuries that include thoracic aortic damage?
9. What are the current management strategies for blunt aortic injury?
10. What are the perioperative clinical and anesthetic pitfalls that can be encountered during management of patients with thoracic aortic injuries, and how should they be managed?
11. Describe the clinical management of transmediastinal gunshot wounds.

A 46-year-old man is admitted to the trauma bay of the emergency department approximately 30 minutes after he was struck by a bus. The primary survey reveals no signs of upper airway obstruction, but there is significant respiratory distress with chest wall splinting. Systemic blood pressure (BP) is 130/80 mm Hg, heart rate is 120 beats per minute, and Glasgow Coma Scale score is 15 with movement of all extremities. No open wounds are observed. The secondary survey reveals a left distal humerus fracture and left (5, 6, 7, 8, and 9) and right (6, 7, and 8) rib fractures as well as abdominal guarding. Computed tomography (CT) demonstrates a grade 4 splenic injury, necessitating emergency laparotomy.

## 1. What are the consequences of thoracic trauma?

Of the 112,000 annual deaths caused by unintentional injuries, almost half result from motor vehicle–related trauma, which carries a high risk of chest injury. Similarly, of the 55,000 deaths caused by intentional injuries, 20,000 are also likely to involve injuries to the chest. It is estimated that 12%–21% of all trauma deaths result primarily from blunt and penetrating chest injury. For each chest trauma–related death, there are approximately 100 nonfatal thoracic injuries. Not all intrathoracic organs are at equal risk of injury. The chest wall (50%–71%) and lungs (21%–26%) are the most commonly involved structures. The heart (7%–9%), aorta and great vessels (4%), esophagus (7%), and diaphragm (0.5%–7%) are less likely to be injured.

The immediate threat to life also varies with different thoracic organ injuries. Immediately life-threatening injuries include major airway trauma with airway obstruction, tension pneumothorax, open pneumothorax, cardiac tamponade, massive hemothorax, and free rupture of the thoracic great vessels. Potentially life-threatening injuries include partial tracheal disruption, contained rupture of the great vessels, myocardial contusion, valvular or septal injuries, pulmonary contusion, esophageal disruption, and diaphragmatic tear. Flail chest can be immediately or potentially life-threatening depending on the severity of associated hypoxemia. Risk factors for mortality after blunt chest trauma are patient age >65 years; three or more rib fractures; preexisting diseases, particularly involving the cardiopulmonary system; and pneumonia developing after injury.

Although cardiothoracic trauma is a major contributor to all trauma mortality, it coexists in 80% of cases with other injuries that commonly require major surgery. Some serious thoracic organ injuries may be clinically silent, and active suspicion and sophisticated diagnostic measures may be required to detect them. Physiologic derangements from chest injuries are multi-dimensional, including pulmonary failure, hemorrhage, and cardiac dysfunction, and coexist in varying combinations and severity. Some clinicians use the term “thoracic shock” to describe chest injury–induced physiologic derangements (Figure 75-1). Individually or in combination, each of these physiologic abnormalities can interfere with oxygen delivery, consumption, and extraction. They can potentially shift oxygen use from a flow-independent to a flow-dependent state, with associated anaerobic tissue metabolism and lactic acidosis.

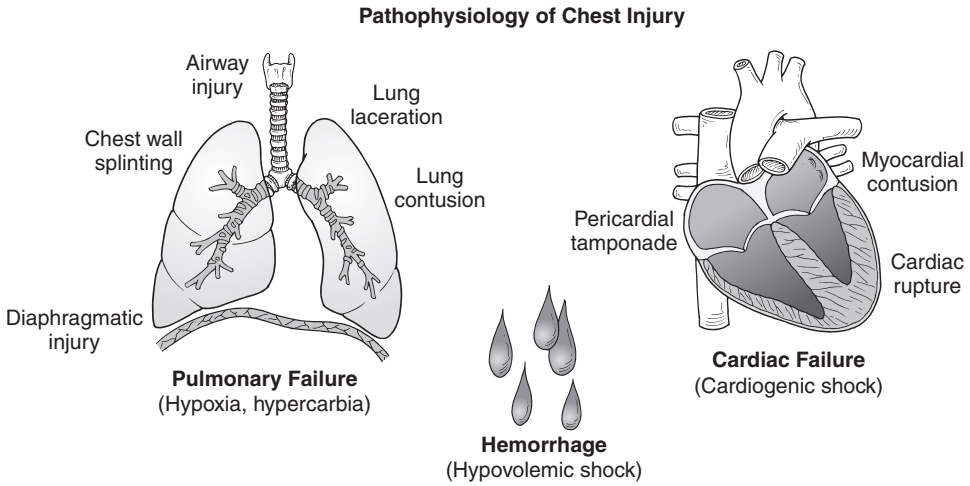


**FIGURE 75-1** ■ Schematic depiction of the pathophysiology of chest injury.

## 2. How are traumatic pneumothorax and hemothorax managed in patients undergoing laparotomy for splenic injury?

Pneumothorax and hemothorax are the most frequent consequences of chest injury and require timely recognition and treatment. They can occur after both penetrating and blunt chest trauma. Both can result from laceration of visceral pleura by sharp objects during assaults or by fractured ribs. However, pneumothorax may also occur after blunt chest trauma without rib fracture. The mechanism of this injury relates to sudden elevation of alveolar pressures, producing alveolar rupture with entry of air into the interstitial space, mediastinum, and visceral pleura.

Concerns about exacerbating spine injuries or producing adverse hemodynamic changes preclude obtaining a chest radiograph in the sitting position, which is required for the diagnosis of a pneumothorax and recognition of the magnitude of a hemothorax. For these reasons, although supine chest radiographs are obtained routinely in all patients with major trauma, additional measures may be necessary to diagnose pneumothorax and hemothorax when their presence is suspected. CT scan of the chest obtained in the supine position is highly specific, so even a small amount of air in the pleural cavity can be recognized by this method.

In some instances, an undiagnosed pneumothorax may enlarge during surgery for associated injuries. Tension pneumothoraces can result in severe hemodynamic and oxygenation abnormalities that can be lethal. Our approach is to place a chest tube for all patients with a diagnosis of pneumothorax and in need of mechanical ventilation for any reason. Not all clinicians agree with this approach. It has been demonstrated that by using CT, the size of a traumatic pneumothorax may be classified as miniscule or limited anteriorly and anterolaterally. In most of these patients, chest tubes may not be indicated, even during mechanical ventilation, if close observation with appropriate monitoring is provided. However, during emergency surgery, such observation and monitoring may not be easy to achieve.

The clinical signs of pneumothorax in anesthetized patients receiving positive pressure ventilation include elevation of peak airway pressure, decreased lung compliance, decreasing oxygen saturation, and decreased breath sounds on the affected side. In extremis, severe hypotension and possibly cardiac arrest can ensue. Chest radiographs can provide the diagnosis even in the supine position if the amount of intrapleural air is large enough; however, chest x-rays may be difficult or impossible to obtain during emergency surgery.

Without a radiologically confirmed diagnosis, placement of a 14-gauge needle between the fourth and fifth ribs (the fourth intercostal space) in the midaxillary line, the thinnest region of the chest wall even in obese patients, may be indicated for unstable patients. Nevertheless, atelectasis, bronchial obstruction, or migration of intraabdominal contents into the chest through a traumatic diaphragmatic defect can mimic the clinical findings of pneumothorax and lead to unnecessary chest tube placement. Sonographic diagnosis of pneumothorax has gained some recognition more recently. Normally, when the lung is imaged by a 3.5- to 7.5-MHz ultrasound probe, sliding of the pleura beneath the chest wall during inspiration and expiration produces multiple echodense spots that originate from the surface of the lungs and project across the lung. These spots are termed comet-tail artifacts. In the presence of a pneumothorax, air between the chest wall and the visceral pleura prevents the appearance of comet-tail artifacts. Ultrasonography may be more sensitive than an anteroposterior chest x-ray for diagnosis of pneumothorax or hemothorax.

Hemothorax may also cause hemorrhagic shock, mediastinal shift, and airway management difficulties. Placement of a large-bore (28F–38F) chest tube in the early phase of management, especially after penetrating injury, provides information about the rate of bleeding and often prevents development of fibrin clot over the lung surface, which may restrict lung expansion and require decortication later. Antibiotic coverage should be provided for the next 24 hours.

The volume and rate of blood drained via the chest tube determine the necessity for video-assisted thoracoscopy or

**BOX 75-1 Pneumothorax and Hemothorax**

**PNEUMOTHORAX**

***Diagnosis***

Chest radiograph in sitting position
CT
Needle aspiration: 14-gauge needle in fourth intercostal space, midaxillary line
Ultrasound: absence of lung movement and "comet-tail" artifact

***Signs and symptoms under anesthesia***

Increased peak airway pressure
Decreased lung compliance
Decreasing oxygen saturation
Decreased breath sounds on affected side
Severe hypotension
Cardiac arrest if recognized late

***Differential diagnosis***

Atelectasis
Bronchial obstruction
Migration of intraabdominal contents through traumatic diaphragmatic defect

**HEMOTHORAX**

***Symptoms***

Hemorrhagic shock
Mediastinal shift

***Indications for thoracotomy***

Chest tube drainage
>1200 mL on placement of chest tube
>200 mL/hour for 4 hours
>100 mL/hour for 4 hours if >60 years old

thoracotomy. Drainage of >1200 mL of blood on placement of the tube, continuing drainage of >200 mL/hour for 4 hours, or >100 mL/hour for 4 hours in patients >60 years are indications for surgical intervention. Other indications for emergency surgery include significant hypotension or tachycardia or both, persistent "white lung" on the chest radiograph in the presence of a properly placed chest tube, difficult ventilation, pericardial tamponade, massive air leak into the chest tube, major tracheal or bronchial injury, and cardiac or great vessel injury. Important management aspects of traumatic pneumothorax and hemothorax are summarized in Box 75-1.

### 3. What are the mechanisms of morbidity and mortality from flail chest?

Flail chest is defined as fracture of several ribs at two or more sites or disarticulation of two or more ribs from their cartilaginous attachments to the sternum in addition to fractures. The resulting respiratory impairment may lead to arterial hypoxemia or hypercarbia or both. Two mechanisms are involved: paradoxical ventilation and pulmonary contusion. Paradoxical chest wall motion—manifested by "caving" of the flail segment on inspiration and "bulging" on exhalation—is dyssynchronous with movement of the uninjured chest wall and diaphragm. By itself, a flail segment may increase the work of breathing, but it usually is not the primary cause of acute respiratory failure unless there is a coexisting pneumothorax from injury to the underlying pleura. The pendelluft effect, a pendulum like motion of gas from one lung to the other during respiration as a result of inequality of pressures between the two hemithoraces, does not seem to be a significant cause of respiratory impairment either. The primary cause of morbidity and mortality after blunt chest trauma is believed to be severe pulmonary contusion. An increase in elastic recoil from this cause makes it difficult to expand the lung during inspiration in spontaneously breathing patients, which not only increases the work of breathing but also causes a decrease in functional residual capacity and lung compliance that may not return to normal for several weeks. All of these events result in exaggeration of paradoxical chest wall movement.

Pulmonary contusion may be present in 30% of adult patients sustaining multiple trauma with injury severity scores >25. Rapid deceleration with a change in velocity ($\Delta V$) >45 mph, seen during free falls or major motor vehicle accidents, is the primary mechanism of pulmonary contusion in civilian trauma. In the military setting, shock waves from explosions and high-speed projectiles are responsible for pulmonary contusion.

The pathophysiology of pulmonary contusion involves several mechanisms. The lung contains gas/fluid interfaces and is vulnerable to alveolar disruption. Also, the low-density alveoli may be stripped during impact by higher density hilar tissues. Finally, alveoli compressed during the impact overexpand immediately afterward. Direct laceration of lung parenchyma by inward displacement of fractured ribs or chest wall compression also can occur.

The pathology of lung contusion involves interstitial and intraalveolar hemorrhage, alveolar disruption, and atelectasis. Although these changes begin within a few minutes after injury, they may take 4 hours to complete. Respiratory function, appearance of plain chest radiographs, and arterial blood gases deteriorate gradually within the first few hours after injury. Increased mucus production, decreased clearance, and impaired surfactant production contribute to the respiratory findings produced by intraalveolar bleeding, ventilation/perfusion ($\dot{V}/\dot{Q}$) mismatching, intrapulmonary shunting, and pulmonary edema. Hypoxemia, wheezing, hemoptysis, hypercarbia, and a rapid respiratory rate with shallow breathing are the main clinical symptoms in spontaneously breathing patients. As a defense mechanism in most instances, hypoxic pulmonary vasoconstriction in the injured lung limits the severity of hypoxemia. However, in patients unable to exert this mechanism, hypoxia may be severe. Generally, age >45 years, preexisting diseases, higher injury severity score, and large fluid volumes predict increased morbidity and mortality.

Pulmonary contusions, if not complicated by inflammation, resolve within a few days. However, when inflammation develops, the likelihood of acute respiratory distress syndrome (ARDS) and pneumonia increases with serious clinical consequences. The long-term outlook after pulmonary dysfunction in patients with flail chest uncomplicated by pulmonary contusion is excellent, generally with complete recovery. The presence

of pulmonary contusion, especially when complicated by ARDS or pneumonia, increases the likelihood of long-term pulmonary dysfunction for at least 6 months.

## 4. What are the management options for flail chest and pulmonary contusion?

### *Diagnosis*

The presence of a flail segment suggests underlying pulmonary contusion, but if breaths are rapid and shallow, this sign may not be evident. However, neither the extent of the flail nor the number of ribs fractured accurately predicts respiratory failure. Chest wall bruising, rib cage deformities, and crepitus or pain or both during palpation of the thorax suggest rib fractures or dislocation even in the presence of a normal chest radiograph, which may not detect cartilaginous injuries and fractures of poorly calcified ribs. The initial film often does not show underlying lung injury because pulmonary edema appears late. If present, a focal infiltrate beneath multiple rib fractures confirms the diagnosis of pulmonary contusion. Clinical signs, such as dyspnea, tachypnea, intercostal muscle retraction, and use of accessory muscles, suggest underlying lung pathology. Monitoring with pulse oximetry in the initial stage is useful only if the patient is breathing room air. Supplemental oxygen administration may mask inadequate ventilation, delaying diagnosis and treatment to restore functional residual capacity and lung compliance toward normal. Likewise, arterial blood gases measured with the patient breathing room air may be useful. Managing these patients without supplemental oxygen necessitates direct observation by a physician or other qualified person. The usual pattern is a progressive decrease in arterial oxygen ($PaO_2$) and increase in arterial carbon dioxide ($PaCO_2$) tensions, resulting in a decrease in pH (i.e., respiratory acidosis). When patients need emergency surgery, as our patient required a splenectomy, hypoxemia and hypercarbia often develop intraoperatively. Frequent intraoperative arterial blood gas measurements should be obtained.

Although arterial hypoxemia may precede radiographic abnormalities, it may not reflect the size of the contusion because blood flow to the injured lung is restricted by hypoxic pulmonary vasoconstriction. A $PaO_2/FiO_2$ <300 after initial resuscitation is considered a risk factor for developing subsequent acute respiratory failure. Because plain chest radiography underestimates contusion volume, CT scans are used for quantifying the contusion size. Patients with a contusion >28% of total lung volume are very likely to require mechanical ventilation, and patients with contusion volumes >20% of total lung volume frequently develop ARDS and pneumonia (Figure 75-2). Although CT is the standard method of diagnosis, patients who are too unstable to be transported to a CT unit may benefit from ultrasound evaluation. Ultrasound may be valuable for detecting rib fractures, pneumothorax, and contusions, although it cannot determine contusion volume. The presence of multiple comet-tail artifacts at the parietal-visceral pleural interface and replacement of the normal transverse A-line pattern by vertical B-lines suggest pulmonary contusion (Figure 75-3). With any of the imaging techniques described, confusion may arise in differentiating contusion from aspiration, atelectasis, hemothorax, fluid overload, transfusion-related acute lung injury, and pulmonary emboli.

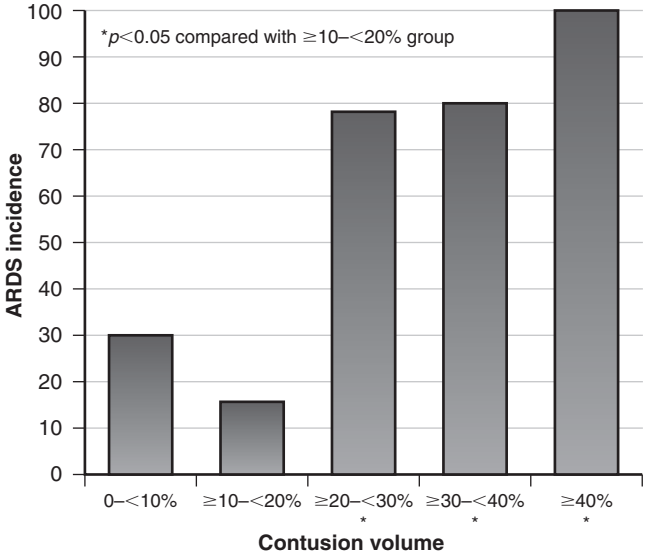


**FIGURE 75-2** ■ Correlation of pulmonary contusion volume with subsequent development of ARDS. (From Miller PR, Croce MA, Bee TK, et al.: ARDS after pulmonary contusion: accurate measurement of contusion volume identifies high-risk patients. J Trauma 51:223, 2001.) *ARDS*, Adult respiratory distress syndrome.

### *Management*

As in our case, patients with pulmonary contusion frequently have associated injuries that may or may not require emergency surgery. Management may need to take into account treatment requirements of associated injuries as well. For example, in a bleeding patient, restricting fluids out of a concern for exacerbating pulmonary contusion may have serious consequences. Many patients with rib fractures and pulmonary contusion also have spinal fractures. Administering continuous epidural anesthesia to these patients because of its salutary effect on contusions would be extremely uncomfortable for the patient and may sometimes be associated with worsening of the vertebral injury or causing spinal cord damage.

During the initial phase, simple measures such as oxygen administration by mask to patients who are hypoxic breathing room air and maintaining the uninvolved lung in a dependent position may help improve oxygenation. Patients with intratracheal bleeding may need a double-lumen endotracheal tube or an endobronchial blocker to prevent contamination of the intact lung and possibly to tamponade the bleeding. Ventilation of the intact lung alone may also be useful in patients with complete unilateral contusions. In patients with bilateral contusions presenting with severe hypoxemia, differential lung ventilation via a double-lumen tube should be considered. When hypoxemia is life-threatening, high-frequency jet ventilation or oscillatory ventilation may improve systemic oxygenation effectively. These modes of ventilation may also improve

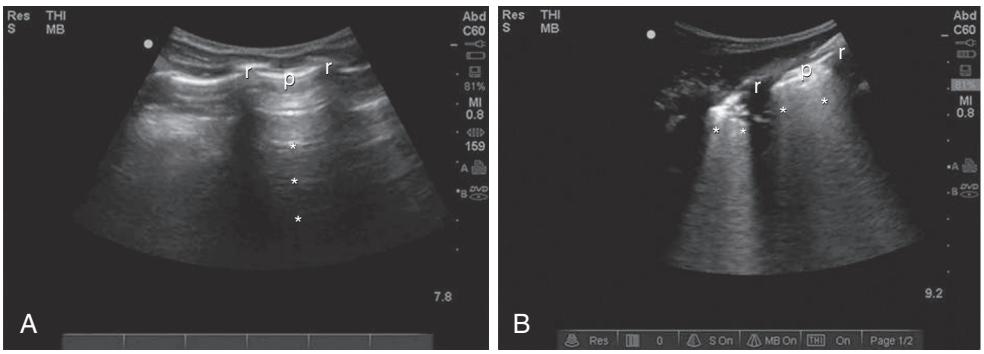


**FIGURE 75-3** ■ Ultrasound diagnosis of pulmonary contusion. **A,** Ultrasound image of the normal lung showing ribs (*r*) and the pleural line (*p*) with A-lines (*asterisks*), which are horizontal reverberation artifacts at equal distances. **B,** Ultrasound image of the contused lung showing ribs (*r*) and the pleural line (*p*) without A-lines. Instead, there are vertical hyperechoic artifacts known as B-lines (*asterisks*), which arise from the pleural line and erase the normal A-line pattern. (From Stone MB, Secko MA: Bedside diagnosis of pulmonary contusion. Pediatr Emerg Care 25:854, 2009.)

depressed cardiac function caused by concomitant myocardial contusion or ischemia.

Early treatment is crucial. A delay of even a few hours may result in progression of underlying lung pathology with increasing morbidity and mortality. The goal is to decrease elastic recoil and the work of breathing and to improve arterial blood gases without adverse hemodynamic effects. In patients without acute respiratory failure or associated injuries requiring tracheal intubation, this goal can be accomplished by continuous positive airway pressure (CPAP) of 10–15 cm $H_2O$ applied by facemask. Noninvasive positive pressure ventilation using titrated bilevel positive airway pressure with both inspiratory (10–12 cm $H_2O$) and expiratory (6 cm $H_2O$) positive pressures can avoid tracheal intubation in more than one half of patients.

Early tracheal intubation and mechanical ventilation with alveolar recruitment maneuvers, the usual practice before 1975, has fallen into disfavor because of a high incidence of tracheobronchitis and pneumonia leading to sepsis, multiorgan failure, and death. At the present time, except in instances when tracheal intubation and mechanical ventilation are necessary (i.e., $PaO_2$ <60 mm Hg in room air, <80 mm Hg with supplemental oxygen, and conditions other than thoracic injury), most patients do well with noninvasive positive pressure ventilation. When impending respiratory failure indicates tracheal intubation, airway pressure release ventilation (APRV) may be a reasonable choice. With this mode of ventilation in a spontaneously breathing patient, CPAP is intermittently decreased for short periods with the device shown in Figure 75-4. In other words, spontaneous breathing is superimposed on mechanical ventilation. In addition to decreased work of breathing, the advantages of this technique over controlled ventilation are improved $\dot{V}/\dot{Q}$ matching, increased systemic blood flow, lower sedation requirements, greater oxygen delivery, shorter periods of intubation, and decreased risk of pneumonia. In patients with severe life-threatening pulmonary contusion, ARDS, or acute lung injury unresponsive to APRV or routine mechanical ventilation, lung recruitment strategies such as high-frequency inverse ratio ventilation, low tidal volume (6 mL/kg) and titrated positive end expiratory pressure (PEEP) ventilation, permissive hypercapnia, or high-frequency oscillatory ventilation may be considered.

Effective removal of tracheobronchial secretions has a significant effect on outcome. Likewise, monitoring with pulse oximetry, an arterial catheter, and a pulmonary artery catheter when indicated is important. A pulmonary artery catheter can not only guide fluid management, which should be adjusted to the minimum consistent with adequate end-organ perfusion, but it also may aid ventilatory management, as it permits calculation of oxygen delivery and intrapulmonary shunt fraction and thus helps to adjust the optimal level of CPAP.

Supplemental oxygen should be administered judiciously to permit the acquisition of maximal information from the initial oxyhemoglobin saturation with pulse oximetry or arterial blood analysis. Supplemental oxygen has detrimental effects, such as absorption atelectasis, interference with hypoxic pulmonary vasoconstriction in damaged lung regions, decreased mucociliary clearance, free radical formation, and decreased surfactant production.

Although the effect of fluids on pulmonary function in the presence of pulmonary contusion has not been conclusively defined, we believe that overzealous fluid administration may result in an increase in the size of the lung contusion and a decrease in $PaO_2$. Although it is possible to remove excess fluid with diuretics, use of diuretics is associated with electrolyte abnormalities, cardiac dysrhythmias, and hypovolemia. At least during initial resuscitation, the type of fluid used does not seem to affect outcome. Crystalloid solutions are favored because they are less expensive. The initial enthusiasm for hypertonic saline in fluid management of pulmonary contusion has not been substantiated. In the presence of concomitant blunt cardiac injury, complications of pulmonary contusion can easily confuse the clinical picture. In this situation, the best guide to fluid management is transesophageal echocardiography (TEE) or, if TEE is unavailable, pulmonary artery and wedge pressures.

Continuous epidural analgesia is the best pain management technique available for patients with blunt chest trauma. It improves lung function and decreases overall morbidity. However, as mentioned earlier, concomitant

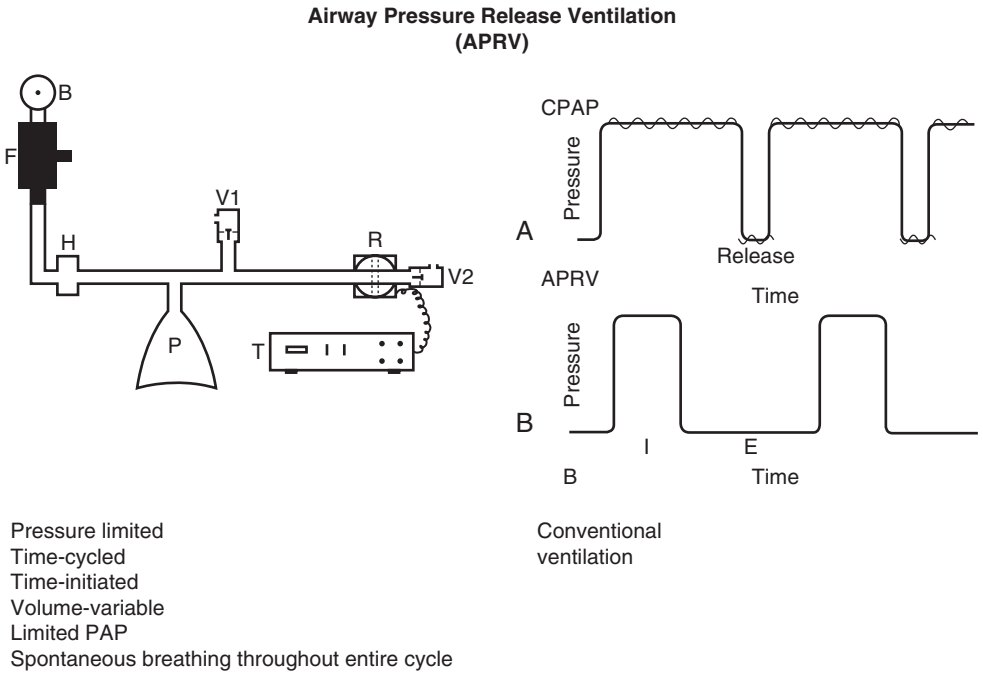


**FIGURE 75-4** ■ *Left panel,* Schematics of the APRV circuit. *Right panel,* Airway pressure pattern produced by APRV **(A)** compared with the airway pressure pattern produced by conventional mechanical ventilation **(B)**. The circuit consists of a flow generator (*F*) that produces continuous positive airway pressure as it exits through a threshold resistor valve (*V1*). APRV breaths are produced by a timer (*T*) controlled release valve (*R*) in the expiratory limb of the circuit. This valve allows the circuit pressure to decrease intermittently below the continuous positive airway pressure; the level is determined by a second threshold resistor valve (*V2*). *B,* Gas source; *H,* humidifier; *P,* patient. Note on the right panel spontaneous breathing superimposed on continuous positive airway pressure (*CPAP*) and the opposite inspiration (*I*)/expiration (*E*) ratios of APRV and conventional ventilation. APRV can be described as a time-cycled, time-initiated, volume-variable device that limits peak airway pressure (*PAP*). (Adapted from Räsänen J, Cane RD, Downs JB, et al.: Airway pressure release ventilation during acute lung injury: A prospective multicenter trial. Crit Care Med 19:1234, 1991; and McCunn M, Habashi NM: Airway pressure release ventilation in the acute respiratory distress syndrome following trauma. Int Anesthesiol Clin 40:89, 2002.)

spine or other injuries and inability of the patient to consent to the procedure preclude this technique. Continuous thoracic paravertebral block with ultrasound guidance may also be considered as a component of multidimensional pain management. Other modalities, such as parenteral opioids, are not nearly as effective, whereas multiple intercostal blocks are labor-intensive and short-lasting and must be repeated at least twice a day. Important management aspects of flail chest and pulmonary contusion are summarized in Box 75-2.

## 5. What are the perioperative management options for traumatic hemopericardium?

Traumatic hemopericardium can develop after both blunt and penetrating chest injuries. In contrast to chronic effusions, in which 600 mL of pericardial fluid may not cause hemodynamic depression, even small accumulations of blood after acute injury result in cardiac tamponade with significant hypotension and cardiac arrest. Inflow occlusion of the atrioventricular valves, resulting from external compression by pericardial blood, leads to decreased ventricular filling, especially in the right heart. Because a relatively small amount of fluid accumulation can cause major hemodynamic changes, evacuation of even a minimal quantity of blood from the pericardium usually restores BP. Hypotensive patients who may have cardiac tamponade could benefit from pericardiocentesis. Transthoracic echocardiography (TTE) or TEE in intubated patients without suspected esophageal injury can aid in diagnosing and evacuating pericardial blood. Diastolic collapse, defined as approximation of the (usually right) ventricular walls during diastole, is a sign of tamponade and is associated with systemic BP reductions of ≥15%–20%. During evacuation, simultaneous imaging of the needle and the pericardial sac prevents cardiac perforation.

The clinical signs characteristic of chronic hemopericardium are virtually useless in acute traumatic tamponade. Beck's triad (i.e., cervical venous distention, hypotension, and muffled heart sounds) is seen in <50% of traumatic tamponade cases. Agitation, combativeness, and cool vasoconstricted extremities are seen in patients with cardiac tamponade, but they are also present in patients with hypovolemic shock. Paradoxical inspiratory distention of the neck veins (i.e., Kussmaul's sign) is characteristic of cardiac tamponade, but it may be extremely difficult to demonstrate in patients with acute trauma.

Paradoxical pulse, although not specific for cardiac tamponade, is probably the most reliable clinical sign in these circumstances. Paradoxical pulse refers to a >10 mm Hg decline in systolic arterial pressure during inspiration in a spontaneously breathing patient and is simply an exaggeration of the normal 3–6 mm Hg respirophasic variation. This sign lacks specificity because it can also occur in patients with uncomplicated hypovolemia. Its absence does not exclude cardiac tamponade. Concurrent septal defect, severe left ventricular failure, or aortic regurgitation may

## BOX 75-2 Flail Chest and Pulmonary Contusion

**Definition**

Flail chest: rib fractures at two or more sites, with or without disarticulation
Pulmonary contusion: atelectasis, interstitial and intraalveolar hemorrhage, alveolar disruption

**Diagnosis**

***Clinical symptoms***

Dyspnea
Tachypnea
Intercostal muscle retractions
Use of accessory muscles of respiration

***Physical examination***

Chest wall bruising
Rib cage deformities
Crepitus/pain on palpation

***Radiologic examination***

Chest radiograph not always diagnostic
Infiltrate seen in area of trauma
CT scan

***Laboratory***

Progressive hypoxia
Progressive hypercarbia
Respiratory acidosis

**Treatment**

CPAP 10–15 cm $H_2O$ by facemask
Tracheal intubation
Mechanical ventilation
  Pressure/volume controlled ventilation
  Airway pressure release ventilation
  Differential lung ventilation
  High-frequency jet ventilation
Limit fluids
Epidural analgesia if no contraindication exists
Paravertebral block, intercostal block, or parenteral opioids

**Monitoring**

Pulse oximeter
Arterial catheter
Transthoracic or transesophageal echocardiogram to demonstrate tricuspid regurgitation
Pulmonary artery catheter
  Calculate oxygen delivery and intrapulmonary shunt fraction to adjust optimal CPAP

*CPAP*, Continuous positive airway pressure; *CT*, computed tomography.

preclude a paradoxical pulse. The following two synergistic mechanisms during inspiratory reduction of intrathoracic pressure are responsible for development of paradoxical pulse:

- Increase in transmural aortic pressure and in left ventricular afterload
- Underfilling of the left ventricle because of leftward displacement of the interventricular septum

Increased venous pressure during inspiration in normovolemic patients makes the paradoxical pulse more obvious because it increases right ventricular filling and enhances the leftward septal shift. However, in hypovolemic trauma patients, right ventricular filling and the septal shift are limited, rendering pulsus paradoxus less perceptible.

Equalization of elevated intrapericardial and right ventricular filling pressures is an inevitable phenomenon in compensated cardiac tamponade. With further accumulation of blood, these pressures increase toward the left ventricular diastolic pressure. With diastolic underfilling, cardiac output becomes rate dependent. A decrease in heart rate may result in catastrophic hypotension and cardiac arrest. Severe cardiac tamponade can also produce a reduction in coronary blood flow, but myocardial ischemia and decreased contractility are unlikely, probably because of a proportional decrease in myocardial work resulting from decreased systemic BP and stroke volume.

Associated injuries often overshadow the clinical manifestations of cardiac tamponade even when the classic signs of this entity are evident. It is important to be familiar with the ancillary diagnostic findings of cardiac tamponade. Radiographic findings are not helpful. Cardiomegaly is unlikely to be present in patients with traumatic cardiac tamponade and is nonspecific. Findings on electrocardiogram (ECG) are also not specific, although ST segment elevation and diminished QRS voltage may be observed if significant pericardial blood accumulates. Electrical alternans (i.e., phasic alteration of R wave amplitude) may be more specific but can also occur in patients with tension pneumothorax. Total electrical alternans (i.e., phasic alteration of P and R wave amplitudes), although rare, is considered a pathognomonic sign. As mentioned, echocardiography is the most reliable diagnostic tool for this entity. Of the four sites examined during a focused abdominal sonographic study (FAST), the first involves exploration of the pericardium via a subxiphoid window. Transthoracic and transesophageal views can also be used. Ultrasound may demonstrate not only pericardial blood and its volume but also right ventricular diastolic collapse. Diastolic collapse may be absent in patients with a hypertrophic right ventricle or in patients with high intraventricular pressures from tricuspid regurgitation.

Management priorities depend on preexisting cardiac conditions, the type and extent of associated injuries, intravascular volume, the quantity of pericardial blood, and patient cooperation. If the severity of associated injuries permits, pericardiocentesis with echocardiographic guidance or surgical drainage and intravascular volume restoration should precede any anesthetic. In contrast to pleural blood, pericardial blood clots easily. It may be possible to drain only a fraction of pericardial fluid, but even small amounts can produce significant hemodynamic improvement.

Any drug that decreases myocardial contractility or produces peripheral vasodilation may precipitate hemodynamic depression. The classic anesthetic induction agent is ketamine, but even with this drug BP may deteriorate. Positive pressure ventilation should be carefully maintained with low airway pressures and without PEEP. In most instances of major trauma with pericardial tamponade, invasive monitoring other than an arterial catheter may be difficult to place. However, a pulmonary artery catheter, if present, can be helpful to determine

**BOX 75-3 Cardiac Tamponade**

**Diagnosis**

***Classic signs present <50%***

Cervical venous distention
Hypotension
Muffled heart sounds
Paradoxical pulse (most reliable in acute trauma)

***ECG***

Nonspecific
Elevation of ST segment
Diminished QRS voltage
Electrical alternans

***Echocardiography***

Pericardial fluid
Right ventricular diastolic collapse

**Treatment**

***Before induction of anesthesia***

Pericardiocentesis with echocardiographic guidance
Surgical drainage
Volume replacement

***After induction of anesthesia***

Avoid cardiac depressants and bradycardia
Spontaneous ventilation
If positive pressure ventilation necessary, low airway pressure, no PEEP

*ECG*, Electrocardiogram; *PEEP*, positive end expiratory pressure.

equalization of cardiac chamber pressures, cardiac output, and response to therapeutic interventions. Bradycardia during direct laryngoscopy or surgical manipulation should be avoided at all costs. Important management aspects of traumatic cardiac tamponade are summarized in Box 75-3.

## 6. What are the clinical implications of blunt cardiac trauma?

By definition, blunt cardiac trauma encompasses a wide variety of pathologic conditions, including varying degrees of myocardial damage. Examples include coronary artery injury; cardiac free wall, interatrial, interventricular septal, or valvular rupture; and, with impalement by a fractured sternum or rib, penetrating injury from blunt trauma. The term "blunt cardiac injury" (BCI) refers to myocardial damage involving myofibrillar disintegration, edema, bleeding, or necrosis; this injury was formerly known as myocardial contusion. It manifests clinically as minor ECG changes, cardiac enzyme abnormalities, complex dysrhythmias, or cardiac failure. Some of these injuries may be caused by myocardial damage from direct mechanical injury or occur indirectly as a result of coronary occlusion or exacerbation of preexisting coronary artery disease by the stress of trauma. Cardiac lesions, seen as ECG abnormalities and troponin release, may also be the result of increased catecholamine activity after severe central nervous system injury and hemorrhagic shock with little or no direct trauma to the heart.

In major trauma, multiple injuries frequently coexist with BCI. The perioperative physician must be able to do the following:

- Anticipate cardiac-induced hemodynamic and rhythm abnormalities that may occur despite an initial stable clinical course
- Determine the contribution of cardiac trauma to the overall circulatory abnormality caused by hemorrhage, hypothermia, acid-base and electrolyte abnormalities, or various other causes
- Implement the most appropriate management based on these findings

The incidence of BCI in blunt thoracic trauma is approximately 20%, although it may be 76% in severe injuries. Nevertheless, major cardiac complications requiring treatment are considerably less likely to occur; however, when they do happen, they may be fatal.

### Diagnosis

BCI may be associated with direct precordial impact, crush injury of the chest causing compression of the heart between the sternum and the spine, deceleration injuries, and blast injuries. Suggestive signs and symptoms include chest pain, angina responding to nitroglycerin, dyspnea, chest wall ecchymosis, and fractures of ribs or sternum or both. There is no "gold standard" for diagnosing blunt cardiac trauma. However, ECG, blood concentration of troponin I, and echocardiography are important. In addition, coronary angiography or ventriculography may rarely be indicated to diagnose coronary lesions, cardiac rupture, or valve injuries.

A 12-lead ECG is the best screening test. Nonspecific changes, such as tachycardia, bradycardia, or occasional atrial or ventricular premature contractions, occur in 50%–70% of patients and usually do not require treatment. More serious alterations, such as ST or T wave changes, conduction delays, and complex atrial and ventricular dysrhythmias, occur less frequently (4%–30%) but often need to be treated. Although sensitive, ECG is not specific, and a normal tracing cannot rule out BCI. The right ventricle, because of its anterior position, is injured more frequently than the left. Standard leads, which are primarily useful to detect left-sided abnormalities, miss some right heart events. Overall, the sensitivity, specificity, and negative predictive value of ECG for predicting cardiac complications are 100%, 47%, and 90%, respectively. Although delayed (>24 hours) appearance of serious ECG abnormalities may very rarely occur, a normal ECG on admission virtually eliminates the risk of complications of blunt cardiac trauma and the need for further evaluation, as long as the patient is hemodynamically stable, has no history of cardiac disease, is <55 years old, and does not have multiple injuries or significant chest wall trauma. However, if these compromising conditions exist, cardiac monitoring for at least 24 hours in a telemetry ward or intensive care unit is indicated. An abnormal ECG should be followed by continuous cardiac monitoring. Additionally, obtaining serum troponin I concentration 6 and 12 hours after the injury in hemodynamically stable patients and echocardiography in hemodynamically unstable patients should be considered.

Serum creatine kinase (CK) and CK-MB determinations, which were frequently used to diagnose myocardial contusion, are no longer performed because of their low specificity. Skeletal muscle, colon, lung, liver, and pancreatic tissue contain both CK and CK-MB. In patients with multiple trauma, a positive value may not indicate cardiac injury. Troponin I is specific for cardiac muscle. However, negative levels of CK-MB or troponin I do not rule out clinically relevant BCI because muscle disintegration is not significant enough in many patients with cardiac trauma to release detectable enzyme levels. Yet even a small area of myocardial damage can cause dysrhythmias, if it is in a critical location.

Echocardiography may be helpful in many ways in BCI. It provides information about myocardial function (e.g., wall motion abnormalities, increased end-diastolic wall thickness), cardiac structural abnormalities (e.g., echodense areas on the ventricular walls, valve malfunction, hemopericardium, intracardiac thrombi), cardiac preload (e.g., end-diastolic area), systolic cardiac function (e.g., fractional ventricular area change), and air embolism (e.g., air bubbles in the cardiac chambers, patent foramen ovale). Echocardiography can help not only with the diagnosis of BCI but also in hemodynamic management. TEE is a much more valuable monitor than TTE, whose usefulness is limited by mechanical ventilation, pleural effusion, pneumothorax, and difficulty in placing the patient in left lateral decubitus position. Myocardial contusion, hemopericardium, valvular lesions, hemomediastinum, and aortic rupture are more likely to be recognized with TEE than with TTE. Nevertheless, it is important to eliminate esophageal injury before attempting TEE in patients with chest trauma. Dysrhythmias, unexplained hypotension, and heart failure are definite indications for TTE or TEE evaluation.

### *Perioperative Management*

Depending on its type and extent, BCI can increase surgical risk. Although most patients with cardiac chamber perforation do not reach the hospital, some, especially patients with atrial lesions, may arrive in the operating room. Preoperative information about the nature of injury is important. Some retrospective reports have documented an increased incidence of intraoperative dysrhythmias and hypotension in patients with preoperatively diagnosed myocardial contusion. It is unclear whether these occurrences were due to the myocardial injury itself or to the complications of associated injuries. Nevertheless, the combination of atrial fibrillation, old age, and aortic rupture with myocardial contusion appears to increase perioperative mortality. The duration of complications is also a relevant issue for the anesthesiologist because many trauma patients present days to months after injury. In most patients, dysrhythmias last no more than a few days. Ventricular wall motion abnormalities may persist for 1 year, but any increased risk of perioperative complications appears to last for no more than 1 month. An intracardiac thrombus, a well-known complication of myocardial contusion, may be present >1 year after injury, further emphasizing the need for preoperative echocardiography even well after the accident.

The clinical presentation of patients with BCI varies; sometimes more than one compromising condition may be present in the same patient. Orliguet et al. proposed an algorithm describing the management principles for each of these scenarios (Figure 75-5). Dysrhythmias appear to respond readily to antiarrhythmic agents. Hypotension may be caused by hypovolemia, pump failure, or both. Fluid loading, with monitoring of cardiac function by echocardiography or right heart catheterization, improves hypovolemia. Pump failure is usually caused by right ventricular dysfunction exacerbated by increased pulmonary vascular resistance secondary to pulmonary contusion, aspiration of gastric contents, or ARDS. An initial right ventricular free wall dilation may be followed by leftward ventricular septal shift, which alters the geometry and compliance of the left ventricle, increasing left ventricular filling pressure and decreasing cardiac output. This condition should by no means be a signal to decrease fluid loading. On the contrary, volume replacement should continue with concomitant use of inotropes and pulmonary vasodilators. Positive pressure ventilation may also be adjusted to minimize intrathoracic pressure and right ventricular afterload. High-frequency jet ventilation or oscillation with its relatively low mean airway pressure may be beneficial in these circumstances. As shown in the algorithm, hemopericardium is treated by drainage, either surgically or by placement of a large-bore catheter with echocardiographic guidance. Anticoagulants, if used, should be stopped. Myocardial infarction and valvular, septal, and coronary vascular injuries are treated in the same way as they would be in the absence of trauma. Severe trauma may dictate surgery before angioplasty, coronary artery bypass, repair of injured cardiac valves, or closing a septal defect.

Rarely, pump failure may be unresponsive to pharmacologic measures and requires cardiac assistance. The ventricular balloon pump has been used in these rare

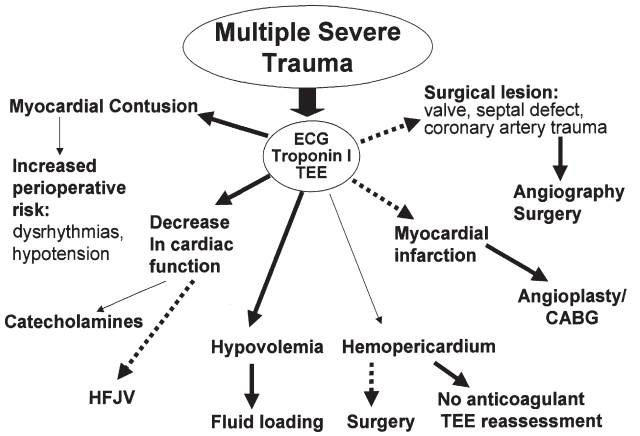


**FIGURE 75-5** ■ Algorithm for management of various clinical scenarios produced by severe BCI. Multiple severe trauma-induced BCI is evaluated with ECG, troponin I, and TEE. *Arrows* represent the frequency of occurrence of each scenario and the frequency of management measures. *Thick arrows* represent high-frequency occurrences, *thin arrows* represent low-frequency occurrences, and *dotted arrows* represent very rare occurrences. *BCI,* Blunt cardiac injury; *CABG,* Coronary artery bypass graft; *ECG,* electrocardiogram; *HFJV,* high-frequency jet ventilation; *TEE,* transesophageal echocardiography. (Adapted from Orliaguet G, Ferjani M, Riou G: The heart in blunt trauma. Anesthesiology 95:544, 2001.)

cases of BCI. However, in most patients, dysfunction originates from the right ventricle. If assistance is needed, biventricular assist devices would be preferable.

### 7. When should traumatic thoracic aortic injury be suspected, and how is it diagnosed?

Traumatic thoracic cardiovascular injury is a potentially lethal sequela of chest trauma, associated with an almost 80% mortality in the first hour after injury. It should be suspected in every patient with blunt chest trauma. Most patients sustain thoracic vascular injury from sudden deceleration after a motor vehicle or motorcycle accident, free falls, or auto versus pedestrian accidents. Other mechanisms, such as sudden compression of the thoracic vessels between the spine and sternum or ribs, can also produce this injury. In almost 90% of cases, the aorta is injured at the isthmus, the junction of its free and fixed portions, which is distal to the origin of the subclavian artery (Box 75-4). Most isthmus injuries occur at the medial aspect of the aorta and are thought to result from sudden increases in intraluminal pressure (>1000 mm Hg) and rotation of the vessel.

Injuries to the ascending portion and the aortic arch are much less frequent than isthmic injuries. The likelihood of ascending aortic injury is enhanced by a history of violent deceleration; impact to the side of a vehicle involved in an accident; ejection of an unrestrained passenger; death of anyone involved in the accident; a motor vehicle and pedestrian or bicycle collision; or the presence of high-impact injuries such as diaphragmatic rupture, mesenteric tear, or pelvic fracture. In the presence of pelvic fracture, the overall incidence of blunt aortic injury increases from <0.5% to 1.4%. Additionally, a patient with chest trauma who develops unexplained hypotension, external signs of direct chest injury, a pulse deficit between the right and left arms or between the upper and lower extremities, a requirement for mechanical ventilation, retrosternal or interscapular pain, hoarseness, precordial systolic murmur, or lower extremity neurologic deficit may also have an aortic injury (Box 75-4).

The radiologic diagnosis of blunt aortic injury has changed over the last decade. Although all patients with major trauma receive a routine supine chest radiograph, findings with this diagnostic modality are not reliable enough to confirm or eliminate blunt aortic injury. For example, in only 20%–30% of instances is mediastinal widening (i.e., >8 cm at the level of the aortic knob) on anteroposterior chest films associated with thoracic aortic injury. Bleeding from the neck vessels or vertebra into the mediastinum can produce a similar image. Absence of mediastinal widening also is unreliable because many patients who reach the hospital have a contained aortic injury without much extravasation. Other chest radiographic findings suggestive of aortic injury are blurred aortic contour, wide paraspinal interface, opacified pulmonary window, broad paratracheal stripe, displaced left main stem bronchus, rightward deviation of the esophagus (or a nasogastric tube) and trachea, left apical pleural hematoma (pleural cap), and left hemothorax (Box 75-5).

Contrast-enhanced spiral CT and multiplanar TEE are highly accurate and are the screening methods used currently. CT findings of traumatic aortic injury include polypoid or linear intraluminal areas of low attenuation suggesting clot or medial flap, false aneurysm, irregular aortic wall or contour, pseudocoarctation, intramural hematoma, and aortic dissection.

**BOX 75-4 Traumatic Thoracic Aortic Injury**

**Mechanism of Injury**

Sudden body deceleration
Compression of thoracic vessels between spine and ribs/sternum

**Site of Injury**

Aortic isthmus (90%)
Ascending aorta
Aortic arch

**Suspicious of Injury**

Unexplained hypotension
Evidence of direct chest injury
Pulse deficits
- Between right and left upper extremities
- Between upper and lower extremities
- Mechanical ventilation

Retrosternal or interscapular pain
Hoarseness
Systolic precordial flow murmur
Lower extremity neurologic deficits

**BOX 75-5 Traumatic Thoracic Aortic Injury: Radiographic Findings**

**Chest Radiograph**

Mediastinal widening
Blurred aortic contours
Wide paraspinal interface
Opacified pulmonary window
Broad paratracheal stripe
Displaced left main stem bronchus
Right deviation of esophagus and trachea
Left hemothorax

**Contrast-Enhanced CT Scan**

Polypoid or linear intraluminal areas of low attenuation
False aneurysm
Irregular aortic wall or contour
Pseudocoarctation
Intraluminal hematoma
Aortic dissection

**TEE**

Dilated aortic isthmus with abnormal contour
Acute false aneurysm formation
Intraluminal medial flap
Mobile image appended to thoracic aortic wall
Crescentic or circumferential thickening of the aortic wall

**CT Angiography with Three-Dimensional Reformation**

Directly indicates location and type of lesion (Figure 75-7)

*CT*, Computed tomography; *TEE*, transesophageal echocardiography.

Both CT and TEE are capable of diagnosing aortic injuries that require surgical intervention or conservative management. However, because of its relative invasiveness, conflict about its accuracy, and special skill sets that may be unavailable after hours, TEE has not become a routine screening method. Nevertheless, TEE is valuable in many instances. Most patients do not have major aortic tears, and their hemodynamic abnormality generally originates from other injuries, such as to the spleen or liver, which require immediate surgery without time for further evaluation of the chest. Intraoperative TEE in these instances eliminates uncertainty about the presence of traumatic aortic injury and permits appropriate intervention for other problems while the diagnosis is made by the anesthesiologist.

TEE findings of traumatic thoracic aortic injury include (Figure 75-6) the following:

- Grade 3
  - Dilated aortic isthmus with abnormal contour or acute false aneurysm formation
- Grade 2
  - Intraluminal medial flap associated with subadventitial disruption
- Grade 1
  - Mobile flap attached to the thoracic aortic wall consistent with an intimal tear or a mural thrombus
  - Crescentic or circumferential thickening of the aortic wall suggesting the presence of intramural hematoma

In addition, traumatic hemomediastinum should be considered if the distance between the esophageal probe and the anteromedial wall of the aortic isthmus is >3 mm, or if there is blood between the posterolateral aortic wall and the left visceral pleura. A left-sided hemothorax can be detected if there is blood between the left lung and the thoracic wall. Aortic branch injuries are difficult to detect by TEE. In patients with suspected esophageal injuries, TEE is contraindicated. These patients frequently present with bloody nasogastric tube drainage, severe facial trauma, unstable cervical spine injuries, and pneumoperitoneum.

Definitive diagnosis of a blunt aortic injury is currently made by CT angiography (see Box 75-5). It provides detailed information about the injury, aiding treatment decisions. Multidetector CT scans with three-dimensional reformation have replaced invasive aortography, which was the standard diagnostic method about a decade ago (Figure 75-7).

## 8. How is surgery prioritized in patients with blunt trauma and multiple injuries that include thoracic aortic damage?

Patients with complete or nearly complete circumferential transection of all three layers of the aortic wall are unlikely to arrive in the operating room. These patients die either in the field or in the hospital within 4–6 hours. Patients who survive to surgery with this pathology generally have a small perforation, a partial transection that is temporarily sealed with perivascular clot, or a relatively large transection that bleeds at a relatively slow rate because of hypotension and possibly perivascular barriers such as adjacent tissues or clot sealing the lesion. In our experience, a patient experiencing a 70% transection of the aortic circumference survived until surgery. Most patients who arrive in the operating room have relatively small, sealed, subadventitial, usually posterior wall, injuries, which require intervention because of impending rupture. In

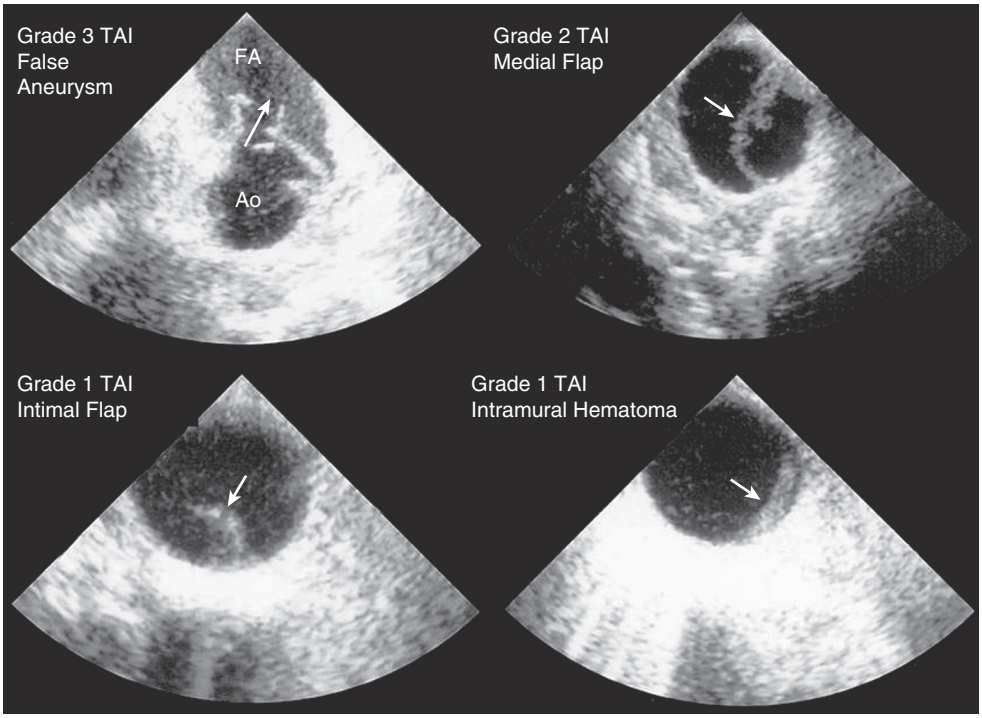


**FIGURE 75-6** ■ TEE images of grades 1, 2, and 3 traumatic thoracic aortic injury (*TAI*). *Ao,* aorta; *FA,* false aneurysm. (From Goarin J-P, Cluzel P, Gosgnach M, et al.: Evaluation of transesophageal echocardiography for diagnosis of traumatic aortic injury. Anesthesiology 93:1373, 2000.)

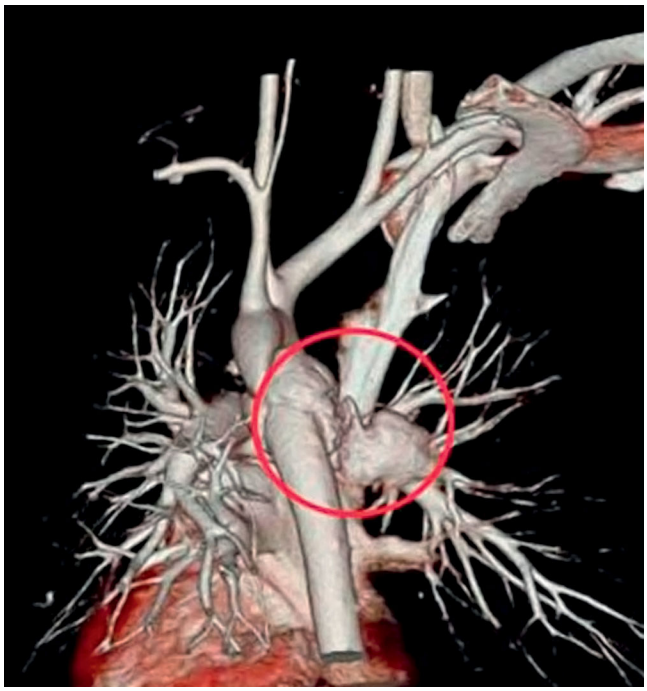

**FIGURE 75-7** ■ CT image with three-dimensional reformation of traumatic thoracic aortic injury with extravasation (*circle*). (From Demetriades D: Blunt thoracic aortic injuries: crossing the Rubicon. J Am Coll Surg 214:247, 2012.)

addition, a significant number of patients have intimal or medial layer injury, or both, which can be managed conservatively with CT scan follow-up in 2–4 weeks. Aortic injury may not heal in some of these patients within this period of time, and intervention is required on an elective basis.

The concept that blunt thoracic aortic injury universally requires emergency intervention has changed during the past decade. A thoracic aortic injury with active bleeding from the site is a life-threatening emergency and necessitates immediate surgery. Hemodynamically stable patients with contained periaortic hematomas require immediate BP control to prevent rupture. In the rare instance when this type of aortic injury manifests as an isolated entity, emergency intervention after CT evaluation is indicated within a few hours of trauma.

Patients with unstable associated injuries and a stable aortic injury first must be treated with stabilization of the other injuries. For example, traumatic intracranial lesions and gross bleeding into body cavities are more emergent than stable aortic injuries verified by CT scan. In most instances, hypotension in these patients is caused by associated injuries rather than the aortic injury, and rushing these patients to the operating room without radiologic investigation may increase morbidity and mortality. As mentioned, TEE helps to determine the extent of aortic injury intraoperatively under these circumstances while other injuries are managed. There is ample evidence to support delayed (few days) versus early (approximately 10 hours) repair. In an American Association for the Surgery of Trauma (AAST)–sponsored study in which the groups compared were similar in injury severity, major associated injuries, type of aortic injury, and type of aortic repair (conventional vs. endovascular), mortality was higher (22%) in the early group compared with the delayed intervention group (3%). The beneficial effect of delayed repair may be related to operating under more optimal patient-related and environment-related factors. Delayed repair has become the standard of care in patients with stable thoracic aortic injury.

Actively bleeding aortic injuries with hemodynamic instability have the highest surgical priority. If an unstable aortic injury occurs concomitantly with unstable abdominal, pelvic, or head injury, which is a rare event, simultaneous intervention may be considered. In the absence of unstable associated injuries, the aortic injury should be repaired as early as possible once optimal patient-related and facility-related conditions are established.

Surgical repair of the thoracic aorta requires clamping of the vessel. In the presence of intracranial pathology, this maneuver may result in an uncontrollable increase in intracranial pressure. A significant intracranial hematoma must be evacuated with at least a burr hole. For small intracranial traumatic lesions, monitoring of the intracranial pressure during aortic repair may suffice.

## 9. What are the current management strategies for blunt aortic injury?

The most important aim in initial care of blunt aortic injury is to decrease shearing force or viscous drag of blood flow on injured vessel walls. This aim is achieved by reducing myocardial contractility and maintaining the lowest systemic BP acceptable for tissue perfusion and oxygenation. Drugs used to achieve this goal include β-adrenergic blockers, calcium-channel blockers, and nitroglycerin.

Two new management techniques have almost replaced the conventional surgical management of aortic injuries during the past decade. The first of these strategies involves the use of endovascular repair, which, compared with conventional surgery, is associated with decreased blood loss, reduced mortality, improved tolerance by high-risk patients, and significantly lower risk of paraplegia. It also may preclude the need for general anesthesia and a double-lumen endotracheal tube. Sedation and local anesthesia may suffice in many instances (Table 75-1). For example, the currently reported overall mortality rate of blunt aortic injury with open repair is 23% compared with 7% for endovascular repair. This difference is of higher significance when controlled for age, hypotension, Glasgow Coma Scale, and extrathoracic injuries. Likewise, the rate of paraplegia, which is 6%–19% with open repair, is reduced to <1% with the endovascular technique. Because of these salutary effects, the length of intensive care unit and hospital stay in patients with relatively mild associated injuries is also shorter. However, there are short-term complications associated with endovascular surgery. These include stent-related complications such as endoleak or graft collapse, iliac or femoral artery injury during access causing bleeding intraoperatively or postoperatively, stroke, and left common carotid artery occlusion. Operator experience and the volume of thoracic trauma managed in a

TABLE 75-1 **Change in Management of Blunt Thoracic Aortic Injuries from 1997 to 2007**

| | AAST1 (N = 253) | AAST2 (N = 193) |
|---|---|---|
| **Diagnosis** | | |
| Aortogram | 220 (87%) | 16 (8%) |
| CT scan | 88 (35%) | 180 (93%) |
| TEE | 30 (12%) | 2 (1%) |
| **Repair** | | |
| Open | 207 (100%) | 68 (35%) |
| Endovascular | — | 125 (65%) |
| **Outcomes** | | |
| Mortality | 53/241 (22%) | 25/193 (13%) |
| Paraplegia | | |
| All patients | 18 (9%) | 2 (2%) |
| Open repair | 18 (9%) | 2 (3%) |
| Endovascular | 0 | 1/125 (1%) |
| Renal failure | 18 (9%) | 17 (9%) |
| Repair site complication | 1/207 (1%) | 25/125 (20%) |

*AAST1,* American Association for the Surgery of Trauma 1997 study; *AAST2,* American Association for the Surgery of Trauma 2007 study; *CT,* computed tomography; *TEE,* transesophageal echocardiography.

From Demetriades D, Velmahos GC, Scalea TM, et al.: Diagnosis and treatment of blunt thoracic aortic injuries: changing perspectives. J Trauma 64:1415, 2008.

specific center probably has some effect on the rate of these complications. Although the short-term results of endovascular management are clearly superior to conventional open repair, there is little information about its long-term outlook.

The second relatively new strategy is conservative nonoperative treatment of grades 1 and 2 injuries involving intramural hematomas or intimal tears. Observation with CT scans and BP control appears to suffice for safe management of these patients. Although endovascular and conservative techniques are currently employed in the management of most blunt aortic injuries, open repair is still used in some centers. Specific pitfalls and their management are discussed next.

## 10. What are the perioperative clinical and anesthetic pitfalls that can be encountered during management of patients with thoracic aortic injuries, and how should they be managed?

### *Diagnostic Pitfalls*

More obvious coexisting injuries, failure to obtain appropriate studies, and misinterpretation of radiographic findings may result in diagnostic difficulties. For example, an initially missed aortic injury may be recognized a few days later during emergency sternotomy to relieve cardiac tamponade and to control bleeding caused by cardiac free wall rupture. Likewise, as we have experienced in the past, an aortic injury may be recognized a few days after injury by spiral CT or during the late phase of a pulmonary angiogram obtained to rule out pulmonary embolism.

### *Airway Management Pitfalls*

Airway management difficulties may be encountered for several reasons. Bleeding from the aorta can reach the prevertebral space. A hematoma in this area could shift the larynx and trachea anteriorly, creating difficulty during laryngoscopy and intubation. Prevertebral hematomas are easily detected by cervical CT or lateral neck film. Laryngoscopic visualization may be difficult in the presence of a cervical collar because of limited neck extension. Combined with a prevertebral hematoma, limited neck extension complicates conventional laryngoscopy. However, neck extension should be avoided not only because of the possibility of cervical spine injury but also to prevent sudden hemorrhage from an aortic arch injury. A perivascular hematoma that seals the injury could be distracted by extension of the neck.

Subadventitial and perivascular hematomas or pseudoaneurysms may compress the left main stem bronchus and cause narrowing of its lumen. Double-lumen tubes have the advantage of preventing spillage of blood into the right bronchus from the left lung during dissection of the aorta. However, forcing a left-sided endobronchial tube blindly into the left main stem bronchus may result in a burst of peribronchial bleeding. Visualization of the left main stem bronchus with a fiberoptic bronchoscope before advancing the endobronchial tube can diagnose this potential problem.

### *Central Line Placement Pitfalls*

Bleeding into the left or rarely into the right hemithorax is a frequent complication of thoracic aortic rupture. A large quantity of blood sometimes may fill the pleural cavity, not only causing collapse of the lung and mediastinal shift but also giving false information when attempting to cannulate the internal jugular or subclavian vein. Free-flowing blood may not indicate vascular puncture; it may be secondary to entry into the blood-filled interpleural space. If this situation is not recognized, rapid infusion of fluids into the pleural space may result in catastrophic complications.

### *Pitfalls Related to Use of Anesthetic Drugs*

The primary goal of anesthetic management in patients with vascular injuries is to avoid bleeding from dislodgment of perivascular clots. This goal can be accomplished by deep anesthesia and complete muscle relaxation, which is easily accomplished in hemodynamically stable patients. However, deep anesthesia may not be possible in unstable trauma victims, who tolerate only oxygen, muscle relaxation, and possibly a minimal dose of intravenous anesthetic.

Another important objective of anesthesia is to decrease viscous drag, the frictional force of flowing blood against

the vascular wall, which may displace a clot sealing the site of injury. It is proportional to viscosity and blood flow and inversely proportional to the fourth power of the radius. It is important to decrease the force of myocardial contraction. In a young, healthy patient, force of cardiac contraction may increase to maximum levels to compensate for hypovolemia. Interfering with compensatory mechanisms could produce a catastrophic outcome. These conflicting objectives may be addressed by careful titration of the anesthetic while monitoring myocardial contractility with TEE and measurement of systemic BP. Control of BP in the preoperative period and before clamping of the aorta during surgery is crucial to prevent rupture. Preoperative β-adrenergic blocking or calcium channel–blocking agents with or without sodium nitroprusside can usually maintain systolic BP at 80–90 mm Hg.

As discussed previously, the surgical mortality rate from traumatic aortic injury averages 20% (range, 5%–35%). Mortality appears to correlate with patient age, preoperative hypotension, delayed diagnosis and late surgical treatment, and location of the lesion. Proximal aortic injuries have a greater mortality than isthmic injuries. Also injuries located <1 cm from the origin of the left subclavian artery are associated with a greater likelihood of technical difficulty, rupture, and mortality during surgical manipulation than injuries in other locations.

### *Pitfalls Related to Spinal Cord Ischemia*

Spinal cord ischemia resulting in paraplegia or paraparesis is a well-known complication of thoracic aortic injury and its repair. A preoperative neurologic evaluation should be documented to avoid confusion about neurologic deficits after surgery. The blood supply to the spinal cord is from one anterior and two posterior spinal arteries, which originate from branches of the vertebral artery at the base of the skull and descend along the cord. The anterior spinal artery supplies the anterior two thirds and the posterior spinal arteries the posterior one third of the cord. Anastomoses between the anterior and posterior blood supply of the cord are weak, and there are areas with marginal blood supply within the spinal cord. The anterior spinal artery receives a few radicular branches that originate from the thoracic intercostals. The largest of those is the great radicular artery of Adamkiewicz (arterial radicularis magna).

There are two common mechanisms of spinal cord ischemia in traumatic aortic injury. The first is occlusion of a subclavian artery, which supplies the vertebral and the spinal arteries. Injury or surgical clamp placement during repair account for many of these cases. The second mechanism of spinal cord ischemia is surgical interference with intercostal vessels supplying the artery of Adamkiewicz. The blood supply to the artery of Adamkiewicz originates from the last four thoracic segments in 75% of patients, from L1 or L2 in 15%, and from the fifth to eighth intercostal arteries in 10%. Surgical technique is the likeliest cause of spinal cord injury in patients without a preoperative neurologic deficit or long periods of hypotension.

There are three techniques for surgical repair of aortic injuries: clamp and sew, passive shunting between proximal and distal aorta, and cardiopulmonary bypass. The last-mentioned may be achieved in several ways: partial femoral-femoral bypass, left heart bypass (left atrioaortic or atriofemoral), and right atrial-to-distal aortic bypass. The advantage of left or right atrial-to-distal aortic bypass techniques is that they can be used with minimal or no anticoagulation.

Clamping and sewing is associated with the highest rate of spinal cord complications. However, the incidence of paraplegia is lower if clamp time is <30 minutes. Passive shunt placement between proximal and distal aorta does not significantly decrease the incidence of neurologic deficit. Partial bypass (e.g., femoral-femoral) decreases the rate of paraplegia, but the need for heparinization is a significant disadvantage. Left atriofemoral bypass is more frequently used than left atrioaortic or right atrioaortic techniques. If used with a centrifugal pump, these approaches result in the best spinal cord protection. Heparin-bound cannulas are used, which obviate the need for systemic heparinization. Left heart bypass also has two important additional advantages in that unloading of the left heart may decrease cardiac complications and possibly decreases ischemic reperfusion injury. The particular surgical technique is dictated by surgeon preference and other associated injuries.

## 11. Describe the clinical management of transmediastinal gunshot wounds.

Injuries to internal organs caused by this type of trauma are unpredictable. Any organ, even outside the thorax, may be injured depending on the path of the bullet. Penetrating trauma to the cardiac window, defined as a quadrangle bounded by the midclavicular lines laterally, the clavicles superiorly, and eleventh ribs inferiorly, is highly likely to damage the heart. Evaluation must include not only the heart but also the other intrathoracic organs. Diagnostic algorithms for transmediastinal gunshot wounds recommend transferring unstable patients directly to the operating room. Stable patients may be evaluated by chest radiograph, transthoracic ultrasound, and spiral CT. A patient with abnormal ultrasound findings should be transferred directly to the operating room. Patients with abnormal spiral CT findings may need further study with esophagography, angiography, bronchoscopy, or esophagoscopy. Positive findings in any of these examinations requires surgery.

Patients with penetrating injury and, to a lesser extent, blunt injury who require intubation and ventilation may develop systemic air embolism. This complication results from entry of higher pressure alveolar air into injured lower pressure pulmonary veins. Clinical signs and symptoms of this frequently fatal complication include sudden cyanosis, hypotension, cardiac arrest, loss of consciousness, and air bubbles in the radial, retinal, or coronary arteries. Although surgical measures, such as emergency thoracotomy and clamping the hilum of the lacerated lung, have been recommended, the immediate measure to minimize further embolism is to ventilate with the lowest possible peak inspiratory pressure. Placement of a double-lumen tube or a bronchial blocker to isolate and avoid ventilation to the injured lung is another measure when time and equipment become available.

Anesthetic management of these patients is challenging. The requirement for massive fluid and blood replacement necessitates insertion of large-bore intravenous lines. Abnormal coagulation requires factor and platelet replacement. Airway management may be difficult because of airway injury or mediastinal shift from hematoma, often necessitating fiberoptic-guided intubation to avoid entry into a false passage. Acid-base and electrolyte balance should be maintained. Cardiac injuries must be repaired immediately, possibly requiring cardiopulmonary bypass for safe repair of major coronary artery injuries.

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CASE 76

# Burns

Jaroslav Usenko, MD

## QUESTIONS

1. What is the epidemiology of burns in the United States?
2. Describe how burns are classified, how the percentage of total body surface area burned is estimated, and the extent of injury that occurs with different burn depths.
3. Which patients require care in specialized burn centers?
4. What is the pathophysiology of burn injury, what are the local and systemic effects, and how do burns affect different organ systems?
5. What fluid should be used for fluid resuscitation of a burn patient, and what are the possible complications of fluid resuscitation?
6. What is smoke inhalation injury, what are the implications of inhalation injury, and how is inhalation injury managed?
7. What is the pathophysiology of carbon monoxide poisoning, and how is carbon monoxide poisoning treated?
8. What is cyanide poisoning, and how is it treated?
9. Explain the concept of direct thermal upper airway injury, when it is suspected, and its consequences.
10. What techniques may be used to secure the airway for airway management of burn patients, and is succinylcholine acceptable for rapid-sequence intubation?
11. Explain the surgical management of burns, discuss the timing of surgery, and identify anesthetic considerations for burn surgery.

A 52-year-old man was brought to the emergency department by ambulance after being injured in a house fire, and you were asked to assess him for inhalation injury and to assist with airway management. The patient's injuries appeared to be partial-thickness burns to both upper arms, most of the anterior trunk, and right thigh. His vital signs were heart rate 108 beats per minute, respiratory rate 25 breaths per minute, blood pressure 158/92 mm Hg, and oxygen saturation 93% with supplemental oxygen by nasal cannula. When he complained of pain, his voice sounded hoarse, and you noticed carbonaceous sputum.

## 1. What is the epidemiology of burns in the United States?

Burns (thermal injuries) cause many complications and deaths. In the United States, >1.2 million people sustain thermal injuries every year. Most cases are minor, but approximately 50,000 burn cases are moderate to severe and require hospitalizations. Of these cases, 4000–5000 patients die from complications of thermal injury.

Deaths resulting from burns usually occur in a bimodal distribution—either immediately after injury or weeks later, from multiorgan failure. About one third of burn-related injuries and deaths occur in children. House fires account for 75% of all burn-related deaths.

Morbidity and mortality rates associated with thermal injury are decreasing; deaths and hospital admissions in the United States declined 50% over a 20-year period. This decline is attributed to prevention efforts resulting in a decreased number of patients with potentially fatal burns and improvements in the clinical care of patients with severe burns.

## 2. Describe how burns are classified, how the percentage of total body surface area burned is estimated, and the extent of injury that occurs with different burn depths.

Burns are classified according to the total body surface area (TBSA) involved, the depth of burn, and the presence or absence of inhalation injury. Additionally, burns are classified into five causal categories, as follows: injury from flame, hot liquids (scald), hot or cold, chemicals, and electricity.

The TBSA burned is calculated using the rule of nines (Figure 76-1). In adults, each upper extremity and the head and neck are 9% each of the TBSA, the lower extremities and the anterior and posterior aspects of the trunk are 18% each of the TBSA, and the perineum and genitalia are 1% of the TBSA. Children have a larger proportion of body surface area contributed by the head and neck relative to the surface area of the lower extremities. The Lund-Browder chart can be used to estimate the TBSA in children (Figure 76-2).

Burn depth is classified according to the degree of injury in the epidermis, dermis, subcutaneous fat, and

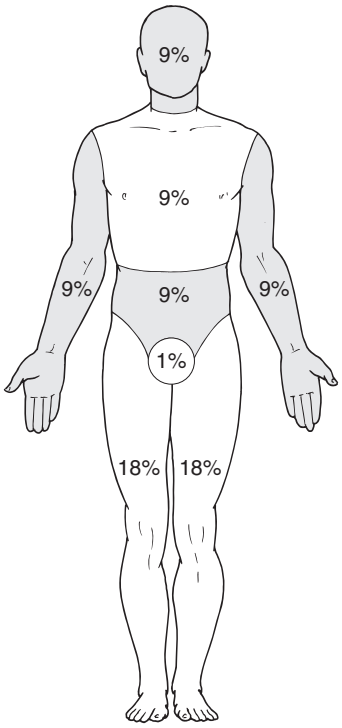
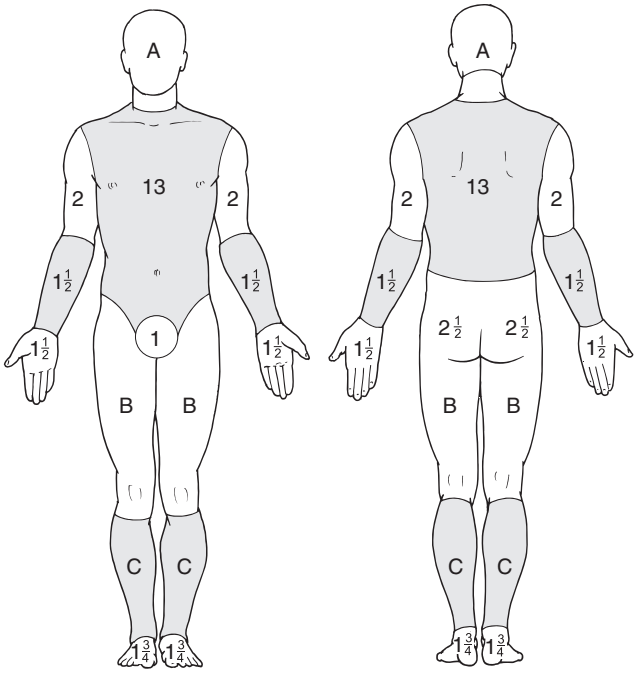



**FIGURE 76-1 ■ Rule of nines for determining the percentage of body surface area burned in adults.** (Adapted from MacLennan N, Heimbach DM, Cullen BF. Anesthesia for major thermal injury. Anesthesiology 1998;89(3):749–70.)




Relative percentage of areas affected by growth

| | (Age in years) | | | | | |
|---|---|---|---|---|---|---|
| Area | 0 | 1 | 5 | 10 | 15 | Adult |
| A: Half of head | 9-½ | 8-½ | 6-½ | 5-½ | 4-½ | 3-½ |
| B: Half of thigh | 2-¾ | 3-¼ | 4 | 4-¼ | 4-½ | 4-¾ |
| C: Half of leg | 2-½ | 2-½ | 2-¾ | 3 | 3-¼ | 3-½ |

**FIGURE 76-2 ■ Lund-Browder chart for determining percentage of body surface area in children.** (Adapted from MacLennan N, Heimbach DM, Cullen BF: Anesthesia for major thermal injury. Anesthesiology 89(3):749–770, 1998.)

underlying structures (Table 76-1). First-degree burns are confined to the epidermis, are painful and erythematous, and do not result in scarring. Second-degree or partial-thickness burns are classified further as superficial and deep. Superficial second-degree burns are erythematous and painful, spontaneously heal in 7–14 days, and may result in skin discoloration. Deep second-degree burns appear pale and mottled but remain painful to pinprick, heal in 14–35 days by reepithelialization, and often result in severe scarring. Third-degree or full-thickness burns are characterized by eschar that is painless and black, white, or cherry red and result in scarring and some limitation of function. Fourth-degree burns involve organs beneath the skin, such as muscle and bone; require complete excision; and result in limited function.

Burn depth is most accurately assessed by the clinical judgment of experienced practitioners. It is important to determine burn depth accurately because of implications for management.

## 3. Which patients require care in specialized burn centers?

Specialized burn centers offer resources and experienced personnel that can optimize outcome after thermal injury. The American Burn Association established the following criteria to determine which burn patients should be acutely transferred to a burn center:

- Greater than 10% TBSA partial-thickness burns
- Full-thickness burns of any size
- Involvement of special areas of function or cosmesis (face, hands, feet, genitalia, perineum, or major joints)
- Smoke inhalation injury
- Serious chemical injury
- Electrical injury including lightning
- Trauma where burns are the major problem
- Pediatric patients if the referring hospital has no specific pediatric capabilities
- Smaller burns in patients with multiple comorbidities

The above-listed criteria also define the components of a major burn injury.

## 4. What is the pathophysiology of burn injury, what are the local and systemic effects, and how do burns affect different organ systems?

Burns cause coagulative necrosis of the epidermis and underlying tissues with the depth of injury determined by the temperature and duration of exposure. After the initial focus of injury is removed, the response of local tissues can lead to injury in deeper layers. The area of injury is divided into three zones, as follows:

- *Coagulation* contains irreversibly damaged necrotic tissue.
- *Stasis* surrounds the necrotic zone and has a moderate degree of damage with decreased tissue perfusion.

TABLE 76-1 **Classification of Burns**

| Classification | Depth of Injury | Appearance/Sensation | Outcome |
|---|---|---|---|
| First degree | Epidermis | Erythematous<br>Painful | No scarring |
| Second degree (partial thickness) | | | |
| Superficial | Epidermis and superficial dermis | Erythematous<br>Painful | Heals in 7–14 days<br>Skin discoloration |
| Deep | Epidermis and into deep dermis | Pale, mottled<br>Painful to pinprick | Heals in 14–35 days<br>Severe scarring |
| Third degree (full thickness) | Epidermis, dermis, and into subcutaneous fat | Leathery eschar (black, white, or cherry red)<br>Painless | Requires excision<br>Scarring with some limitation of function |
| Fourth degree | Epidermis; dermis; subcutaneous fat; and into muscle, fascia, or bone | Brown, charred<br>Painless | Requires excision<br>Limitation of function |

Depending on the wound environment, the zone of stasis can either survive or progress to coagulative necrosis.

- *Hyperemia* is characterized by vasodilation from inflammation surrounding the burn wound and contains viable tissue from which the healing process begins.

Mediators released from the burn wound contribute to local inflammation and wound edema. Oxygen-free radicals, histamine, bradykinin, vasoactive amines, and interleukins have been implicated. In major burns, local injury triggers the release of inflammatory mediators into the circulation, resulting in a systemic response characterized by immune suppression, hypermetabolism, and protein catabolism. Systemic inflammation may progress to sepsis and multiorgan failure.

The cardiovascular system is affected by fluid shifts associated with major burn injury and effect of circulating mediators on contractility and systemic vascular resistance. Hypovolemic shock, described as burn shock, can occur immediately after a burn and primarily results from altered microvascular permeability of both burned and nonburned tissue in response to the above-described mediators. This altered microvascular permeability results in protein loss from the intravascular compartment to the interstitial compartment. There is also a marked transient decrease in interstitial pressure caused by the release of osmotically active particles, causing a vacuum effect whereby fluid is pulled in from the intravascular space. The rapid influx of fluid into the interstitium neutralizes the vacuum effect but does not prevent further edema formation. Finally, an increase in interstitial space compliance adds to changes in oncotic and hydrostatic pressures, exacerbating tissue edema formation further.

Initially, cardiac output is decreased independent of intravascular volume status. Cardiac contractility is reduced because of circulating mediators, decreased responsiveness to catecholamines, and decreased coronary blood flow. Systemic vascular resistance is increased. After successful resuscitation and the first 24–48 hours after burn injury, the cardiovascular response evolves into systemic inflammatory response syndrome, manifested by increased cardiac output and reduced systemic vascular resistance.

Burn injury affects the lungs directly and indirectly. Direct effects include upper airway obstruction and smoke inhalation injury (discussed in further detail subsequently). Indirect injury occurs as a result of the effects of circulating inflammatory mediators, complications of burn therapy, and infection. Pulmonary edema and pulmonary hypertension can also occur.

The kidneys are affected by diminished plasma volume and cardiac output. Increased levels of catecholamines, angiotensin, aldosterone, and vasopressin cause systemic vasoconstriction and contribute to renal dysfunction. Decreased renal blood flow and glomerular filtration rate result in oliguria, which, if left untreated, progresses to acute tubular necrosis and renal failure. Early resuscitation decreases the incidence of renal failure.

Mucosal atrophy, changes in digestive absorption, and increased intestinal permeability are gastrointestinal responses to a burn. The extent of atrophy of the small bowel mucosa is proportional to the burn size. There is reduced uptake of glucose and amino acids and decreased absorption of fatty acids. Gut permeability is increased further when burn wounds become infected. Gastric mucosal stress ulceration occurs with major burns but may be minimized by enteral feeding.

Hypermetabolism develops after major burns and resuscitation. It is characterized by tachycardia, increased cardiac output, elevated energy expenditure, increased oxygen consumption, increased carbon dioxide production, and catabolism. These changes in metabolism are due partly to release of catabolic hormones, which include catecholamines, glucocorticoids, and glucagon. The ambient temperature when below thermoneutral (28°–32° C) further increases metabolic rate in burn patients, and this should be avoided.

Burns cause global depression in immune function, which places burn patients at risk for infectious complications, including bacterial wound infection, pneumonia, sepsis, and multiorgan failure. Immune system impairment results from depressed cellular function in all parts of the immune system, including decreased activation and activity of neutrophils, macrophages, and T and B lymphocytes. When >20% of the TBSA

is affected by burns, impairment of immune function becomes proportional to burn size.

The hematologic and coagulation systems are affected by burns based on the magnitude of injury and time from injury. In the immediate injury, hematocrit increases as noncellular fluid moves to the interstitial space. Despite fluid resuscitation, hematocrit tends to remain elevated during the first 48 hours. Anemia then develops secondary to erythrocyte loss from wounds, bleeding during operations, and shortened erythrocyte half-life. Platelet counts are decreased secondary to dilution and formation of microaggregates. Both thrombotic and fibrinolytic mechanisms are activated after major burns. Table 76-2 summarizes the pathophysiologic effects of burns on different organ systems.

TABLE 76-2 **Pathophysiologic Effects of Major Burns**

| | |
|---|---|
| Cardiovascular | Early<br>Burn shock, hypovolemia<br>Impaired cardiac contractility<br>Late<br>Increased cardiac output, hypertension, tachycardia |
| Respiratory | Direct effects<br>Early<br>Upper airway obstruction<br>Smoke inhalation, asphyxia<br>Late<br>Chest wall restriction with thoracic burns<br>Indirect effects<br>Early<br>Effects of inflammatory mediators<br>Complications of resuscitation (pulmonary edema)<br>Late<br>Complications of ventilation ($O_2$ toxicity, barotrauma)<br>Complications of intubations (tracheal stenosis) |
| Metabolism | Increased metabolic rate<br>Increased $CO_2$ production and $O_2$ utilization<br>Impaired thermoregulation |
| Hematology and coagulation | Early<br>Hemoconcentration<br>Hemolysis<br>Activation of thrombotic and fibrinolytic systems<br>Late<br>Anemia |
| Renal | Early<br>Decreased renal blood flow and function<br>Myoglobinuria<br>Late<br>Increased renal blood flow<br>Variable drug clearance |
| Infection and immunity | Impaired immune function<br>Endotoxemia<br>Multiple organ failure |
| Gastrointestinal | Stress ulceration (Curling ulcers)<br>Impaired intestinal barrier function<br>Endotoxemia |

Adapted from MacLennan N, Heimbach DM, Cullen BF: Anesthesia for major thermal injury. Anesthesiology 89:749, 1998.
$CO_2$, carbon dioxide; $O_2$, oxygen.

## 5. What fluid should be used for fluid resuscitation of a burn patient, and what are the possible complications of fluid resuscitation?

Adequate resuscitation from burn shock is the most important intervention in burn treatment and should be initiated as soon as possible. Delays in initiating resuscitation of burned patients result in poorer outcomes and must be minimized. Lactated Ringer's solution most closely resembles normal body fluids and is usually the fluid of choice in adult burn patients. Lactated Ringer's solution with 5% dextrose should be considered in children <2 years old. Additional fluid options for resuscitation are discussed subsequently.

Several resuscitation formulas have been described; most rely on intravenous fluid administered in proportion to the TBSA. Any such formula should be regarded as a resuscitation guideline because all fluid resuscitation must ultimately be adjusted to individual patient needs. The most widely used formula, the Parkland formula, has been renamed the Consensus formula and is supported by the Advanced Burn Life Support curriculum for resuscitation in burn injury. The Consensus formula is:

$$4 \text{ mL/kg/\% TBSA}$$

The calculated amount is administered as lactated Ringer's solution in the first 24 hours after burn injury. Half of the fluid is administered in the first 8 hours, and the remaining half is given over the next 16 hours. For example, in a 70-kg patient with a 40% TBSA:

$$4 \text{ mL} \times 70 \times 40 = 11{,}200 \text{ mL}$$

Over the first 24 hours, 5600 mL is given over the first 8 hours (initial rate 700 mL per hour), and the remaining 5600 mL is given over the next 16 hours.

A child with a burn comparable with that of an adult requires more resuscitation fluid per kilogram. Modified formulas, such as the Galveston formula, are commonly used for children with burns to account for changes in the ratio of surface area to mass. The Galveston formula is:

$$5000 \text{ mL/m}^2 \text{ TBSA burned} + 2000 \text{ mL/m}^2 \text{ TBSA}$$

The calculated fluid is administered in the first 24 hours and accounts for both the maintenance needs and the increased fluid requirement of a child with a burn.

As discussed earlier, isotonic crystalloids, such as lactated Ringer's solution, are used most frequently as the primary resuscitation fluid. Most experts do not recommend colloids in the first 24 hours because they are no more effective than crystalloids in restoring intravascular volume; this may be due to increased vascular permeability after burn injury. Albumin and hypertonic saline warrant special mention. In a review of existing studies on the critical care of burn patients, Latenser (2009) concluded that there is no clinical advantage of using albumin, given conflicting results in the

literature. Similarly, the use of hypertonic saline has yielded disappointing results, with a fourfold increase in renal failure and a twofold increase in mortality compared with patients given lactated Ringer's solution.

Tissue edema is a hallmark of burn pathophysiology. Although fluid resuscitation can correct hypovolemia, it can also exacerbate edema. The possible consequence is increased compartment pressure in the extremities, the abdomen, and the orbit. The increased compartment pressures may progress to compartment syndromes, and require release by escharotomies. The abdominal compartment is clinically monitored with a Foley catheter and pressures greater than 30 mm Hg require interventions, such as escharotomy and possibly decompressive laparotomy.

Some burn patients do not respond to fluid resuscitation guided by the Consensus formula. Although it is sometimes impossible to predict accurately who will fail fluid resuscitation, patients with electrical burns, in whom resuscitation is delayed, and patients using alcohol or illicit drugs routinely require additional fluid. Patients with smoke inhalation injury, discussed in detail next, also frequently have increased fluid requirements.

### 6. What is smoke inhalation injury, what are the implications of inhalation injury, and how is inhalation injury managed?

Smoke inhalation injury results from toxins that cause chemical damage to the airway. Products of combustion, such as ammonia, nitrogen dioxide, sulfur dioxide, and chlorine, combine with water in the respiratory tract to produce strong acids and alkalis. These chemicals induce bronchospasm, edema, and mucous membrane ulceration. Another hallmark of inhalation injury is the separation of ciliated epithelial cells from the basement membrane, which contributes to exudate formation within the airway. The exudate eventually coalesces to form fibrin casts, which can be difficult to clear.

Patients who present with a history of a closed-space fire, such as in a small apartment or a car, are at high risk for smoke inhalation injury. Bronchoscopy is the "gold standard" for establishing the diagnosis. A clinical presentation of facial burns, singed nasal hairs, carbonaceous sputum, hoarseness, and respiratory distress increases the index of suspicion for inhalation injury. Each of these findings has poor sensitivity and specificity, but the presence of two or more of these clinical parameters increases the likelihood of positive bronchoscopic findings.

Smoke inhalation injury is a major factor that increases morbidity and mortality in burn patients. It increases the amount of time spent on mechanical ventilation. The addition of inhalation injury to a cutaneous burn of any size doubles mortality. Acute upper airway obstruction occurs in 20%–33% of hospitalized patients with inhalation injury and is a major hazard because of the risk of rapid progression from mild pharyngeal edema to complete upper airway obstruction. Early tracheal intubation may be necessary.

Inhalation injury complicates fluid management of burn patients. The presence of inhalation injury is associated with increased resuscitation fluid requirements. The pulmonary edema seen in smoke inhalation injury is not prevented by fluid restriction. However, although overhydration could increase pulmonary edema, inadequate fluid resuscitation increases the severity of pulmonary injury. Resuscitation is adequate if normal cardiac index or urine output is maintained.

The management of smoke inhalation injury is directed at maintaining airway patency and maximizing gas exchange. Care is primarily supportive. In burn patients intubated for airway protection or for respiratory failure, an important goal of mechanical ventilation is to minimize barotrauma. Current Adult Respiratory Distress Syndrome (ARDS) Network protocols are widely used to minimize positive airway pressure delivered by ventilators. Permissive hypercapnia may be used to help minimize plateau pressures. Arterial oxygen tension >60 mm Hg is acceptable to minimize oxygen toxicity to the lungs. Routine pneumonia prevention strategies should be employed. Prophylactic antibiotics for inhalation injury are not indicated. As patients recover from lung injury, tracheal extubation should be done as soon as clinically possible to minimize the occurrence of ventilator associated pneumonia and because the airway is more effectively cleared by patient coughing than by suctioning through an endotracheal tube. Additionally, prolonged intubation risks laryngeal and tracheal injuries.

### 7. What is the pathophysiology of carbon monoxide poisoning, and how is carbon monoxide poisoning treated?

Carbon monoxide is a major component of most open fires. It causes tissue hypoxia and metabolic acidosis by the following mechanisms:

- Carbon monoxide has 250 times more affinity for hemoglobin than oxygen does and, by displacing oxygen, decreases oxygen-carrying capacity of hemoglobin.
- Carbon monoxide shifts the oxyhemoglobin dissociation curve to the left, reducing the unloading of oxygen to the tissues.
- Carbon monoxide binds to cytochrome oxidase and impairs the activity of several intracellular enzymes.

Carbon monoxide poisoning should be considered in all patients who sustained burns in enclosed spaces. Patients who present with smoke inhalation injury are at high risk for carbon monoxide poisoning. Clinical presentation depends on carboxyhemoglobin levels (Table 76-3). Delayed neuropsychiatric sequelae have been described in patients exposed to toxic levels of carbon monoxide.

TABLE 76-3 **Carbon Monoxide Toxicity**

| Carboxyhemoglobin Level | Signs and Symptoms |
|---|---|
| <20% | Headache, tinnitus, nausea |
| 20%–40% | Weakness, drowsiness |
| >40% | Severe neurologic dysfunction (may be permanent), coma |
| 55%–70% | Cardiac dysrhythmias (often fatal), brain injury |

Carbon monoxide poisoning is diagnosed based on clinical findings and by measuring carboxyhemoglobin levels. Oxyhemoglobin saturation measured by commonly used pulse oximeters may be normal because the pulse oximeters read carboxyhemoglobin as saturated hemoglobin. A cooximeter, which measures the percentage of hemoglobin, oxyhemoglobin, carboxyhemoglobin, and methemoglobin, is necessary to obtain accurate oxygen saturations.

Carbon monoxide poisoning is treated with supplemental oxygen. The patient's inspired oxygen should be maintained at the highest possible concentration. A fractional concentration of oxygen of 1.0 in inspired gas decreases the blood half-life of carboxyhemoglobin from 4 hours, seen when breathing room air, to 60–90 minutes. Hyperbaric oxygen treatment further shortens the half-life of carboxyhemoglobin. Hyperbaric oxygen treatment should be considered in patients with carboxyhemoglobin levels >30%, if this poses no delay to or interference with treatment of other, more life-threatening injuries.

## 8. What is cyanide poisoning, and how is it treated?

Hydrogen cyanide is a product of the incomplete combustion of certain plastics and other synthetic materials. Cyanide may be inhaled or absorbed through mucous membranes. Cyanide causes tissue asphyxia by inhibiting cytochrome oxidase activity, which prevents mitochondrial oxygen consumption. Cyanide also interferes with the tricarboxylic acid cycle, causing affected cells to rely on anaerobic metabolism to generate adenosine triphosphate, which results in lactic acidosis.

Similar to carbon monoxide toxicity, a history of smoke inhalation and fire in an enclosed space raises the suspicion of cyanide toxicity. In fact, carbon monoxide toxicity, smoke inhalation injury, and cyanide poisoning may be present in the same patient. A definitive diagnosis can be made only by measuring the blood cyanide level. Symptoms range from dizziness, headache, and tachycardia to lethargy, seizures, and cardiopulmonary failure, depending on the blood cyanide level.

Initial treatment of cyanide toxicity is the administration of supplemental oxygen and hemodynamic support. The half-life of cyanide is about 1 hour. Specific antidotes exist, such as sodium thiosulfate, which accelerates hepatic metabolism of cyanide, and nitrites, which accelerate nonhepatic metabolic pathways by increasing levels of methemoglobin. However, there is some controversy as to whether specific treatments are necessary or helpful, given the short half-life of cyanide.

## 9. Explain the concept of direct thermal upper airway injury, when it is suspected, and its consequences.

Thermal upper airway injury results from inhalation of superheated air or steam. Heat is dispersed in the upper airways, so direct thermal injury to the lower airways and lungs is rare. Brief exposure of the epiglottis or larynx to either dry air at 300° C or steam at 100° C leads to airway edema.

Stridor, dysphonia, hoarseness, dysphagia, facial burns, and soot in the mouth or nose should raise the suspicion of thermal upper airway injury. The diagnosis can be confirmed with fiberoptic laryngoscopy, which provides direct information about glottic and periglottic structures. Fiberoptic bronchoscopy can provide information about the lower airways. Smoke inhalation injury, which is primarily a chemical injury, may also be present in a burn patient with thermal upper airway injury.

Glottic and periglottic edema that results from thermal upper airway injury may rapidly progress to complete airway obstruction. This is particularly concerning in pediatric patients, whose airways are of smaller diameter and may be occluded by minimal swelling. Prophylactic intubation may be required.

## 10. What techniques may be used to secure the airway for airway management of burn patients, and is succinylcholine acceptable for rapid-sequence intubation?

Airway management of burn patients requires a focused history and physical examination to assess whether the airway needs to be secured and to anticipate challenges in securing the airway. Information regarding the presence of preexisting airway abnormalities, a history of head and neck surgery, and a history of difficult airway management should be obtained. Burn patients should be evaluated for current airway injury and for signs of airway obstruction.

Once the information is obtained, an important management decision is to determine if the patient requires tracheal intubation. Patients with abnormal airways, signs of airway obstruction, or impending respiratory failure need prompt airway management. Intubation may be required for associated injuries or to facilitate emergency diagnostic studies and treatment when patients are agitated or uncooperative. There is also a role for prophylactic intubation in patients whose airway injuries are not immediately apparent if there are concerns for edema progression and rapid airway obstruction. It is generally better to intubate a burn patient early than late.

When it is decided a burn patient needs tracheal intubation, the technique depends on whether the airway is normal or abnormal. If there is no airway abnormality, tracheal intubation may be achieved with rapid-sequence induction in the emergency department trauma bay. Patients should continue to receive supplemental oxygen in preparation for intubation. An induction agent (type and dose based on the clinical situation) and a rapidly acting muscle relaxant (succinylcholine or rocuronium) are administered, followed by rapid intubation of the trachea with conventional direct laryngoscopy.

The use of succinylcholine warrants additional consideration. After a burn, extrajunctional acetylcholine receptors proliferate, which results in exaggerated release of potassium after administration of succinylcholine. Rapid elevations of serum potassium >9 mEq/L have been documented and are associated with cardiac arrest. The process of receptor proliferation takes several days, and there is an initial window of safety of unknown duration. The general agreement is that administration of succinylcholine is safe in the first 24 hours after a burn injury and should be avoided afterward.

In a cooperative adult burn patient with an abnormal airway or upper airway obstruction, an awake technique

may be selected. An awake intubation is most frequently achieved with a flexible fiberoptic bronchoscope. Adequate topical anesthesia is a key requirement for a successful awake intubation. Intravenous opioids may be appropriate for an alert patient in pain, and small doses of sedatives may be given to alleviate anxiety, but care must be taken to avoid exacerbating respiratory problems. Monitored transport to the operating room should be considered for patients with markedly abnormal airways. The operating room generally provides skilled assistance, multiple airway devices, and an anesthesia machine and is the best environment for a surgical airway should that become necessary.

Pediatric patients with abnormal airways present special challenges. Most young children do not cooperate with an awake technique. Inhalation induction with oxygen and a nonpungent volatile agent, such as sevoflurane, is likely to be the safest technique. Once the patient is anesthetized, several methods of intubation are available based on the experience of the anesthesiologist. A pediatric bronchoscope, a conventional laryngoscope, or one of the many airway devices currently available [GlideScope® (Verathon Inc. Bothell, WA), Airtraq optical laryngoscope (Airtraq, Fenton, MO), LMA Fastrach™ (LMA North America, Inc. San Diego, CA)] may be used. The key is to choose a device with which one is most skillful to facilitate urgent or emergent airway management.

### 11. Explain the surgical management of burns, discuss the timing of surgery, and identify anesthetic considerations for burn surgery.

Deep second-degree and third-degree burns do not heal in a timely fashion without surgery. The surgical management of burns involves excision of eschar and coverage of viable tissue with an autograft or temporary cover. Tangential excision and fascial excision are the two surgical approaches. In tangential excision, which is a procedure performed more frequently, thin slices of burn eschar are shaved sequentially with dermatomes until a healthy wound bed is developed. Blood loss is usually diffuse and can be large. Laparotomy pads soaked with epinephrine 1:100,000 are applied to the wound to control bleeding. Systemic absorption of epinephrine may cause tachycardia and increases the probability of dysrhythmias. Tourniquets are usually used to minimize blood loss for tangential excision of extremities.

Fascial excision involves removal of burn eschar and all the underlying fat en bloc to the level of muscle fascia or deeper structures. It can be performed more rapidly and with less blood loss than tangential excision. However, fascial excision results in marked cosmetic deformities and functional limitations. It is generally reserved for patients with fourth-degree burns or very extensive, life-threatening third-degree burns.

After excision of tissues and attainment of hemostasis, wounds are covered. An autograft is used for coverage when the wound bed is deemed suitable, a donor site is available, and the patient is stable. Wounds involving 20%–30% of the TBSA can usually be covered with an autograft of split-thickness skin, harvested from the patient's own donor site. Harvesting a split-thickness skin graft at the dermal level produces bleeding, which is controlled with epinephrine-soaked laparotomy pads. If an autograft is unavailable, temporary coverage with an allograft, xenograft, or biologic dressing is used.

Early excision and grafting of burn wounds is currently practiced because reports have shown benefits in terms of survival, incidence of sepsis, and length of hospitalization. One of the goals is to remove eschar, a potential nidus for inflammation and infection, before secondary sepsis supervenes. The excision usually starts on days 2–5 following the burn, after completion of fluid resuscitation, and is performed every 2–3 days, depending on the patient's condition.

Major burn surgery is usually performed under general endotracheal anesthesia. Regional anesthesia is often impractical given that an operation in a single patient may involve multiple excision and donor sites. Laryngeal mask airways may be considered for minor cases that are not expected to result in significant blood loss and when the anesthesiologist has access to the patient's airway.

Patients may be brought to the operating room already tracheally intubated. The anesthesiologist should note the position of the tracheal tube and ensure that it is properly secured, especially if patient positioning changes are anticipated for the case. In patients who are not intubated, an airway assessment should be performed, as with any patient requiring anesthesia. Specific airway considerations in burn patients have been discussed in detail earlier; however, it bears repeating that if muscle relaxation is used to facilitate airway management, succinylcholine must be avoided 24 hours after burn injury. Additionally, patients with large burns develop decreased sensitivity to nondepolarizing muscle relaxants and require 1.5 times the usual intubating dose.

Blood loss is a primary consideration during major burn surgery. Because blood loss can be rapid and massive, blood products should be available in the operating room before starting the case. Blood loss may be difficult to estimate because it is generally not collected into the suction canister. Vigilant monitoring and close communication with the surgical team are essential to provide timely resuscitation.

Hypothermia is another important consideration. Burn patients lose heat rapidly without intact skin and with large exposed surfaces. Hypothermia causes many complications and exacerbates hypermetabolism seen in major burns. The patient's temperature should be monitored, areas out of the operative field should be covered and warmed, and the operating room ambient temperature should be maintained at $>28°$ C (thermoneutral) to minimize heat loss.

At the end of the case, the anesthesiologist has to decide whether extubation is possible. Patients who are brought to the operating room after tracheal intubation usually remain intubated and are transported back to the burn unit. Patients who did not undergo tracheal intubation preoperatively may be extubated if they meet criteria. It is necessary to rule out the presence of airway edema if a case involved large blood loss and fluid resuscitation, especially if performed in the prone position.

Additional considerations are to provide adequate postoperative analgesia and to ensure a smooth emergence.

Analgesic requirements may be difficult to estimate because the patients are already receiving high doses of opioids preoperatively. If a split-thickness skin graft has been applied, it is especially important to avoid uncontrolled patient movement on emergence because of the risk of graft dislodgment.

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CASE 77

# Abdominal Trauma

J. David Roccaforte, MD

## QUESTIONS

1. What injuries and abnormalities can be anticipated from the history?
2. Explain the primary and secondary surveys according to advanced trauma life support.
3. After the primary and secondary surveys are performed, what are the options for definitive care, and what further diagnostic studies or therapeutic interventions must be considered before transport?
4. What are the airway management options?
5. What are the intraoperative surgical objectives during damage control laparotomy?
6. What is the best resuscitation fluid?
7. What are the appropriate endpoints of resuscitation for this patient?
8. Explain the value of a massive transfusion protocol.
9. What are the anesthesiologist's intraoperative priorities?
10. What are the goals for subsequent postanesthesia care unit care?

A 26-year-old man shoveling snow from the roof of a five-story apartment building slips and falls to the ground. On arrival to the emergency department 20 minutes later, he is awake and alert and can accurately state his name. He is not oriented to place, and he cannot recount what happened. He is complaining of pain. On physical examination, he is shivering, has a grossly deformed right proximal femur, and has a tender abdomen to palpation. His vital signs are heart rate 135 beats per minute, blood pressure 88/69 mm Hg, respirations 22 breaths per minute, and oxygen saturation by pulse oximetry ($SpO_2$) 99% on facemask oxygen.

The primary survey reveals a patent, well-protected airway; adequate oxygenation with supplemental oxygen; impaired ventilation secondary to pain and splinting; clear breath sounds bilaterally; sinus tachycardia; hypotension responsive to rapid fluid boluses of 100–200 mL; intact cranial nerves; normal pupillary examination; intact sensation; and movement in all four extremities. He has two 16-gauge intravenous (IV) catheters in his upper extremities.

After tracheal intubation, the patient is brought to the radiology department. He continues to have ongoing fluid-responsive hypotension, and packed red blood cell transfusions are initiated. Computed tomography (CT) scan of the brain is unremarkable, although diffuse axonal injury cannot be excluded. CT scan of the pelvis reveals an unstable, "open-book" pelvic fracture. The abdominal CT scan demonstrates an avulsed, grade 5 right kidney injury with significant retroperitoneal bleeding. The patient proceeds directly to the operating room for a damage control laparotomy. The planned procedures are exploratory and decompressive laparotomy; right nephrectomy; and pelvic, right femoral, and right ulnar external fixations. Trauma, urology, and orthopedic surgical teams will operate concurrently. Significant intraoperative blood loss is anticipated.

### 1. What injuries and abnormalities can be anticipated from the history?

In general, our ability to anticipate significant injuries is poor. The best marker of severe injuries after trauma is a recorded systolic blood pressure <90 mm Hg. Other associations are far less valuable predictors, especially pertaining to the mechanism of injury. Frequently, hearsay reports arrive before or concurrent with the patient describing a fall of several floors, an occupant ejected from a motor vehicle, or a through-and-through gunshot wound. Subsequent evaluation of the patient reveals no injuries. Just as often, patients are brought in with vague histories, such as falling from a standing position, bicycling-pedestrian accident, or extremity stabbing, and they are found to have significant, life-threatening injuries.

Because of these frequent discrepancies, all patients in whom significant trauma is considered possible must be managed using a protocol-driven system specified by the American College of Surgeons advanced trauma life support (ATLS). The objectives of ATLS are quick and accurate diagnosis and initiation of treatment for all life-threatening injuries. *All* patients are managed similarly initially focusing on the primary and secondary surveys of ATLS. The price paid to expedite diagnosis and treatment of trauma patients as well as to avoid missing occult severe injury is that some patients receive otherwise "unnecessary" testing; evaluation; and possibly even nontherapeutic interventions, such as tracheal intubation, tube thoracostomy, or exploratory laparotomy.

Specifically for this patient, it is relevant to appreciate that a fall of four stories is associated with approximately 50% mortality. Given that he has arrived at the hospital alive and talking, it is likely that his fall was broken somehow during descent. First aid initiated by bystanders and emergency medical services (EMS), especially tourniquets and pressure applied to bleeding areas, must be maintained during transfer to the hospital trauma team. Injuries from the following categories can be anticipated (Table 77-1).

## Neurologic Injury

### Traumatic Brain Injury

The Glasgow Coma Scale (GCS) is the traditional means of quickly assessing neurologic function when traumatic brain injury is suspected. The GCS is a coarse screening tool that encompasses eye-opening, verbal, and motor responses (Table 77-2). GCS scores range from 3–15. A score of 3 represents a completely nonresponsive patient with a predicted mortality rate of 65%–90%. A GCS score of 13 predicts mortality rates of <10%. Although the GCS score on admission correlates with survival outcomes, more importantly, the specific details of neurologic function should be accurately noted. Often, loss of consciousness is reported from the field, yet when patients arrive at the hospital, they are awake with normal GCS scores. This finding does not exclude neurologic injury; the "lucid interval" of a potentially fatal epidural hematoma follows precisely this pattern. The presence of seizures has a high correlation with positive findings on CT scans of the brain (80%). Headache, amnesia,

TABLE 77-1 **Suspected Injuries after Trauma**

| Type | Injury | Comments |
|---|---|---|
| Neurologic | Traumatic brain injury | Glasgow Coma Score |
| | Spinal injury | Cervical immobilization<br>Careful logrolling |
| Penetrating wounds | Hemorrhage | Apply pressure to bleeding areas<br>Place extremity tourniquet proximal to bleeding site |
| Orthopedic | Long bone fractures | Splint fractures to avoid fat embolism syndrome and disruption of clots<br>Expect 1–3 units of blood loss per closed fracture |
| | Pelvic fracture | Immobilization<br>Expect several liters of blood loss |
| Thoracic | Rib fractures | Excruciatingly painful<br>Leads to splinting, hypoventilation, and hypoxia |
| | | Hemothorax<br>Pneumothorax<br>Pulmonary contusion |
| | Hemothorax/pneumothorax | Chest tube insertion should not be delayed waiting for chest x-ray |
| | Diaphragmatic rupture | Herniation of abdominal contents into thoracic cavity |
| Cardiac | Impaired ventricular function | Most common presentation |
| | Arrhythmias | Monitor electrocardiogram for at least 24 hours |
| | Cardiac rupture | In extreme cases |
| | Valvular dysfunction | |
| | Coronary occlusion | |
| Aortic | Avulsed at ligamentum arteriosum | Rapid deceleration |
| | Rupture | Death before arrival to hospital |
| | Dissection | May be occult |
| | | Manifests later with hypotension, stroke, aortic valve insufficiency, or myocardial infarction |
| Abdominal | Bowel | Vascular injury and ischemia |
| | Liver and spleen | Most common after blunt trauma |
| | Kidneys and pancreas | Less common |
| Systemic | Shock | Lactic acidosis |
| | Hypothermia | Exposure at scene and emergency department |
| | | Room temperature intravenous fluids |
| | Coagulopathy | Shock, hypothermia, and acidosis |
| | | Consumption of coagulation factors |
| | | Coagulation factors diluted by crystalloid solution resuscitation |

TABLE 77-2 **Glasgow Coma Scale**

| | |
|---|---|
| Eye opening | 1—none<br>2—to pain<br>3—to loud voice<br>4—spontaneously |
| Verbal | 1—none<br>2—moaning<br>3—incomprehensible words<br>4—confused or disoriented<br>5—alert and oriented |
| Movement | 1—none<br>2—decerebrate extension<br>3—decorticate flexion<br>4—withdraws<br>5—localizes<br>6—obeys commands |

and vomiting are each associated with structural brain injury in 40%–45% of cases. Brief loss of consciousness predicts positive CT scan findings in only 29% of cases.

### *Spinal Injury*

In a patient who has sustained blunt injury, the default approach is to presume that the spinal column is unstable until proved otherwise. Consequently, neck immobilization must be maintained, and logrolling must be carefully performed when examining or transferring the patient. In a patient who is hemodynamically unstable, clearance of the cervical spine is not a priority, even if the airway must be managed. For the cervical spine to be clinically cleared, the patient must be able to do the following:

- Focus fully on the examination (no distractions)
- Localize and discriminate mildly noxious stimuli
- Move and feel all extremities

For this patient, full spinal immobilization would be maintained until detailed imaging and clinical clearance could be possible. Imaging would be obtained nonurgently. Provided that no radiographic abnormalities were noted, a clinical evaluation for clearance could be performed at a later time.

### *Penetrating Wounds*

During the patient's fall and on landing, it is possible that a sharp object (e.g., debris, tree branch) could have impaled the patient. Pressure should be applied and maintained to all bleeding areas. Tourniquets must be appropriately applied (i.e., proximal to any extremity bleeding) and maintained.

### *Orthopedic Injuries*

#### *Long Bone Fractures*

Obvious deformities should be noted and the involved limb maintained splinted so as to minimize fat embolism syndrome and disruption of formed blood clots. For each closed fracture, 1–3 units of blood loss should be anticipated.

#### *Pelvic Fractures*

If a pelvic fracture is suspected, the pelvis must be immobilized as soon as possible with a tied sheet or binder. A rich venous plexus resides on the anterior surface of the pelvis. Pelvic fractures disrupt these veins, and neither embolization nor suturing can be performed. A tremendous amount of bleeding can occur, eventually filling the retroperitoneum and providing venous tamponade. Until that occurs, a blood loss of several liters should be anticipated.

### *Thoracic Injuries*

#### *Rib Fractures*

Even small rib fractures can be excruciatingly painful leading to respiratory splinting, hypoventilation, and hypoxia. Larger, multiple (flail chest), and comminuted rib fractures are associated with hemothorax or pneumothorax and are markers for significant pulmonary contusion.

#### *Hemothorax or Pneumothorax*

If hemothorax or pneumothorax is suspected from the physical examination (i.e., absent breath sounds, tracheal shift, distended jugular veins, hypotension, or hypoxia), chest tube insertion should not be delayed for a chest radiograph.

#### *Pulmonary Contusion*

Pulmonary contusion may not manifest initially. However, hypoxia, decreased lung compliance, and infiltrates develop within hours. Care is supportive.

#### *Diaphragmatic Rupture*

Diaphragmatic rupture can occur when high pressure develops acutely in the abdomen. Depending on the object hit and the patient's position at impact, abdominal contents may eviscerate into the thoracic cavity.

#### *Blunt Cardiac Injury*

Most cases of blunt cardiac injury manifest as impaired ventricular function. Death, when it occurs, is usually due to malignant arrhythmias. Consequently, when blunt cardiac injury is suspected, the patient must have continuous electrocardiogram monitoring. If no arrhythmias are noted in 24 hours, monitoring may be discontinued. In extreme cases, blunt cardiac injury can lead to cardiac rupture, valvular dysfunction, or coronary occlusion.

#### *Aortic Injury*

During rapid deceleration, the aorta can be avulsed at the ligamentum arteriosum, where the arch is tethered. Aortic rupture is catastrophic and usually results in

death before arrival at the hospital. However, aortic tears and dissections can be occult initially and manifest later with hypotension, stroke, aortic valve insufficiency, or myocardial infarction.

### Abdominal Injuries

Abdominal wall laxity and the absence of anterior bony protection results in abdominal contents being particularly vulnerable to blunt trauma. Forces applied anteriorly can compress abdominal contents against bony structures of the spine or pelvis. Additionally, tremendously high or even brief increases in intraabdominal pressure during impact can rupture both solid and hollow viscera. Shear forces during deceleration are another mechanism of injury, which can manifest immediately as solid organ rupture or hours later as vascular insufficiency leading to bowel necrosis.

### Bowel Injury

Bowel injury is generally less common following blunt trauma compared with penetrating trauma. When bowel injury occurs after blunt force trauma, it is often associated with vascular injury and ischemia. A late mechanism of bowel and renal injury is abdominal compartment syndrome.

### Solid Organ Injuries

The liver and spleen are the most commonly injured intraperitoneal abdominal organs from blunt trauma. If the patient is hemodynamically stable, nonoperative management may be appropriate in select cases of hepatic and splenic trauma. The kidney is occasionally injured following blunt trauma, and the pancreas is injured less frequently. Both the kidneys and the pancreas reside in the retroperitoneal space.

### Systemic Abnormalities

### Shock

A reliable marker for a shock state does not exist. In this patient, hemorrhagic shock is presumed because he has hypotension, tachycardia, altered mental status, and distended abdomen. Lactic acidosis develops as a consequence of hypoperfusion. The degree of metabolic acidosis present on admission correlates with mortality.

### Hypothermia

Although the patient was in the field for only 20 minutes, he is shivering. The largest contributor to hypothermia is depressed metabolism that accompanies shock. Additional factors contributing to this patient's hypothermia include exposure to cold temperatures in the field and in the emergency department when fully disrobed and treatment with room temperature IV fluids.

### Coagulopathy

The development of coagulopathy is inexorably linked to the patient's shock, acidosis, and hypothermia. Patients surviving massive blunt trauma arrive at the hospital with a measurable coagulopathy. This coagulopathy is exacerbated further by consumption and dilution by EMS-administered crystalloid solutions of coagulation factors.

## 2. Explain the primary and secondary surveys according to advanced trauma life support.

Trauma care follows a standardized approach starting in the field and continues through evacuation, triage, primary survey, resuscitation, secondary survey, and definitive care.

### Primary Survey

The primary survey is the initial evaluation on arrival at the hospital. Objectives of the primary survey are to assess and address quickly life-threatening conditions. The sequence is easily remembered by the mnemonic *A*, *B*, *C*, *D*, *E*.

### Airway Maintenance with Cervical Spine Protection

The initial focus is on airway patency. The ability to phonate and converse is usually sufficient proof of an adequate airway. Many of the criteria for immediate tracheal intubation of trauma patients are similar to criteria typically used for other patients (i.e., hypoxemia, hypoventilation, lack of airway reflexes). The presence of oropharyngeal bleeding or stridor is always cause for concern. Other times, the threshold for tracheal intubation of the trauma patient is lowered. For example, if victims are intoxicated, combative, and actively bleeding, they may need tracheal intubation expeditiously despite the presence of adequate cough, gag and swallow reflexes. By default and until proved otherwise, trauma patients are presumed to have a full stomach and cervical spine instability.

Cervical spine protection begins with immobilization in the field using minimally padded extrication collars made of stiff, thin plastic. Cervical spine clearance is usually deferred until after the primary and secondary surveys have been completed. If the airway needs to be secured, the risk of exacerbating a cervical spine injury is negligible provided that adequate precautions are maintained. These precautions include manual in-line stabilization, minimizing neck extension, and management of the airway by an experienced laryngoscopist.

Extrication cervical spine collars and backboards can quickly lead to decubitus ulcer formation, sometimes in $<1$ hour. As soon as possible, backboards should be removed, and the extrication collar should be changed to one that is padded and designed for longer term use.

### Breathing and Ventilation

In a spontaneously breathing patient, auscultation of both lung fields is performed to establish the presence of bilateral breath sounds. In a hypotensive tracheally intubated patient, unilateral right-sided breath sounds (later discovered to be from a right main-stem intubation) occasionally lead to the avoidable placement of an emergent left thoracostomy tube for suspected pneumothorax.

Trauma patients generally arrive at the emergency department on supplemental oxygen. If the only monitor of ventilatory adequacy is oxygen saturation, significant hypoventilation could be missed because oxygen saturation can be maintained with a fraction of inspired oxygen ($FiO_2$) of 100% oxygen despite very low tidal volumes.

### Circulation with Hemorrhage Control

Blood pressure is the initial vital sign used to establish adequacy of circulation. However, in severe hypovolemia, especially in young, healthy victims, compensatory mechanisms can maintain blood pressure until precipitous circulatory collapse occurs. Active hemorrhage is controlled with applied pressure or tourniquets. If it has not been done so already, large-bore peripheral IV access is established. Fluids administered from this point forward should be warmed.

### Disability (Neurologic Evaluation)

This stage of the primary survey encompasses a quick assessment of both central and neuraxial integrity. The GCS score (Table 77-2) is correlated with survival in traumatic brain injury and is commonly used as a shorthand method of communicating mental status. Patients with a GCS score <8 are unlikely to be able to protect their airway and may require tracheal intubation.

Beyond the GCS score, it is crucial to assess and document specific findings of an immediate baseline neurologic examination, including cranial nerve function, pupillary size, movement of extremities, lateralizing signs, sensation (if the patient is able to cooperate), and higher functions. Any deterioration from baseline requires immediate investigation.

### Exposure and Environmental Control

The patient should be fully undressed (exposure) while maintaining cervical spine immobilization and kept warm with blankets (environmental control); this facilitates the head-to-toe examination, which is part of the secondary survey.

### Secondary Survey

When the primary survey objectives are met and stable (or supported) and adequate vital signs are achieved, the secondary survey can begin. The secondary survey comprises a head-to-toe physical examination and a review of the patient's history, if available. The findings during the secondary survey guide a further focused physical examination as well as obtaining appropriate ancillary diagnostic tests (e.g., laboratory, radiographic, ultrasound). If the patient's condition deteriorates, the primary survey is repeated.

## 3. After the primary and secondary surveys are performed, what are the options for definitive care, and what further diagnostic studies or therapeutic interventions must be considered before transport?

Subsequent steps after the secondary survey involve further evaluation and treatment. Possible options include monitoring and observation, additional diagnostic evaluation, interventional angiography, and surgery. Decisions hinge on the patient's known and suspected injuries in addition to hemodynamic stability. Severe, refractory hypotension is easy to recognize as hemodynamic instability. However, a finding of isolated tachycardia or a normal blood pressure sustainable only with ongoing fluid boluses, vasoconstrictors, or both might not be as obvious.

For hemodynamically stable patients without obvious injury, monitoring and observation are appropriate. At the other extreme, a hemodynamically unstable patient with an acute abdomen following penetrating trauma would likely proceed directly to the operating room for exploratory laparotomy. Other scenarios require a balance between the value of imaging and the risk of delaying treatment.

Bedside surface ultrasonography, referred to as focused abdominal sonography for trauma (FAST), has become the routine for evaluating intraabdominal, pericardial, and intrathoracic bleeding. In experienced hands, FAST is able to confirm free fluid in the peritoneal cavity; however, it is an unreliable method for excluding hollow viscera injury. Diagnostic peritoneal lavage is a complementary tool for evaluating intraabdominal bleeding and diagnosing gastrointestinal perforation (Figure 77-1).

Whenever possible, as dictated by hemodynamic stability, further delineation of injuries by radiologic evaluation (e.g., CT scan) can be accomplished before an intervention or procedure. Bleeding from certain injuries may be addressed by angiography with arterial embolization. Injuries amenable to embolization include pelvic fractures, splenic and hepatic lacerations, and occasionally renal injuries (Figure 77-2).

This patient's secondary survey reveals obvious bony distortions of the right forearm and femur; multiple scrapes and soft tissue contusions; and a distended, tender abdomen. Initial x-rays demonstrate an unstable pelvic fracture; essentially normal chest; and confirmed comminuted, displaced right ulnar and femur fractures.

FAST was negative for free fluid, and diagnostic peritoneal lavage was normal. Throughout this period (20 minutes), the patient's systolic blood pressure decreased into the low 80s with maintained mental status. Intermittent crystalloid solution boluses of 100–200 mL increased the systolic blood pressure >90 mm Hg. He

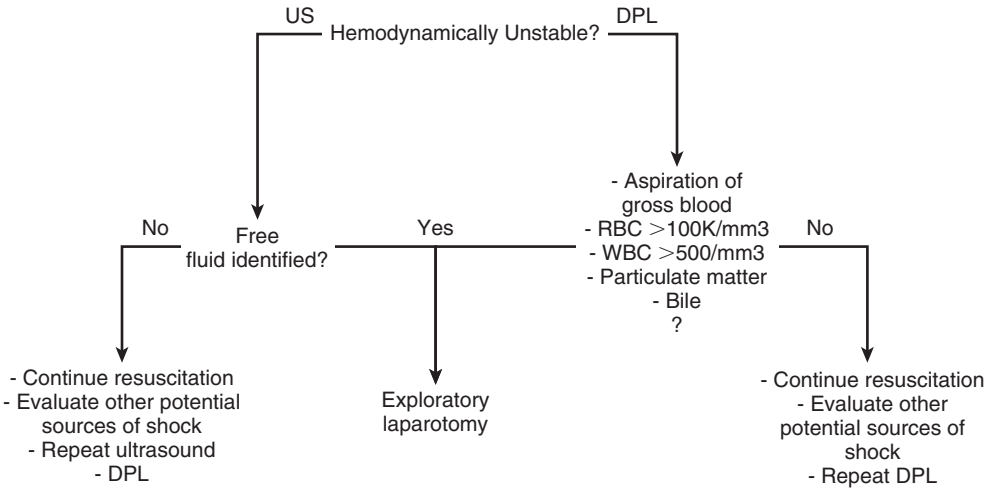


**FIGURE 77-1** ■ Evaluation of blunt abdominal trauma in a hemodynamically unstable patient. *DPL,* Diagnostic peritoneal lavage; *US*, ultrasound. (From Hoff WS, Holevar M, Nagy KK, et al.; Eastern Association for the Surgery of Trauma: Practice management guidelines for the evaluation of blunt abdominal trauma: the East Practice Management Guidelines Work Group. J Trauma 53:602, 2002.)

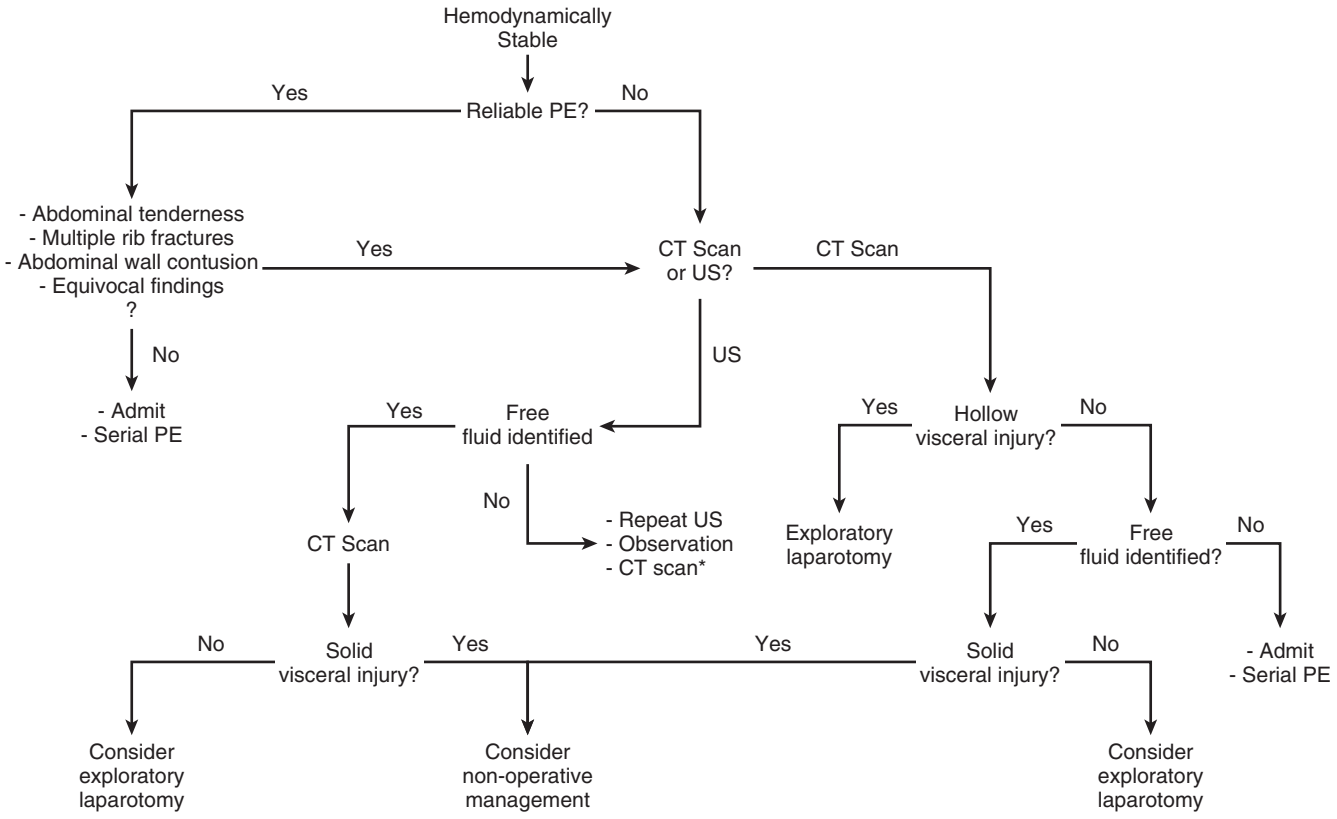


**FIGURE 77-2** ■ Evaluation of blunt abdominal trauma in a hemodynamically stable patient. *Abd,* Abdominal; *DPL,* diagnostic peritoneal lavage; *fxs,* fractures; *PE,* physical examination; *US,* ultrasound. (From Hoff WS, Holevar M, Nagy KK, et al.; Eastern Association for the Surgery of Trauma: Practice management guidelines for the evaluation of blunt abdominal trauma: the East Practice Management Guidelines Work Group. J Trauma 53:602, 2002.)

had received 2 L of normal saline (NS) in the field, and another 2 L were infusing. There were 4 units of packed red blood cells (PRBCs) and fresh frozen plasma (FFP) in the process of crossmatching.

Anticipating the source of bleeding to be a retroperitoneal hematoma secondary to pelvic fracture, the plan was to continue monitoring and resuscitation, while transporting the patient to radiology for a CT scan to evaluate his brain, abdomen, and pelvis. Until serious injuries have been objectively excluded, appropriate monitoring and personnel must accompany trauma patients when they are transported. Personnel must be able to recognize physiologic deterioration and respond. Before transport, this patient was tracheally

intubated and sedated to alleviate pain, optimize imaging, and facilitate transition to a definitive care procedure, such as angiography with embolization or surgery.

## 4. What are the airway management options?

The decision to secure this patient's airway is a judgment call. Anticipating that the patient will soon require tracheal intubation for a definitive procedure, the author prefers to secure the airway in a controlled manner, rather than emergently during transport or while in the CT scanner. The disadvantage of sedation and tracheal intubation is the inability to assess the patient's neurologic status. Neurologic assessment of the awake patient is the best monitor of brain function. Consequently, CT evaluation of the brain for bleeding, contusion, or mass effect becomes the priority.

As long as full stomach and cervical spine precautions are maintained, there is no evidence-based strategy for managing induction and tracheal intubation that yields superior outcomes. Generally, there is no benefit to awake, nasal, blind, or fiberoptic intubation compared with asleep oral direct laryngoscopy. On the contrary, awake techniques are likely to result in excessive patient movement, Valsalva, coughing, bleeding, and delay of treatment and should be employed only for specific indications.

Airway management begins with ensuring appropriate personnel and equipment, such as oxygen, vascular access, medications, endotracheal tubes, laryngoscope blades, and suction. Next, the plan is articulated to involved personnel, and contingencies are outlined in the event that primary intubation attempts fail. Optimally, there should be one person assigned to administer medications, a second to hold cricoid pressure, a third to maintain in-line cervical stabilization, and a fourth to manage the airway.

A theoretical concern about cricoid pressure is the potential for an unstable C5 vertebral body to be displaced posteriorly into the spinal cord. In many cases, the force applied during Sellick maneuver is insufficient to occlude the esophagus. Consequently, cricoid pressure must be firm but not excessive.

The choice of medications administered is controversial. Of induction agents available, etomidate is often chosen for induction because of its ability to maintain hemodynamic stability in euvolemic patients. Although etomidate has been associated with adrenal suppression, this is of questionable clinical significance. Propofol administered to hypovolemic patients with high sympathetic drive often results in severe hypotension, especially after institution of positive pressure ventilation, which impairs venous return and cardiac preload. Reduced doses of propofol, especially following small doses of a benzodiazepine, provide sufficient hypnosis (and often amnesia), while preserving blood pressure better. Ketamine offers several advantages, such as analgesia, better preservation of respiratory drive and airway reflexes, and increased sympathetic tone.

Choice of neuromuscular blocking agents is equally controversial. No prospective trial has demonstrated survival benefits with either succinylcholine (1.5 mg/kg), or rocuronium (1.2 mg/kg) for rapid-sequence induction. The choice may be guided by the anticipation of difficult intubation (favoring succinylcholine) or by concerns for hyperkalemia (favoring rocuronium). *Regardless, a neuromuscular blocking agent should not be excluded or underdosed.* Laryngoscopy without neuromuscular blockade can stimulate gagging and a vigorous Valsalva response, which can increase intraabdominal (risking regurgitation and pulmonary aspiration), venous (disrupting formed clots), and intracranial (compromising cerebral blood flow) pressures.

Successful denitrogenation is accomplished with high-flow oxygen and an airtight facemask seal. $SpO_2$ values of 100% are insufficient proof that oxygen has replaced nitrogen in the lungs. For adequate preoxygenation, 3 minutes of spontaneous ventilation or eight maximum breaths in 60 seconds is generally recommended. Although prolonged hyperventilation is no longer recommended to treat closed head trauma, slight hyperventilation with 100% oxygen before induction helps prevent hypoxia during laryngoscopy and avoids elevated arterial carbon dioxide tension ($PaCO_2$) exacerbating increased intracranial pressure (ICP).

There is no need to wait for hypnosis before dosing the neuromuscular blocker. The induction agent and neuromuscular blocker should be dosed in rapid sequence (except for thiopental, which must be flushed before rocuronium administration to avoid precipitation). Likewise, there is no need to wait for defasciculations or twitches on the neuromuscular monitor to disappear before removing the facemask and attempting to open the mouth. Care must be taken not to induce a gag or cough reflex, but advances should be made to secure the airway as long as the patient tolerates gentle laryngoscopy. The greatest risk of aspiration occurs between the time when patients cannot protect their airway and inflation of the tracheal tube's cuff in the trachea.

## 5. What are the intraoperative surgical objectives during damage control laparotomy?

Traditionally, surgery follows the standard sequence: access, exposure, hemostasis, resection, and reconstruction. Damage control surgery endeavors to complete the minimum life-threatening repairs that are necessary and then seek safe harbor in the postanesthesia care unit (PACU) or intensive care unit. Further repair of additional injuries and reconstruction are done in a staged manner. Objectives for damage control laparotomy are as follows:

- *Control bleeding.* Bleeding from arteries and large veins is addressed with clamps and staples. Bleeding from smaller veins is controlled with packing. Time-consuming microvascular repair is not attempted.
- *Control enteric spillage.* Control is accomplished quickly with stapling devices or creating blind loops, if necessary. Time-consuming complex anastomoses and ostomies are not performed.
- *Immobilize long bone and unstable pelvic fractures.* Immobilization is accomplished with external fixation devices or splinting. It is important to minimize bony fragments from moving past each other, which

can lead to ongoing bleeding, fat embolism syndrome, and significant systemic inflammatory response. Internal fixation and joint replacement are too time-consuming and are deferred.

Temporary abdominal closure is preferred to facilitate subsequent planned (and possibly unplanned) reoperations. It also decreases the likelihood of developing abdominal compartment syndrome, which is associated with edema of splanchnic viscera from the inflammatory response to trauma and shock.

Ideally, initial damage control surgery should last <1 hour. Implementation of damage control surgery, coordinated with resuscitation, is probably the biggest factor contributing to improved survival after severe trauma in the past decade.

In this patient, the combination of injuries is particularly concerning. Generally, venous bleeding from pelvic fractures is managed conservatively with external fixation and allowed to tamponade in the retroperitoneum. Pelvic arterial bleeding is addressed by endovascular embolization. However, severe renal injuries necessitate nephrectomy that would open the retroperitoneum and expose the patient to significant ongoing venous blood loss until the abdomen can be packed.

## 6. What is the best resuscitation fluid?

The fluids chosen and the resuscitation strategy for massive bleeding must meet three objectives.

### *Anticipate and Avoid Severe Anemia*

Dilutional anemia can develop quickly when the loss of whole blood is replaced with non–red blood cell resuscitation fluids and the patient's own mobilization of interstitial and intracellular fluids to auto-resuscitate intravascular volume. The degree to which anemia is tolerated (considered "severe" anemia) is a function of the patient's cardiac and systemic reserves. The adaptive response, which maintains oxygen delivery in the setting of reduced hemoglobin, is increased cardiac output. If cardiac output is limited by intrinsic myocardial or valvular disease, the degree of shock and likelihood of survival are significantly worse. In the context of severe, uncontrolled bleeding, even with adequate cardiac function, the development of anemia must be anticipated and PRBCs should be transfused aggressively, without waiting for systemic compromise or documentation of anemia.

There is an inherent delay in crossmatching type-specific blood. Rare patients require immediate $O^-$ transfusion. Controversy exists regarding the need to continue with $O^-$ PRBCs to prevent a hemolytic reaction when switching back to type-specific products. The best way to avoid the controversy is to limit $O^-$ transfusions to $\leq 4$ units and to switch to type-specific blood as soon as it is available.

For less severe bleeding or when bleeding is controlled, the need for further PRBC transfusion is based on traditional transfusion triggers (i.e., hematocrit, hemodynamic stability, end-organ function). Excessive PRBC transfusions have been associated with an increased risk of infection secondary to immunosuppression.

### *Treat Coagulopathy*

Frequently observed trauma-related coagulopathy was traditionally thought to be a result of consumption, dilution, and dysfunction from acidosis and hypothermia. Although these factors eventually contribute to the problem, more recent studies have demonstrated that a posttrauma coagulopathy exists even before significant resuscitation occurs. Speculation is that early coagulopathy reflects the degree of shock present, as do the other two markers, acidosis and hypothermia, of the so-called triad of death.

Three strategies address platelet and factor consumption. First, ongoing surgical bleeding must be addressed as soon as possible. Second, clots that have formed can be disrupted and flushed away with hyperresuscitation (so-called popping the clot). Arterial and venous pressures should be allowed to decrease to the lowest tolerated values, and cyclic hyperresuscitation (fluid administration → disrupting clots → bleeding → hypovolemia and hypotension → further fluid administration) should be avoided, if possible. Third, the dysfunctional and depleted coagulation system must be aggressively replenished with FFP, platelets, and cryoprecipitate. The inherent delay in thawing FFP must be accounted for. Once surgical bleeding is addressed and hemodynamic stability is achieved, further platelet and factor transfusions are administered based on traditional triggers. Excessive FFP administration has been associated with acute respiratory distress syndrome, infections, and transfusion-related acute lung injury.

### *Avoid Severe Hypovolemia*

The fluid of choice for treating simple hypovolemia in a nonbleeding patient is an isotonic crystalloid solution. In a bleeding trauma patient, treating hypovolemia with only crystalloid solutions quickly leads to both dilutional anemia and coagulopathy. For ongoing blood loss, PRBCs and factors are preferable. If hypovolemia persists after the anemia and coagulopathy have been adequately addressed by blood product transfusions or if the blood bank cannot provide appropriate products, the fluid of choice is an isotonic crystalloid solution, such as 0.9% sodium chloride (NS), or lactated Ringer solution (LRS).

The type of crystalloid solution administered is based on several considerations. To avoid infusing a potassium-containing solution to patients in renal failure, NS is typically used by EMS in the field. NS is slightly hypertonic and unlikely to exacerbate cerebral edema in patients with traumatic brain injury. It is associated with improved survival in this setting compared with albumin. However, NS increases serum chloride out of proportion to the increase in serum sodium; predictably, this results in a non–anion gap hyperchloremic metabolic acidosis, which is rarely of clinical significance. Historically, a commonly used marker for the adequacy of volume resuscitation has been the base deficit. When the base deficit is associated with lactic acidosis, it reflects the degree of hypoperfusion. The base deficit cannot differentiate between an anion gap (lactic) and a non–anion gap (hyperchloremic) etiology of acidosis. If NS is used as a resuscitation fluid and base deficit

alone is used to assess the need for further resuscitation, a vicious cycle is initiated that can lead to excessive fluid administration.

LRS does not cause a hyperchloremic acidosis because lactate is metabolized by the liver into bicarbonate, which helps to maintain a normal pH balance. LRS is the most commonly used trauma resuscitation crystalloid solution in hospitals. However, LRS has some shortcomings.

- *LRS contains potassium.* Trauma patients typically are exposed to multiple renal insults, including episodes of hypotension, hypoxia, anemia, IV contrast, and rhabdomyolysis. When LRS is used, judicious attention must be paid to serum potassium levels to avoid hyperkalemia.
- *LRS contains calcium.* This may be beneficial because transfusion of multiple PRBC units can lead to severe hypocalcemia from the sodium citrate used as an anticoagulant. However, combining LRS and PRBCs in the same infusion set results in clotting. As a precaution, infusion sets should be flushed with NS between PRBC transfusions and LRS.
- *LRS is slightly hypotonic.* Theoretically, this may exacerbate cerebral edema, increasing ICP in patients with traumatic brain injury.

The functional improvement to coagulation with colloid infusions (e.g., FFP, cryoprecipitate, platelets) provides utility above and beyond their volume expansion properties. There is no survival benefit associated with nonfunctional colloid solutions (e.g., albumin, hetastarch). The only potential advantage of nonfunctional colloid solutions may be to "catch up" quickly with severe hypovolemia. However, albumin-based resuscitation is associated with worse outcomes in patients with traumatic brain injury. Hetastarch infused in larger volumes is associated with platelet dysfunction and bleeding. In adults, hetastarch is typically limited to 1000 mL in 24 hours.

The idea that crystalloid-based resuscitation causes edema is not supported by physiology. In the setting of an inflammatory response, capillary pores leak (especially in the gut), even large molecules such as albumin, and the lymphatic system shuts down. Excess interstitial fluid is not cleared, resulting in edema formation. Although total body water increases in this setting, intravascular volume decreases. The result is organ hypoperfusion and dysfunction and hypovolemic shock. In the absence of an inflammatory response, excess crystalloid administration is eliminated by the kidneys and does not result in edema formation.

## 7. What are the appropriate endpoints of resuscitation for this patient?

A universal marker of adequate resuscitation does not exist. Single endpoints of resuscitation have the potential to provide a false sense of security or generate unnecessary cause for alarm. Patient comorbidities often render commonly used parameters unreliable. For instance, β-adrenergic blockers could prevent tachycardia in response to hypovolemia, and hepatic insufficiency may interfere with lactate clearance. Trauma patients frequently arrive without medical histories. The best strategy for treating a trauma patient in shock is to collect and trend as many endpoints of resuscitation as reasonably possible and determine which parameters improve or deteriorate as bleeding and resuscitation continue.

Endpoints of resuscitation can be categorized as markers of global (Table 77-3) or regional (Table 77-4) organ-specific perfusion. The goal is to narrow the focus to at least one marker from each group that together would optimize the ability to assess the degree to which the patient is resuscitated and provide an early warning of deterioration.

Vital sign targets are not clear-cut. It may be unnecessary to return blood pressure and heart rate to normal, especially before surgical hemostasis. Resuscitation objectives vary depending on the status of surgical bleeding and the ability of the patient to tolerate compensated hypovolemia and hypotension. Aiming for supranormal endpoints of resuscitation, although associated with better survival retrospectively, has not been shown to improve outcomes in prospective randomized trials and probably simply reflects the patient's baseline physiologic reserve.

Permissive hypotension, similar to the strategy employed for leaking abdominal aortic aneurysms, may decrease blood loss before obtaining hemostasis. Low mean arterial pressures (MAPs) must be tolerated with caution in the setting of traumatic brain injury and elevated ICP because even brief episodes of low cerebral perfusion pressure (CPP) are associated with significantly worse neurologic outcomes. The default approach is to target normotension and allow hypotension only with MAP $\leq$55 mm Hg when ICP is normal and no evidence of cardiac ischemia exists. With ongoing blood loss such as the case described, even targeting hypotensive endpoints of resuscitation may still require tremendous volumes of resuscitation fluids. When surgical and medical hemostasis is achieved, resuscitation goals should target restoration of normal vital signs.

## 8. Explain the value of a massive transfusion protocol.

Traditionally, massive transfusion was defined as the infusion of one blood volume in 24 hours. Trauma patients often receive this amount in 10–15 minutes, and multiple blood volumes are replaced over the first 24 hours. In reality, survival of patients with massive hemorrhage is determined in the first few hours, during which hemostasis must be obtained surgically. The objective of resuscitation in this context is to keep up with blood loss, and speed is essential. For ongoing, uncontrolled bleeding, blood products are transfused without regard to vital signs or laboratory values. When bleeding is controlled, further resuscitation and blood products are administered based on objective triggers, such as vital signs and laboratory values.

A massive transfusion protocol serves to expedite blood product availability, especially FFP and platelets. These protocols decrease the amount of time required for the blood bank to provide adequate blood products; this is beneficial in the initial stage of management, when a bleeding patient is at risk for exsanguination. Controversy

TABLE 77-3 **Endpoints of Resuscitation—Markers of Global Perfusion**

| Markers of Global Perfusion | Notes/Pitfalls |
|---|---|
| Mean arterial pressure | Generally well compensated until late |
| | Unknown baseline |
| Lactate | Impaired clearance with hepatic dysfunction |
| Heart rate | Unknown β-adrenergic blocker use |
| Base deficit | May reflect non–anion gap acidosis |
| pH | May reflect respiratory or non–anion gap acidosis |
| Anion gap | May be elevated for reasons other than lactic acidosis |
| $ETCO_2$; $PaCO_2$-$ETCO_2$ gradient | Elevated with chronic obstructive pulmonary disease |
| $SvO_2$ | Requires pulmonary artery catheter |
| | Abnormal in shock syndromes other than hypovolemia |
| Core temperature | Hypothermia is a marker of late or advanced shock |
| | Fever is the most common transfusion reaction |
| Pulse pressure | Difficult to interpret if accompanied by bradycardia |
| Cardiac output | Requires pulmonary artery catheter |
| | Abnormal in shock syndromes in addition to hypovolemia |
| $PaO_2$; $PaO_2$:$FiO_2$ | Lower from: |
| | Shunt (e.g., pulmonary contusion, aspiration) |
| | Hypovolemia-related $\dot{V}/\dot{Q}$ mismatch |
| | Hypoxemia from shunt does not generally respond to supplemental oxygen |
| | Hypoxemia from $\dot{V}/\dot{Q}$ mismatch easily corrected with supplemental oxygen |
| Respiratory systolic pressure variation | Difficult to interpret with obesity or with abdominal compartment syndrome |

*$ETCO_2$,* End-tidal carbon dioxide; *$FiO_2$,* fraction of inspired oxygen; *$PaCO_2$,* arterial carbon dioxide tension; *$PaO_2$,* arterial oxygen tension; *$SvO_2$,* mixed venous oxygen saturation; $\dot{V}/\dot{Q}$, ventilation/perfusion.

TABLE 77-4 **Endpoints of Resuscitation—Markers of Regional Perfusion**

| Markers of Regional Perfusion | Notes/Pitfalls |
|---|---|
| Mental status | Unavailable during general anesthesia<br>Unreliable with intoxication |
| Urine output | Unreliable with acute or chronic renal failure, SIADH, or neurogenic DI |
| Electrocardiogram | Unknown baseline for comparison |
| Echocardiography | Requires special operator skills<br>Absent esophageal or gastric pathology |
| Capillary refill | Unknown baseline for comparison |
| Sublingual tonometry | Not routinely available |
| Jugular bulb saturation | Not routinely available |
| NIR spectrometry | Not routinely available |
| CPK levels | Too slow for acute changes |
| Troponin levels | Too slow for acute changes |

*CPK,* Creatinine phosphokinase; *DI,* diabetes insipidus; *NIR,* near infrared; *SIADH,* syndrome of inappropriate antidiuretic hormone.

exists regarding the optimal ratio of blood products to administer. The approximate ratios present in whole blood are effectively reconstituted with 1 unit of PRBCs + 1 unit of FFP + 1 unit of platelets. Although no prospective randomized data have demonstrated a survival benefit of transfusing a 1:1:1 ratio, it would seem as good as any strategy in the initial severe blood loss stage. When bleeding has been controlled, the massive transfusion protocol ends, and the 1:1:1 ratio may not be necessary. Because transfusions can be harmful, subsequent blood products are administered to correct documented abnormalities, not to meet a predetermined ratio.

## 9. What are the anesthesiologist's intraoperative priorities?

Besides volume resuscitation, anesthesiologists have other responsibilities that must be prioritized. For complex cases such as the one described here, it is impossible for a single anesthesiologist to keep up with all the necessary tasks. Help of additional anesthesiologists is required to do the following:

- *Provide immobility and amnesia.* Although awareness under anesthesia can be devastating, when blood pressure is already marginal, depth of anesthesia is

generally reduced. The initial priority should be to provide neuromuscular blockade and amnesia. Agents to consider are benzodiazepines at low doses, scopolamine, nitrous oxide (if oxygenation is adequate), and ketamine (provided that ICP is normal). If blood pressure is inadequate, short-term vasopressor therapy may be used until intravascular volume is improved. If hypotension persists, alternative explanations of shock (i.e., cardiogenic, distributive, mechanical) should be investigated. When blood pressure is stable, other agents can be added to provide balanced anesthesia addressing hypnosis (volatile anesthetics) and analgesia (opioids).

- *Establish reliable IV access.* In the field, two short length catheters are routinely placed in the antecubital fossae. As resuscitation proceeds, edema formation in subcutaneous tissue expands the distance between vein and skin where the IV catheter is fixed. Consequently, the tip of the IV catheter begins to retract out of the vessel. For massive transfusions, large-bore (introducer) venous access should be established. Femoral or saphenous venous lines should be used with caution if injuries involve the pelvic or abdominal central veins.
- *Monitor arterial blood pressure.* An arterial catheter should be inserted to monitor blood pressure continuously, to calculate CPP accurately, and to enable frequent arterial blood gas sampling. Femoral, dorsalis pedis, or axillary arteries may be used if the radial arteries are unavailable.
- *Manage CPP.* For patients with concomitant head injuries, ICP monitoring should be initiated in the operating room as soon as possible, and CPP should be maintained >55 mm Hg (CPP = MAP − ICP). This may require augmentation of blood pressure using α-agonist agents or efforts to decrease ICP (e.g., mannitol, hypertonic saline), or both.
- *Maintain normothermia.* Shock induces hypothermia as metabolism slows. It can be challenging to maintain normothermia in an exsanguinating trauma patient. All fluids should be infused through warmers, and warming blankets should be placed on all exposed, nonoperative parts of the body. If the patient's temperature continues to decrease, ambient temperature in the operating room may need to be increased.
- *Diagnose and treat medical issues and electrolyte abnormalities.* Occasionally, vehicular trauma and falls may occur after a person loses consciousness from a medical condition (e.g., stroke, sepsis, myocardial infarction, arrhythmia, hypoglycemia, seizures). Those medical conditions warrant investigation and treatment concurrently with the management of traumatic injuries. Prophylactic antibiotics may need to be redosed if blood levels are diluted by large-volume resuscitation.
- *Maintain accurate documentation.* Accurate recording of medications, fluids, and blood products should be ongoing.

### 10. What are the goals for subsequent postanesthesia care unit care?

After surgical bleeding has been addressed and operative damage control objectives have been met, priorities transition to correction of abnormal physiology. Immediately on arrival in the PACU, this patient would require active warming, correction of coagulopathies and anemia, invasive monitoring, sedation, and antibiotics. Complete blood count, coagulation profile, electrolyte panel, arterial blood gas, and creatinine phosphokinase (to screen for rhabdomyolysis) should be obtained.

If possible, sedation should be decreased, and a basic neurologic examination should be performed. If a neurologic examination is not possible or if any gross neurologic abnormalities are noted, repeat CT scan of the brain should be considered. A chest x-ray is performed to confirm line placement, to confirm tracheal tube location above the carina, and to rule out pneumothorax. A head-to-toe physical examination is repeated, and additional imaging is obtained as indicated to evaluate for missed injuries (commonly hand, foot, or digital fractures). IV catheters placed in the field or under less than sterile conditions are removed. Tetanus booster injection should be administered. Extrication cervical spine collar is changed to one designed for long-term use (Miami-J or Philadelphia type).

Worsening shock should prompt rapid evaluation for new surgical bleeding, which is treated with either angiographic embolization or surgery. Sequential compression devices are placed on uninjured limbs for deep vein thrombosis prophylaxis, and subcutaneous heparin is started as soon as acute bleeding concerns have ceased. A plan for nutrition should be established. Family members should be contacted and updated regarding the patient's condition and prognosis. When the patient's abnormalities are corrected, one should anticipate returning to the operating room in 24–48 hours for staged procedures including internal fixation of orthopedic fractures, removal of abdominal packing, and reconstruction and closure of the abdomen.

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SECTION **15**

# POSTANESTHESIA CARE UNIT

CASE 78

# Asthma

**Andrew B. Leibowitz, MD • Elvis Umanzor Velasquez, MD**

## QUESTIONS

1. What is asthma, and how is it diagnosed?
2. What are the characteristic pulmonary function test findings seen in obstructive and restrictive lung disease, asthma, and chronic obstructive pulmonary disease?
3. What is the pharmacology of medications available to treat asthma; which medications are used for long-term control, and which medications are used for acute attacks; and what would be a treatment plan based on the degree of severity?
4. What are the indications for mechanical ventilation in severe asthma (status asthmaticus), and what are the specific concerns?
5. What preoperative evaluation and preparation would you order for this patient; would you cancel the case if the patient said that she was just recovering from a "bad cold" and had a few scattered wheezes on auscultation?
6. Would you choose general anesthesia (endotracheal intubation versus laryngeal mask airway) or a neuraxial block for this patient?
7. What are the signs and potential causes of perioperative bronchospasm?
8. After uneventful induction of general anesthesia and intubation, the patient's peak airway pressures suddenly increased during the procedure, and wheezing was heard on auscultation; what would you do?

A 30-year-old woman presented for elective uterine myomectomy. She had a long history of asthma, treated with an unknown inhaler, as needed. Preoperatively, her chest was clear to auscultation.

### 1. What is asthma, and how is it diagnosed?

Asthma is a common disease characterized by reversible airway obstruction with components of hyperresponsiveness and inflammation. Asthma "attacks" are characterized by episodes of shortness of breath, wheezing, and often cough. These episodes usually follow exposure to known triggers (e.g., pollen, dust, animal dander, smoke, change in weather, viral illness). The diagnosis is most commonly made by history and examination alone. Measurements of peak expiratory flow (PEF) rate and forced expiratory volumes and their response to bronchodilator administration may sometimes be necessary.

### 2. What are the characteristic pulmonary function test findings seen in obstructive and restrictive lung disease, asthma, and chronic obstructive pulmonary disease?

Pulmonary function tests (PFTs) comprise spirometry and flow-volume loops. An arterial blood gas and diffusion of carbon monoxide can also be included. Typical values in obstructive and restrictive lung disease are shown in Table 78-1.

Asthmatics usually have normal PFTs between exacerbations. Narrowing limited to small airways may yield a normal ratio of forced expired volume in the first second ($FEV_1$) to forced vital capacity (FVC), but the more sensitive forced expiratory flow between 25% and 75% of FVC ($FEF_{25\%-75\%}$) would be decreased. Also, the $FEV_1$/FVC ratio is effort dependent and requires patient cooperation for accurate measurement, whereas $FEF_{25\%-75\%}$ does not depend on patient effort. $FEF_{25\%-75\%}$ is obtained by dividing the volume expired between 25% and 75% of the FVC by the time elapsed between these two points. Occasionally, bronchospasm may be intentionally triggered during PFT evaluation with methacholine or histamine to assess airway reactivity in patients with normal baseline PFTs who are suspected to have asthma.

For patients with chronic obstructive pulmonary disease (COPD), measurements are repeated after inhaled bronchodilators to evaluate the degree of reversibility. The fixed component of COPD is due to inflammation and airway destruction.

Flow-volume curves may also be helpful. A normal curve and typical curves from patients with obstructive and restrictive disease are shown in Figure 78-1. By convention, inspiration is below the *x* axis, and expiration is above the *x* axis. In restrictive disease, airway resistance is normal with no flow limitation, whereas lung volumes are reduced. In obstructive disease, the expiratory flow curve shows a characteristic flattening secondary to increased airway resistance.

Curves from patients with fixed airway obstruction and variable extrathoracic and intrathoracic obstructions are shown in Figure 78-2. Fixed obstruction, exemplified by tracheal stricture or compression by a tumor or goiter,

**TABLE 78-1 Results of Pulmonary Function Tests in Obstructive and Restrictive Lung Disease**

| Value | Obstructive | Restrictive |
|---|---|---|
| FVC | Normal or decreased | Decreased |
| $FEV_1$/FVC | Decreased | Normal or increased |
| MMEFR ($FEF_{25\%-75\%}$) | Decreased | Normal |
| MBC | Decreased | Normal |
| TLC | Normal or increased | Decreased |
| RV | Increased | Decreased |
| DLCO | Decreased in COPD<br>Normal in asthma | Decreased |

*COPD,* Chronic obstructive pulmonary disease; *DLCO,* diffusion capacity of the lung for carbon monoxide; *$FEF_{25\%-75\%}$,* forced expiratory flow between 25% and 75% of forced vital capacity; *$FEV_1$,* forced expired volume in the first second; *FVC,* forced vital capacity; *MBC,* maximum breathing capacity; *MMEFR,* maximal midexpiratory flow rate; *RV,* residual volume; *TLC,* total lung capacity.

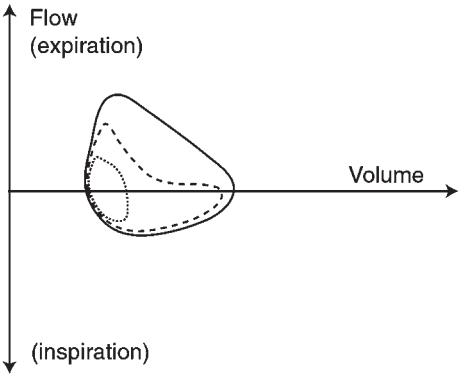


**FIGURE 78-1** ■ Flow-volume curves in a normal patient *(continuous curve)*, in a patient with obstructive lung disease *(dashed curve)*, and in a patient with restrictive lung disease *(dotted curve)*.

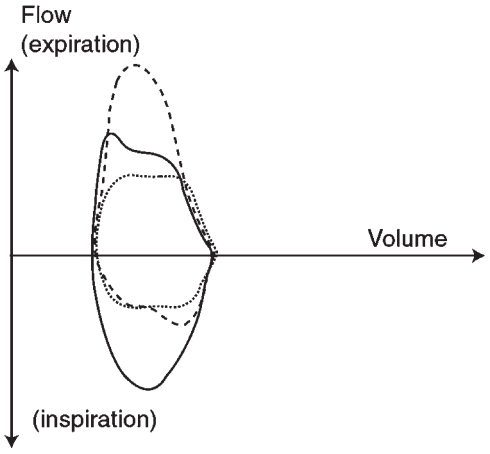


**FIGURE 78-2** ■ Flow-volume curves in a patient with fixed airway obstruction *(dotted curve)*, in a patient with variable extrathoracic obstruction *(dashed curve)*, and in a patient with variable intrathoracic obstruction *(continuous curve)*.

causes decreases in inspiratory and expiratory flows. Variable extrathoracic obstruction, such as vocal cord paralysis or marked pharyngeal muscle weakness, causes airway collapse during inspiration because negative inspiratory pressure is transmitted to the extrathoracic airway. Mobile surrounding tissues are drawn into the airway, obstructing the flow of gas. With variable intrathoracic obstruction (e.g., caused by tracheal or endobronchial tumor), airway narrowing increases during forced expiration.

### 3. What is the pharmacology of medications available to treat asthma; which medications are used for long-term control, and which medications are used for acute attacks; and what would be a treatment plan based on the degree of severity?

An overview of the medications used to treat asthma is presented in Table 78-2. Short-acting $\beta_2$ agonists and systemic steroids are used for the treatment of acute attacks. All other medications are used for long-term control of asthma. Products combining $\beta_2$ agonists (usually long-acting) and steroids (e.g., fluticasone and salmeterol) are commonly prescribed for patients with moderate and severe persistent asthma, although the efficacy and safety of long-acting $\beta_2$ agonists have been questioned. Patients with severe disease occasionally need oral steroids for long periods. A detailed discussion of the long-term treatment of asthma is beyond the scope of this chapter, and recommendations vary among authors. Suggested regimens are as follows:

- Intermittent asthma: Inhaled short-acting $\beta_2$ agonist used on an as-needed basis
- Mild persistent asthma: Low-dose inhaled corticosteroids or leukotriene antagonists as long-term treatment, in addition to inhaled short-acting $\beta_2$-agonist inhalers used as needed
- Moderate persistent asthma: Medium dose of inhaled corticosteroid possibly with an inhaled long-acting $\beta_2$ agonist
- Severe persistent asthma: High dose of inhaled corticosteroid and a long-acting $\beta_2$ agonist; in addition, long-term oral steroids are often required

TABLE 78-2 **Pharmacology of Medications Used to Treat Asthma**

| Drug Class | Representative Medications | Onset | Duration | Side Effects | Other Comments |
|---|---|---|---|---|---|
| $\beta_2$ Agonist short-acting | Albuterol<br>Metaproterenol | Immediate | 3–4 hours | Tachycardia, hypokalemia | |
| $\beta_2$ Agonist long-acting | Salmeterol<br>Formoterol | Days | Days | Tachycardia, hypokalemia | Increased risk of death (?); never used as monotherapy in severe asthma |
| Inhaled steroid | Fluticasone<br>Triamcinolone<br>Beclomethasone | Days | Days | Minimal | |
| Oral and intravenous steroids | Prednisone<br>Hydrocortisone<br>Methylprednisolone | 6 hours | Days | Hyperglycemia, infection, myopathy, avascular femoral necrosis | |
| Inhaled anticholinergics | Ipratropium<br>Tiotropium | Days | Days | Cough, dry mouth, blurred vision | Best for COPD and if patient also taking a β blocker |
| Leukotriene antagonists | Montelukast<br>Zileuton<br>Zafirlukast | Days | Days | Churg-Strauss syndrome (vasculitis of small arteries and veins) | Not for immediate or severe asthma treatment; also used for seasonal allergies |
| Chromones | Cromolyn<br>Nedocromil | Minutes | Hours | Sore throat and cough | Best used before exposure to known trigger |

*COPD,* Chronic obstructive pulmonary disease.

Acute attacks not responding to a self-administered metered-dose inhaler $\beta_2$ agonist are usually treated with $\beta_2$-agonist nebulizers and systemic steroids (e.g., methylprednisolone, 40-60 mg intravenously), which are tapered over a few days.

### 4. What are the indications for mechanical ventilation in severe asthma (status asthmaticus), and what are the specific concerns?

The indications for tracheal intubation and mechanical ventilation in severe asthma are hypercapnia and impending physical exhaustion, despite treatment. Hypoxemia and somnolence likely indicate that tracheal intubation was delayed too long. Tracheal intubation can acutely worsen airway obstruction because of bronchial hyperresponsiveness, and a treatment plan for this possibility needs to be established ahead of time.

The main concerns of mechanically ventilating asthmatic patients are increased airway resistance, high peak insufflation pressures, prolonged expiration times, auto-PEEP (positive end expiratory pressure), and breath "stacking." Reasonable initial settings are fraction of inspired oxygen ($FiO_2$) of 1.0, respiratory rate of 8–12 breaths per minute, and tidal volume of 6–8 mL/kg of lean body weight. Increasing expiratory time, high inspiratory peak flows (80–100 L per minute if using an intensive care unit–style ventilator), and low inspiratory/expiratory ratio (e.g., 1:4–1:6) are helpful. Most modern ventilators allow auto-PEEP to be measured by triggering an expiratory pause (provided that the patient is sedated enough to prevent spontaneous breathing). Occasionally, in patients with extreme bronchospasm, neuromuscular blockade might be used to increase chest wall compliance and make ventilation easier.

### 5. What preoperative evaluation and preparation would you order for this patient; would you cancel the case if the patient said that she was just recovering from a "bad cold" and had a few scattered wheezes on auscultation?

History and physical examination usually suffice for the preoperative evaluation. The key historical points to ascertain are the frequency and severity of attacks, response to treatment, need for emergency department visits, hospital admissions and mechanical ventilation, use of systemic steroids (dose, duration, last use), and long-term medications. If the patient uses a PEF device, the best PEF and the current value should be compared. There is no benefit in obtaining preoperative PFTs for a patient with asthma.

The key physical examination finding is the presence or absence of wheezing. If there is any wheezing, prolongation of the expiratory phase of respiration and use of accessory muscles should be noted. Severe bronchospasm may manifest with absence of breath sounds

and no wheezing, but many asthmatics when examined carefully always wheeze, even when asymptomatic.

Patients who are asymptomatic with a history of mild asthma do not need any special testing or preparation. Their usual medications should be continued per usual routine, and an inhaled $\beta_2$ agonist should be administered before entering the operating room. Perioperative steroids should be reserved for asthmatics with moderate or severe asthma. Treatment should be initiated the day before surgery with prednisone, 40 mg daily, or its equivalent. A postoperative nausea and vomiting prophylactic dose of dexamethasone (e.g., 8 mg) is equivalent to approximately 50 mg of prednisone. In the absence of problematic asthma complicating the immediate perioperative course, this dose of steroid either can be discontinued after 2–3 days or rapidly tapered over 4–7 days without risk.

A history of recent respiratory viral infection increases airway reactivity in normal patients and is one of the main triggers for exacerbations in asthmatics. In an adult patient with a clear chest examination, it is probably safe to proceed, but postponement may be the safer course of action in the presence of fever, erythematous throat, and productive cough. In this patient, with known asthma and an abnormal chest examination, postponement is indicated.

### 6. Would you choose general anesthesia (endotracheal intubation versus laryngeal mask airway) or a neuraxial block for this patient?

Regional anesthesia is generally preferable because airway instrumentation would be avoided, but patients undergoing regional anesthesia are not completely immune from intraoperative bronchospasm. Two often cited concerns that are rarely an issue are (1) a high block may adversely affect pulmonary function, and (2) sympathetic blockade would cause unopposed vagal tone leading to bronchospasm. As with any regional anesthetic, there is a risk of failure and need for general anesthesia.

General anesthesia can almost always be safely administered. Basic principles include the need to obtain a deep plane of anesthesia before laryngoscopy and tracheal intubation and consideration of ketamine as the induction agent. Laryngeal mask airway insertion has been shown to be associated with less increased airway resistance compared with endotracheal intubation and might be preferable. However, a laryngeal mask airway does not always protect against aspiration of gastric contents, and in the case of abdominal surgery in which there is peritoneal irritation and need for neuromuscular blockade, a tracheal tube is preferable.

### 7. What are the signs and potential causes of perioperative bronchospasm?

Bronchospasm is recognized by auscultation of expiratory wheezing accompanied by a prolonged expiratory time. Tachypnea and dyspnea are usually present in an awake patient, but increased airway resistance with an increase in inflation pressures is usually noted first in anesthetized mechanically ventilated patients. In addition to asthma, other causes of bronchospasm include tracheal tube obstruction (e.g., kink, secretions), congestive heart failure, allergic reactions (e.g., drugs, blood transfusion reaction), increased histamine release (e.g., secondary to morphine), and rarely pneumothorax and pulmonary embolus.

### 8. After uneventful induction of general anesthesia and intubation, the patient's peak airway pressures suddenly increased during the procedure, and wheezing was heard on auscultation; what would you do?

An orderly approach to wheezing, even in the absence of a history of asthma, is a basic skill every anesthesiologist must be able to perform reflexively. A reasonable checklist that can be modified to suit the specific patient, operation, and incident severity follows:

1. Immediately increase $FiO_2$ to treat or in anticipation of decreased oxygen saturation. Short-term $FiO_2$ of 1.0 is completely safe.
2. Rule out mechanical causes of wheezing, including main stem intubation, tracheal tube tip abutting the carina, tracheal tube kink, and obstruction by secretions (pass a "whistle tip" suction catheter through the tracheal tube). Always consider pneumothorax in the differential diagnosis.
3. Deepen the anesthetic by increasing the volatile agent concentration, and optimize neuromuscular blockade if diaphragmatic or chest wall compliance is possibly contributory.
4. Administer an inhaled short-acting $\beta_2$ agonist (e.g., albuterol) by metered-dose inhaler or nebulizer. High doses may be given with minimal side effects.
5. Administer steroids (e.g., hydrocortisone 100–200 mg or methylprednisolone 40–60 mg intravenously). Onset might take 6 hours, but if bronchospasm persists, early administration would be advantageous.
6. If life-threatening bronchospasm occurs, consider magnesium sulfate (e.g., 2 g intravenously) and as a last resort intravenous epinephrine (e.g., 5–10 μg).
7. Consider inhaled ipratropium in patients with a chronic obstructive component or if the patient also takes a β blocker.
8. Remember basic mechanical ventilation principles. A normal or low tidal volume with prolonged expiratory time would be advantageous. Respiratory acidosis is generally very well tolerated.

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CASE 79

# Hypothermia

Andrew B. Leibowitz, MD • Gene Tulman, MD

## QUESTIONS

1. How is hypothermia defined and graded?
2. What mechanisms lead to hypothermia in surgical patients under general anesthesia?
3. Explain the physiologic responses to hypothermia.
4. Describe the physiologic consequences of hypothermia.
5. Are there any benefits to mild intraoperative hypothermia?
6. Where are the commonly used temperature monitoring sites?
7. How is hypothermia prevented?
8. Is hypothermia prevention warranted for patients receiving central neuraxial blockade?

A 71-year-old man underwent subtotal colectomy complicated by hypothermia. He was brought to the postanesthesia care unit (PACU) with a temperature of 31.9° C.

### 1. How is hypothermia defined and graded?

Hypothermia is defined as a core body temperature <35° C. It is often further characterized as mild (32°–35° C), moderate (28°–32° C), and severe (<28° C).

### 2. What mechanisms lead to hypothermia in surgical patients under general anesthesia?

The first phase of hypothermia is due to redistribution. Core temperature decreases by 0.5°–1.5° C during the first hour after induction of general anesthesia if warming measures are not instituted on entry to the operating room. During this time, heat is redistributed from the core to the periphery. The second phase is due to heat loss in excess of heat production and lasts 2–3 hours. Heat production decreases by approximately 20% after induction of general anesthesia. Core temperature plateaus after 3–4 hours because of peripheral vasoconstriction that is triggered by a core temperature of 33°–35° C. However, peripheral temperature continues to decrease.

There are four mechanisms of heat loss, as follows:

- Radiation is the movement or transfer of heat from a warm object to a colder one that is not in direct contact and accounts for approximately 60% of heat loss.
- Evaporation is heat lost as body fluids leave the liquid (water) state and enter the gaseous phase and typically accounts for 15%–20% of heat loss (e.g., respiratory tract, open abdomen, or thorax).
- Convection is the movement or transfer of heat from the patient to the passing cooler air and typically accounts for 15%–20% of heat loss.
- Conduction is the movement or transfer of heat from the patient to an adjacent object and typically accounts for ≤5% of heat loss (e.g., the operating table).

In other settings, hypothermia can result from loss of central thermoregulation (e.g., stroke, head trauma, spinal cord injury), drugs (e.g., alcohol or barbiturate overdose), or metabolic derangement (e.g., hypoglycemia, hypothyroidism, sepsis, burns, hepatic failure).

### 3. Explain the physiologic responses to hypothermia.

There are three physiologic responses to hypothermia.

#### *Vasoconstriction*

Vasoconstriction is the result of sympathetic stimulation. Volatile agents reduce the threshold for vasoconstriction by 2°–4° C. The vasoconstrictive threshold is also reduced by approximately 1° C in elderly patients, who are at higher risk for hypothermia.

#### *Shivering Thermogenesis*

Shivering thermogenesis is an involuntary oscillatory muscular activity that augments the basal metabolic rate by a factor of two to four times. The threshold for shivering is usually about 1° C less than the vasoconstriction threshold. Shivering is a "last resort" response and is metabolically much less efficient than vasoconstriction. The shivering threshold is decreased by potent inhalation anesthetics even more than the vasoconstriction threshold. Two types of patterns are seen, as follows:

- A *tonic* pattern resembles normal shivering at four to eight cycles per minute and has a waxing and waning component.
- A *phasic* pattern resembles clonus with a 5- to 7-Hz burst pattern seen most specifically in the postanesthesia period. This pattern is often secondary to volatile anesthetic administration and probably results from anesthetic-induced disinhibition of normal descending control over spinal reflexes.

Shivering in the postoperative period can increase oxygen consumption by 300%–500% contributing to a potentially significant oxygen/demand mismatch that can lead to myocardial ischemia in susceptible patients. It can also increase the serum potassium level.

### *Nonshivering Thermogenesis*

Nonshivering thermogenesis is the mechanism of heat production in infants that is not associated with muscle activity. This mechanism may double the metabolic heat production in infants, but it does not play a significant role in adults. (See Chapter 64 for a detailed explanation of nonshivering thermogenesis.)

## 4. Describe the physiologic consequences of hypothermia.

The physiologic consequences of hypothermia are summarized in Table 79-1. Electrocardiogram (ECG) changes

TABLE 79-1 **Physiologic Consequences of Hypothermia**

| Parameter | Change | Implication |
|---|---|---|
| Oxygen and $CO_2$ solubility | Increased | pH increases by 0.015 per 1° C decrease |
| Volatile anesthetics solubility | Increased | May contribute to prolonged emergence from general anesthesia with potent inhalation anesthetics |
| MAC | Decreased | Delayed awakening<br>Postoperative confusion |
| Cardiac output | Decreased | Blood flow decreases in the following order: muscle, kidneys and gut, brain and heart |
| Speed of induction | Unchanged | No change seen because both MAC and cardiac output are decreased |
| Oxygen consumption and $CO_2$ production | Decreased | Decreased by 7%–9% per 1° C decrease |
| $PaCO_2$ | Decreased | Decreased by 1.5% per 1° C decrease (i.e., $PaCO_2$ equals temperature [° C]) |
| Plasma catecholamines | Increased | Hypertension<br>Tachycardia<br>Hyperglycemia |
| Plasma insulin | Decreased | Hyperglycemia from activation of glycogenolysis and gluconeogenesis |
| Hemoglobin affinity for oxygen | Increased | Increased by 6% per 1° C decrease (left shift in oxyhemoglobin dissociation curve) |
| Hypoxic ventilatory drive | Depressed | Hypercarbia driven ventilation |
| Bronchomotor tone | Decreased | Increased anatomic dead space |
| Hypoxic pulmonary vasoconstriction | Decreased | Worsening of ventilation/perfusion mismatch |
| Threshold for ventricular fibrillation | Decreased | Risk of ventricular fibrillation becomes significant at $<$32° C |
| Systemic vascular resistance | Increased | May contribute to left ventricular failure |
| Pulmonary vascular resistance | Increased | May contribute to right ventricular failure |
| Hepatic blood flow | Decreased | Proportional to decrease in cardiac output |
| Renal blood flow | Decreased | Decreases proportionately more than cardiac output |
| Diluting and concentrating capacity; tubular transport of sodium, chloride, water, and potassium | Decreased | "Cold diuresis" can lead to hypovolemia and hemoconcentration |
| Blood viscosity | Increased | Increased by 2%–3% per 1° C decrease |
| Coagulation | Impaired | Decreased circulating factors<br>Platelets sequestered in portal circulation |
| Platelet function | Impaired | Perioperative bleeding may contribute to increased transfusion requirements |
| Urinary nitrogen excretion | Increased | Remains high for several days postoperatively |
| Drug metabolism | Decreased | Effect of most intravenous pharmacologic agents requiring end-organ metabolism (e.g., vecuronium, propofol) is prolonged |
| Immune function | Impaired | Reduced monocyte HLA-DR surface expression<br>Delayed clearance of TNF-α<br>Increased IL-10 release |

*$CO_2$,* Carbon dioxide; *HLA-DR,* human leukocyte antigen, DR subregion; *IL-10,* interleukin-10; *MAC,* minimum alveolar concentration; *$PaCO_2$,* arterial carbon dioxide tension; *TNF-α*, tumor necrosis factor-α.

include sinus bradycardia, widened P–R interval, widened QRS, and prolonged Q–T interval. The Osborn wave is characteristic for hypothermia (Figure 79-1). This wave is a deflection at the J point (the junction between the QRS complex and the ST segment) in the same direction as that of the QRS complex, with a height proportional to the degree of hypothermia. It is frequently mistaken for genuine ST segment elevation.

Several deleterious clinical consequences have been well documented, including the following:

- Impaired coagulation has been shown to lead to higher transfusion requirements in patients undergoing total hip replacement.
- The incidence of wound infection is increased because of direct impairment of the immune function and a decrease in oxygen delivery to the tissue edges.
- The incidence of postoperative myocardial infarction and ventricular dysrhythmias is increased.
- Hospital length of stay is increased.

The current recommendation is to maintain temperature at ≥36° C to avoid hypothermia-related adverse outcomes. This temperature goal is emerging as a standard for reporting to various regulatory authorities. Failure to maintain normothermia could subject institutions to financial penalties. Hypothermic patients, especially patients with coronary artery disease, might benefit from remaining under anesthesia into the postoperative period until adequate rewarming is achieved to avoid the potential shivering-related increased oxygen consumption and resultant myocardial ischemia.

## 5. Are there any benefits to mild intraoperative hypothermia?

For years, hypothermia had been postulated to confer protection against cerebral hypoxia. However, the Intraoperative Hypothermia for Aneurysm Surgery Trial (IHAST) failed to demonstrate any neuroprotective benefits of mild hypothermia in patients undergoing temporary clipping during cerebral aneurysm surgery. In contrast, hypothermia acutely applied to patients who survive cardiac arrest but are comatose has become widely accepted in recent years. Recommendations at the present time are for cooling to 32°–34° C for 12–24 hours.

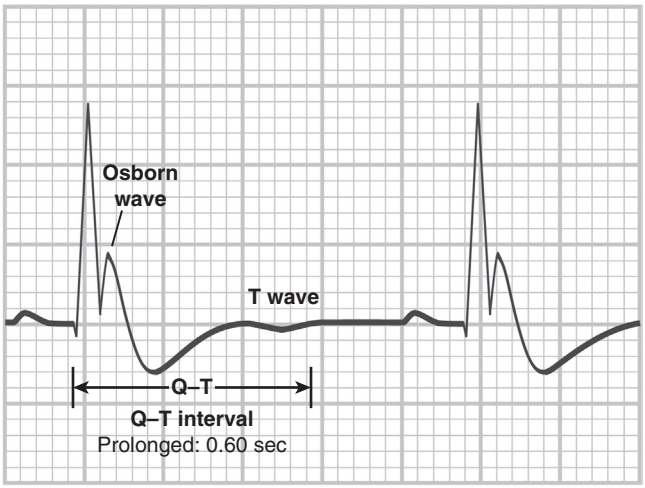


**FIGURE 79-1** ■ Osborn wave and prolonged Q–T interval seen on ECG in hypothermic patients.

## 6. Where are the commonly used temperature monitoring sites?

Temperature may be monitored via oral, rectal, esophageal, nasopharyngeal, and tympanic membrane sites. It can also be monitored via pulmonary artery catheter or urinary bladder catheter. With the exception of the oral route, all other methods provide a generally accurate and reproducible measurement of core temperature in general surgical patients.

Skin temperature monitoring is usually accomplished using liquid crystal–containing strips or probes with thermistor tips, but the potential large difference between core and peripheral temperature makes skin monitoring suboptimal intraoperatively and may be inaccurate on admission to the PACU.

During hypothermic cardiopulmonary bypass, significant gradients can exist between core, blood, and peripheral temperatures. Pulmonary artery catheters measure temperature of blood from the cardiopulmonary bypass pump. Core temperature (esophageal, nasopharyngeal, and tympanic) lags behind. Envelope (rectal) temperature takes even more time to equilibrate during both cooling and rewarming.

## 7. How is hypothermia prevented?

The four mechanisms of heat loss should be kept in mind. Redistribution and loss that is primarily due to radiation are the largest largely preventable mechanisms by early application of skin warming. Even in the absence of active warming, simply increasing the ambient (room) temperature is very helpful because radiation heat loss is proportional to the fourth power of the difference between the absolute temperatures of surfaces. Radiation heat loss can be limited simply by increasing ambient (room) temperature. Radiant warmers are used only for infants and are effective only while the patient is exposed. Use of radiant warmers can preclude the need to increase room temperature. However, intervening drapes render radiant warmers ineffective, and increasing distance between the patient and the warmer diminishes its effectiveness.

Warming of inspired gas and intravenous fluid has limited efficacy. Less than 10% of heat loss occurs in the respiratory tract. Fluid warming becomes more important as larger volumes are administered over shorter times. Body temperature is decreased by about 0.25° C with 1 L of crystalloid at room temperature or 1 unit (250 mL) of refrigerated blood.

Insulation with one layer of fabric (sheet or blanket) decreases heat loss by only 30%. There is little additional benefit from additional layers. Forced-air warming (e.g., Bair Hugger Blanket; Arizant Healthcare Inc., Eden Prairie, MN) is the most effective warming and rewarming method. It works best when patients are vasodilated. It is better to maintain normothermia from the time of entry into the operating room rather than to have to rewarm postoperatively. Rewarming a vasoconstricted

patient can lead to hypotension secondary to vasodilation, especially if volume status is not maintained, which is a frequently seen complication in the PACU. Circulating-water mattresses placed on the operating room table have little efficacy. A minimal amount of the patient's body surface area actually contacts the mattress, substantially limiting its effectiveness.

Forced-air warmers are effective but must be used with caution. They can produce burns if applied directly to the skin. Hot-water bottles and forced hot air warming without the appropriate blanket should absolutely be avoided. They are frequent causes of perioperative thermal injury according to the American Society of Anesthesiologists Closed Claims Project database.

Shivering can be treated by skin-surface warming and pharmacologically, most commonly with meperidine, 12.5–50 mg intravenously. The exact mechanism of action of meperidine is unknown, but it is likely associated with its multireceptor activity including the $\alpha_{2b}$-adrenergic receptor and the kappa receptor. Dexmedetomidine, an $\alpha_2$ agonist, has also been reported to be effective but is a very expensive option with a propensity to reduce blood pressure and promote bradycardia. The mechanism of action of dexmedetomidine involves a decrease of vasoconstriction and shivering thresholds. Another rarely employed adjunct in the PACU is buspirone, a serotonin 5-$HT_{1A}$ partial agonist, which is now frequently used in post–cardiac arrest hypothermia–related shivering algorithms.

### 8. Is hypothermia prevention warranted for patients receiving central neuraxial blockade?

Neuraxial blockade results in a functional sympathectomy in the anesthetized area causing loss of autoregulation and vasodilation. Additionally, shivering is precluded by motor blockade. Central control is impaired secondary to elevated skin temperature from cutaneous vasodilation. Significant hypothermia can occur, leading to discomfort and possible shivering, although the shivering threshold is reduced in this setting. Measures to prevent hypothermia should be used during central neuraxial blockade.

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CASE 80

# Postanesthesia Care Unit Discharge Criteria

Andrew B. Leibowitz, MD • Gene Tulman, MD

## QUESTIONS

1. What is the cause of nausea and vomiting?
2. What are the risk factors for postoperative nausea and vomiting?
3. What are the incidence and implications of postoperative nausea and vomiting?
4. What are the strategies to reduce the incidence and severity of postoperative nausea and vomiting?
5. What are the treatment considerations for postoperative nausea and vomiting?
6. What complications occur in the postanesthesia care unit?
7. What are the commonly applied postanesthesia care unit discharge criteria?
8. Describe a postanesthesia care unit scoring system used to assess readiness for discharge.

A 36-year-old woman underwent uneventful laparoscopic salpingo-oophorectomy under general anesthesia. In the postanesthesia care unit (PACU), she complained of severe nausea and vomited. She wanted to be discharged home.

### 1. What is the cause of nausea and vomiting?

The vomiting center is located in the medulla. It receives input from the chemoreceptor zone and gastrointestinal tract. The vomiting center may be activated by various stimuli, including medications, body motion, stimulation of the posterior pharynx, odors, and visual images.

### 2. What are the risk factors for postoperative nausea and vomiting?

Risk factors for postoperative nausea and vomiting (PONV) are related to patient characteristics, type of surgery, and anesthetic. The main patient characteristics that increase the risk of PONV are female gender (especially if pregnant or menstruating), prior history of PONV, history of motion sickness, and being a nonsmoker.

Operative procedures particularly associated with an increased incidence of PONV are laparoscopy, breast, strabismus, and ear-nose-throat procedures. Surgical duration >30 minutes also increases the risk of PONV.

General anesthesia entailing potent volatile agents, nitrous oxide, and intravenous opioids increases the risk of PONV, whereas use of a propofol-based general anesthetic reduces the incidence and severity of PONV. There is little benefit if propofol is used only as an induction agent and a significant benefit if it is used as a maintenance infusion. Etomidate is associated with an increased risk of PONV and should be used only when hemodynamic stability is of paramount importance.

The incidence of PONV is similar regardless of type of opioid administered; opioid-sparing techniques should contribute to a risk reduction of PONV. A meta-analysis showed that a single perioperative intravenous dose of 60 mg of ketorolac was associated with a potentially clinically significant opioid-sparing effect and a statistically significant reduction in PONV. Intravenous acetaminophen, which became available in the United States more recently, can be expected to result in similar improved outcomes. Regional anesthetic techniques (e.g., peripheral nerve blocks) without intravenous opioid supplementation are also effective in reducing the risk of PONV.

### 3. What are the incidence and implications of postoperative nausea and vomiting?

PONV is the most common postoperative complication and the leading cause of delayed discharge from the PACU. It has been estimated that 25%–30% of surgical patients experience PONV within 24 hours of surgery. In high-risk surgical patients, the incidence of PONV may be 70%–80%. The incidence of perioperative vomiting in children has been estimated to be twice that of adults. In one review of 8995 pediatric outpatient cases, 26 patients required admission for persistent nausea and vomiting, accounting for 36% of all unanticipated hospital admissions. PONV may contribute to high levels of patient discomfort, delayed PACU discharge, increased need for nursing care, and potential hospital admission. All of these factors may

increase avoidable periprocedural cost and are a main cause of patient dissatisfaction.

### 4. What are the strategies to reduce the incidence and severity of postoperative nausea and vomiting?

The 2007 Society of Ambulatory Anesthesia Guidelines for the Management of Postoperative Nausea and Vomiting recommend the following strategies to reduce PONV:

- Use of regional anesthesia with no or minimal intravenous opioid supplementation
- Use of propofol for induction and maintenance of general anesthesia
- Avoidance of nitrous oxide
- Avoidance of volatile anesthetics
- Avoidance or minimization of intraoperative and postoperative opioids
- Avoidance or minimization of neostigmine given for muscle relaxant reversal
- Administration of adequate hydration
- Prophylactic administration of 5-$HT_3$ antagonists
- Prophylactic administration of additional antiemetic medications to high-risk patients

### 5. What are the treatment considerations for postoperative nausea and vomiting?

Although there may be no consensus to administer antiemetic prophylaxis to all surgical patients, routine administration of some generically available agents is commonplace because of their minimal cost and risk. Considerations to administer pharmacologic antiemetic prophylaxis and treatment of established PONV should be individualized based on the previously discussed risk factors. Patients with several risk factors frequently require more than one agent. The following drugs are commonly administered either prophylactically or as treatment. They are listed in order of clinical usefulness and ease of use-to-risk ratio: 5-$HT_3$ receptor antagonists, dexamethasone, droperidol, scopolamine, and metoclopramide.

- *Ondansetron*, *dolasetron*, *granisetron*, and *palonosetron* are currently available 5-$HT_3$ receptor antagonists approved for the prevention of PONV; ondansetron is the most widely studied. There is no significant difference in efficacy among these drugs when comparing equipotent doses. The recommended adult dose of ondansetron is 4 mg intravenously. Ondansetron is effective when administered after general anesthesia induction or approximately 30 minutes before the end of surgery. 5-$HT_3$ receptor antagonists are the first choice for prophylaxis in children. Although frequently administered to treat established PONV, they are not effective if already administered prophylactically within the previous 4 hours. They all have minimal, if any, clinically significant side effects; however, there have been reports of Q–T interval prolongation similar to that seen with droperidol.
- *Dexamethasone* is a potent synthetic glucocorticoid (0.75 mg of dexamethasone is equivalent to 20 mg of hydrocortisone). It is usually administered prophylactically in a dose of 4–10 mg intravenously after induction of general anesthesia. Administration may be associated with acute vaginal burning in awake female patients and with scrotal burning in male patients, which can be quite disturbing. Routine administration should be standard after induction of general anesthesia. Some studies have suggested that smaller doses (4 mg) are as effective as larger doses. The antiemetic mechanism of action is not well understood. No clinically significant adverse events have been noted after a single bolus dose of dexamethasone but caution is warranted in diabetic patients who are prone to hyperglycemia. The effectiveness of dexamethasone in treating established PONV is not nearly as well documented as the prophylactic effect.
- *Droperidol* is a pharmacologic relative of the more widely used antipsychotic drug haloperidol. It is a potent α-adrenergic antagonist. In small doses (0.625–1.25 mg intravenously), it significantly decreases the incidence of PONV. When given in higher doses, it may be associated with excessive sedation and delayed discharge from the PACU. In 2001, the U.S. Food and Drug Administration (FDA) issued a "black box" warning noting that droperidol can cause Q–T interval prolongation, has been associated with lethal arrhythmias (e.g., torsade de pointes), and should not be administered in the presence of known Q–T interval prolongation. In the absence of a prolonged Q–T interval, it was recommended that patients receiving droperidol should have electrocardiogram (ECG) monitoring for 2–3 hours after administration. The FDA was widely criticized for these warnings and recommendations because this decision was mostly based on reported cases involving much higher doses of the drug than were clinically used in the United States and that low doses had not been associated with arrhythmia or cardiac arrest. Nonetheless, the "black box" warning has contributed to a significant reduction in the use of droperidol for prevention and treatment of PONV. However, in high-risk patients, early administration of droperidol allows for the requisite ECG monitoring period while conferring significant reduction in the risk of PONV.
- *Scopolamine* is an anticholinergic drug that is usually applied as a transdermal patch and is better known for the prevention of motion sickness. It reduces PONV with minimal side effects but should be applied well before the induction of general anesthesia. Intramuscular or intravenous administration is much more likely to cause a central cholinergic syndrome consisting of sedation, amnesia, and euphoria. Consequently, intramuscular and intravenous routes of delivery are less desirable. The transdermal patch may be associated with complaints of dry mouth and visual disturbances.
- *Metoclopramide* is a methoxychlorinated derivative of procainamide and is a dopamine antagonist. It is the weakest of all of the medications discussed here, and its ability to prevent PONV or treat

established PONV has been questioned. Its antiemetic effect results primarily from increasing gastric emptying and lowering esophageal sphincter pressure. Although it may be administered orally and intramuscularly, 10 mg administered intravenously is the standard clinical dose. Extrapyramidal effects are common and frequently very disturbing to patients. Its poor efficacy and substantial side effects have led many clinicians to abandon the use of metoclopramide. It is not even mentioned in the 2007 SAMBA guidelines for the management of PONV.

- *Aprepitant* is a newer $NK_1$ receptor antagonist that is very expensive and not widely used by anesthesiologists.

Administration of intraoperative fraction of inspired oxygen ($F_{IO_2}$) of 0.8 and postoperative supplemental oxygen ($F_{IO_2}$ >0.3) has been associated with decreased PONV in patients receiving general anesthesia; this may be the result of eliminating nitrous oxide administration rather than increasing oxygen concentration. Other nonpharmacologic therapies that are effective include the following:

- Acupuncture
- Acupoint stimulation via wristband
- Acupressure

Combining available therapies in management of PONV has been shown to be highly effective, with vomiting rates approaching 0% versus 7% with ondansetron alone and 22% with placebo. Although gastric suctioning before the completion of surgery empties the stomach and theoretically would reduce the incidence of PONV, this has not been shown to be efficacious.

## 6. What complications occur in the postanesthesia care unit?

The incidence of complications in the PACU is high. A review of >18,000 PACU admissions in a university hospital showed an overall complication rate of 26%; the most common complication was PONV (9.8%). Other complications are airway compromise (6.9%), hypotension (2.7%), dysrhythmias (1.4%), hypertension (1.1%), altered mental status (0.6%), suspected myocardial infarction (0.3%), and other major cardiac events (0.3%). Another review of 120 incidents occurring in the PACU found that two thirds were related to respiratory complications. The incidence of complications and specific frequency of each of these complications are significantly influenced by the patient population and types of surgery performed. Healthy young patients undergoing ambulatory procedures most frequently experience PONV, whereas elderly patients with American Society of Anesthesiologists Physical Status 4 undergoing major abdominal, thoracic, and vascular procedures experience respiratory and cardiac complications.

## 7. What are the commonly applied postanesthesia care unit discharge criteria?

Discharge of patients to home after surgery and anesthesia is safest when predetermined discharge criteria are rigorously applied to all patients. Although criteria may vary from center to center, the following summarizes what typically occurs on discharge.

### *Examination*

1. The patient should have stable vital signs for at least 30 minutes and consistent with his or her age and preanesthetic examination.
2. The patient should be able to swallow and cough.
3. The patient should be able to walk or return to preoperative status.
4. The patient should have minimal nausea and vomiting allowing for the ability to swallow and retain liquids.
5. The patient should have little or no dizziness allowing for ambulation.
6. The patient should have no respiratory distress.
7. The patient should be appropriately alert and oriented.
8. The patient should have no surgical contraindication to discharge (e.g., excessive pain, bleeding).

### *Instructions to Patient*

1. "You may experience sleepiness or fatigue and should not drive, operate machinery, or make any complex decisions until tomorrow."
2. "You may have a sore throat and should gargle with dilute salt water or take acetaminophen."
3. "You may experience muscular soreness that may also be treated with acetaminophen." (This is more likely if succinylcholine has been administered.)
4. "In case of any unforeseen emergent problem, call …." (The patient should be provided with an emergency phone number to contact.)
5. "An adult escort must accompany you home." (The availability of an escort should be ascertained before starting surgery because local law likely mandates this and forbids the discharge of even fully recovered patients on their own recognizance.)

### *Follow-Up*

A member of the anesthesia care team should call the patient on the day after surgery and confirm that there are no complaints and that the recovery is as expected.

## 8. Describe a postanesthesia care unit scoring system used to assess readiness for discharge.

The Aldrete scoring system (Table 80-1) and Postanesthesia Discharge Scoring System (PADSS) (Table 80-2) are two commonly used systems. Many variations, combinations, and permutations of these systems are employed. The Aldrete scoring system is primarily used to determine suitability for discharge from the PACU to an inpatient bed, and most PACUs would require a summative score of at least 9. The PADSS is more appropriate for determination of discharge to home; many PACUs look for a score of 9.

TABLE 80-1 **Aldrete Scoring System**

| Criteria | Points |
|---|---|
| **Respiration** | |
| Able to take deep breath and cough | 2 |
| Dyspnea or shallow breathing | 1 |
| Apnea | 0 |
| **Oxygen Saturation** | |
| >92% on room air | 2 |
| Require oxygen to maintain saturation >90% | 1 |
| <90% on supplemental oxygen | 0 |
| **Consciousness** | |
| Fully awake | 2 |
| Arousable on calling | 1 |
| Not responsive | 0 |
| **Circulation** | |
| BP ± 20 mm Hg of preoperative value | 2 |
| BP ± 20–50 mm Hg of preoperative value | 1 |
| BP ± 50 mm Hg of preoperative value | 0 |
| **Activity** | |
| Able to move all extremities | 2 |
| Able to move two extremities | 1 |
| Unable to move any extremity | 0 |

*BP,* Blood pressure.

TABLE 80-2 **Postanesthesia Discharge Scoring System**

| Criteria | Points |
|---|---|
| **Vital Signs** | |
| BP and pulse within 20% of preoperative values | 2 |
| BP and pulse within 20%–40% of preoperative values | 1 |
| BP and pulse <40% or >40% of preoperative values | 0 |
| **Activity** | |
| Steady gait, no dizziness | 2 |
| Requires assistance | 1 |
| Unable to ambulate | 0 |
| **Nausea and Vomiting** | |
| Minimal, treated with oral medication | 2 |
| Moderate, treated with intravenous or rectal medication | 1 |
| Severe, refractory to treatment | 0 |
| **Pain** | |
| Controlled and acceptable to patient—yes | 2 |
| Controlled and acceptable to patient—no | 1 |
| **Surgical Bleeding** | |
| Minimal—no dressing changes | 2 |
| Moderate—up to two dressing changes | 1 |
| Severe—more than three dressing changes | 0 |

*BP,* Blood pressure.

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CASE 81

# Delayed Emergence, Coma, and Brain Death

**Andrew B. Leibowitz, MD • Elvis Ulmanzor Velasquez, MD**

## QUESTIONS

1. What are the possible causes, work-up, and treatment for delayed emergence after general anesthesia?
2. Computed tomography scan showed a large left thalamic hemorrhage with intraventricular blood and a midline shift, and the patient remained comatose; how would you manage this patient in the intensive care unit?
3. On the following day, the patient responded to noxious stimuli with extensor posturing, and his pupils were 4 mm, fixed, and nonreactive to light; is this patient brain dead, and what are the criteria for brain death?
4. What is an apnea test, and how is it performed?

A 66-year-old man underwent craniotomy for clipping of a saccular aneurysm of the right middle cerebral artery. The aneurysm was discovered during the work-up of persistent headache and did not bleed preoperatively. At the conclusion of the procedure, the patient did not wake up.

### 1. What are the possible causes, work-up, and treatment for delayed emergence after general anesthesia?

#### *Anesthetic Medication Effect*

The effects of intravenous and inhalation anesthetics can be prolonged especially in advanced age and in the presence of hepatic and renal dysfunction. The total amount of medications administered should be reviewed, and special attention should be given to when the last doses were administered. The effects of propofol, midazolam, and volatile agents should rarely last >30–60 minutes if there was no "overdose." Analysis of expired gases can rule out the persistence of volatile agents. Benzodiazepines can be reversed by administration of flumazenil intravenously in 0.2-mg increments up to 1.0 mg, and physostigmine can reverse the effect of some sedatives, especially the central effects of anticholinergic agents such as scopolamine.

A prolonged opioid effect is more common. The patient typically presents with pinpoint pupils, a slow respiratory rate, and normal to high tidal volumes. Both diagnosis and treatment are accomplished by carefully titrating naloxone intravenously in 40-μg increments, up to 400 μg, or in rare cases higher doses if the suspicion is high. Complete opioid reversal is undesirable because it might lead to severe pain or withdrawal symptoms, with tachycardia, dysrhythmias, hypertension, increase in intracranial pressure (ICP), myocardial ischemia, and pulmonary edema. Occasionally, a continuous infusion of naloxone is required to prevent "renarcotization."

Residual neuromuscular blockade must always be suspected. The response to train-of-four stimulation (train-of-four ratio ≥0.9) can easily assess residual neuromuscular blockade. Care must be taken not to stimulate nerves in an area where upper motor neuron disease is present (e.g., hemiplegia) because the response can be normal-appearing, while neuromuscular blockade exists in normally innervated muscle. The typical behavior of a patient with residual neuromuscular blockade is rapid, shallow breathing and "flapping" of the limbs, described as "a fish out of water." When in doubt, additional cholinesterase inhibitors (usual maximum adult dose of neostigmine regardless of weight is 5 mg) can be given for reversal, or one can allow for more time to elapse. If the latter option is chosen, the patient should be adequately sedated to avoid an awake but paralyzed patient. Inadequate reversal of neuromuscular blockade (despite administration of an adequate reversal dose of neostigmine or edrophonium) may result from several circumstances, including (1) the original block was too dense to overcome, (2) severe acidosis, (3) hypothermia, (4) marked hypocalcemia, and, more rarely, (5) administration of antibiotics (e.g., aminoglycosides) or other medications (e.g., magnesium) that potentiate neuromuscular blockade.

#### *Metabolic Disorders*

The blood glucose should be measured to rule out hypoglycemia or marked hyperglycemia and hyperosmolar coma. Hypoglycemia should be treated with intravenous dextrose, at least 50 mL of 50% dextrose (25 g). If the suspicion is high, treatment should be initiated without waiting for the laboratory results. Blood analysis for

electrolytes and an arterial blood gas (ABG) should be performed, and any significant abnormality (especially hypoxemia, hypercapnia, and hyponatremia or hypernatremia) should be corrected. In patients whose immediate preoperative neurologic status is unknown or questionable, other etiologies such as hypothyroidism or adrenal insufficiency should be considered.

### *Neurosurgical Disorders*

A neurologic examination for focal deficits should be performed. If the cause of delayed awakening remains unclear, especially after a craniotomy, a computed tomography (CT) scan of the brain must be performed to search for intracranial pathology, such as intracranial hemorrhage. Ischemic cerebrovascular accidents are often not immediately seen on CT scan. Less commonly, CT scan may demonstrate tension pneumocephalus, caused by nitrous oxide, or global cerebral hypoxic damage. Cerebral hypoxia of any cause results in a reduced level of consciousness that may first appear as delayed emergence.

### *Other Causes*

Alcohol and other recreational drugs ingested preoperatively should be considered, especially in trauma patients. Blood and urine could be quickly sent for a toxicology screen.

Table 81-1 summarizes the differential diagnosis and work-up for delayed awakening.

## 2. Computed tomography scan showed a large left thalamic hemorrhage with intraventricular blood and a midline shift, and the patient remained comatose; how would you manage this patient in the intensive care unit?

The following parameters should be monitored and managed accordingly:

- Maintain close to normal hemodynamics
  - Fluid administration as necessary
  - Vasopressors or inotropes as indicated
- Cerebral perfusion pressure (CPP) should be maintained >70 mm Hg and is calculated as follows:

CPP = MAP − CVP or ICP (whichever is the higher value)
(MAP = mean arterial pressure, CVP = central venous pressure.)

- Mechanical ventilation
  - Airway protection
  - Maintain normal oxygenation
  - Mild hyperventilation (see subsequently)
- Decrease ICP
  - Elevate head of the bed 30 degrees (easiest and most effective measure).
  - Avoid excessive (e.g., >5 cm $H_2O$) positive end expiratory pressure.
  - Avoid agitation and "bucking."
  - Consider administration of mannitol (0.5–1 g/kg intravenously) or hypertonic saline (3% or 25%) to increase serum osmotic pressure.
  - Hyperventilate to arterial carbon dioxide tension ($PaCO_2$) of 30–35 mm Hg.
  - Consider insertion of ICP monitor (e.g., ventriculostomy), which also permits cerebrospinal fluid removal to manage cases of acute intracranial hypertension.
  - In extreme cases, craniectomy can be performed to remove part of the skull vault to control ICP.
- Avoid rebleeding
  - Control blood pressure.
  - Correct any coagulopathy.
  - Avoid anticoagulants (e.g., prophylactic doses of heparin subcutaneously for deep vein thrombosis are controversial but usually avoided).
- Prevent seizures
  - Administer fosphenytoin, 1500 mg (or 15 to 20 mg/kg) intravenously (equivalent to 1000 mg of phenytoin but less likely to cause hypotension in high doses) over 30 minutes, then phenytoin, 100 mg intravenously every 8 hours, adjusted based on plasma levels. Free phenytoin level rather than total phenytoin level may need to be checked.
- Prevent hyperthermia
  - Although the cerebral protective effect of hypothermia is still controversial, the deleterious effect of hyperthermia to the injured brain is well established.
  - Administer antipyretics and active cooling as needed.
- Glucose control
  - Hyperglycemia predicts increased risk of mortality and poor outcome in patients with intracerebral hemorrhage. However, more recent studies reveal an increased risk of hypoglycemic events and associated increased risk of mortality in patients treated with tight glucose control regimens. At the present time, the optimal target glucose is unclear but <180 g/dL is a reasonable goal. Hypoglycemia should be avoided and treated expeditiously.
- Prevent gastrointestinal bleeding
  - Administer anti–histamine $H_2$ agents (e.g., famotidine) or proton pump inhibitors (e.g., omeprazole).
- Prevent deep vein thrombosis
  - Apply sequential compression stockings.

**TABLE 81-1 Differential Diagnosis and Work-up for Delayed Awakening**

| | | |
|---|---|---|
| Metabolic | Hypoxia<br>Hypercapnia<br>Hypoglycemia<br>Electrolyte disturbance<br>Hypothyroidism<br>Adrenal insufficiency | ABG<br><br>Laboratory testing |
| Neurologic | Cerebrovascular accident<br>Pneumocephalus<br>Global cerebral hypoxia | CT scan |
| Other | Alcohol intoxication<br>Recreational drug use | Blood and urine toxicology |

*ABG,* Arterial blood gas; *CT,* computed tomography.

### 3. On the following day, the patient responded to noxious stimuli with extensor posturing, and his pupils were 4 mm, fixed, and nonreactive to light; is this patient brain dead, and what are the criteria for brain death?

The patient is not brain dead, but if he survives, the likelihood of a persistent vegetative state is very high. If the patient does not have a living will stating his wishes, the discussion with the family should first provide information regarding the current status and prognosis in a way that nonmedical people could comprehend. The discussion should center on trying to determine what the wishes of the patient are. If no wishes were clearly stated, the patient's values should be explored to reach a decision regarding pursuit or withdrawal of treatment.

The criteria for brain death are the irreversible absence of brain function including cortex and brainstem in the absence of hypothermia, toxins (e.g., drugs, especially sedative-hypnotics and muscle relaxants), and metabolic disturbances (e.g., marked abnormalities in sodium, hypothyroidism). Precise protocols for determining brain death vary among institutions.

Determination of brain death requires two clinical assessments of brain function, separated by a period of at least 6 hours. The apnea test is typically performed after the second evaluation of brainstem reflexes. The three essential findings in brain death are coma or unresponsiveness, absence of brainstem reflexes, and apnea. The determination of brain death verifies these findings by the following clinical indicators:

- Coma or unresponsiveness
  - No cerebral motor response to verbal command or painful stimulation in all extremities (nail-bed pressure) and supraorbital pressure
- Absence of brainstem reflexes
  - Pupils
    - No response to bright light
    - Size: midposition (4 mm) to dilated (9 mm)
  - Ocular movement
    - No oculocephalic reflex (testing is appropriate only when no fracture or instability of the cervical spine or skull base is apparent); this entails turning the head rapidly from side to side and observing the abnormal lack of eye movement in the direction opposite to the head movement
    - No deviation of the eyes to irrigation in each ear with 50 mL of cold water (tympanic membranes intact; allow 1 minute after injection and at least 5 minutes between testing on each side)
  - Facial sensation and motor response
    - No corneal reflex
    - No jaw reflex (optional)
    - No grimacing to deep pressure on nail bed, supraorbital ridge, or temporomandibular joint
  - Pharyngeal and tracheal reflexes
    - No response after stimulation of the posterior pharynx
    - No cough response to tracheobronchial suctioning
- Clinical observations compatible with the diagnosis of brain death

The following manifestations are occasionally seen and are not evidence of brainstem function:

- Spontaneous movements of limbs other than pathologic flexion or extension response
- Respiratory-like movements (shoulder elevation and adduction, back arching, intercostal expansion without significant tidal volumes)
- Sweating, flushing, tachycardia
- Normal blood pressure without pharmacologic support or sudden increases in blood pressure
- Absence of diabetes insipidus
- Deep tendon reflexes, superficial abdominal reflexes, triple flexion response
- Babinski reflex

Confirmatory tests, such as a cerebral angiogram or a radionuclide scan, demonstrating the absence of blood flow to the brain are sufficient to affirm brain death. Ancillary tests can be used when uncertainty exists about the reliability of parts of the neurologic examination or when the apnea test cannot be performed. Transcranial Doppler showing small systolic peaks with no diastolic flow has similar value. The absence of signal on both electroencephalogram and brainstem evoked potentials is also sufficient. Some of these tests are required by policy in some institutions; however, brain death is commonly determined on clinical criteria alone.

All evidence should be adequately documented in the chart, and two concurring physicians should affirm the diagnosis of brain death. Legally, all physicians are allowed to determine brain death in most states. Neurologists, neurosurgeons, and intensive care specialists may have specialized expertise. It seems reasonable to require that all physicians making a determination of brain death be intimately familiar with brain death criteria and have demonstrated competence in this complex examination. The family can be approached for solid organ and tissue donation. In children, the criteria are slightly different and beyond the scope of this chapter.

### 4. What is an apnea test, and how is it performed?

An apnea test reveals the patient's response to hypercapnia and helps to confirm the diagnosis of brain death (i.e., no response in the case of brain death). It is performed as follows:

- Baseline ABG is obtained
- Establish reliable pulse oximeter signal and disconnect ventilator
- Deliver oxygen into the trachea by placement of nasal cannula deep into the tracheal tube taking care not to occlude the lumen and prevent efflux of gas
- Look closely for any respiratory movements
- Measure arterial oxygen tension, $PaCO_2$, and pH after approximately 8 minutes and reconnect ventilator

If respiratory movements are absent and $PaCO_2$ is $\geq$60 mm Hg, or there is a 20 mm Hg increase in $PaCO_2$ over a baseline normal $PaCO_2$, the apnea test result is positive (i.e., supports the diagnosis of brain death).

If respiratory movements are observed, the apnea test result is negative (i.e., does not support the clinical diagnosis of brain death).

If hypotension, oxygen–desaturation, or cardiac arrhythmias develop, an arterial blood sample should be drawn, and the ventilator should be reconnected. Analysis of ABG as described previously is still possible, but if $PaCO_2$ is <60 mm Hg or $PaCO_2$ increase is <20 mm Hg over baseline normal $PaCO_2$, the result is indeterminate.

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SECTION **16**

# CRITICAL CARE

CASE 82

# Neonatal Resuscitation

**Francine S. Yudkowitz, MD, FAAP**

## QUESTIONS

1. Describe the fetal circulation.
2. What physiologic changes occur at birth?
3. How is neonatal resuscitation managed in the delivery room?
4. How is oxygen administration optimally managed during neonatal resuscitation?
5. How is a newborn managed when meconium is present?
6. What is the Apgar score?

A 42-year-old woman was in labor. The fetal heart rate monitor showed intermittent variable decelerations with good recovery. The obstetrician ruptured membranes and noted that the amniotic fluid was meconium stained. Because the fetal heart rate monitor showed good beat-to-beat variability, it was decided to allow the mother to continue in labor and deliver vaginally. The infant was delivered vaginally 2 hours later and was noted to be meconium stained.

### 1. Describe the fetal circulation.

The fetal circulation (Figure 82-1) is a parallel circuit, in contrast to a series circuit in the adult. In the fetus, gas exchange occurs at the placenta and not the lungs. Blood leaving the placenta enters the fetus via the umbilical vein. This relatively well-oxygenated blood ($pO_2$ 30–35 mm Hg) enters the fetus and predominantly bypasses the liver via the ductus venosus. Most of this blood on entering the right atrium is preferentially shunted across the patent foramen ovale to the left side of the heart and out the ascending aorta to the cerebral and coronary circulation. The brain and heart receive most of the relatively well-oxygenated blood. Blood returning from the cerebral circulation via the superior vena cava, which is considerably less oxygenated ($pO_2$ 12–14 mm Hg), enters the right side of the heart. This blood is preferentially directed to the right ventricle and exits through the pulmonary artery. Because of the high pulmonary vascular resistance (PVR) that exists in utero, only 10% of this blood enters the pulmonary circulation to provide nutrients for lung growth. The remaining blood is shunted across the ductus arteriosus because of the low systemic vascular resistance (SVR). SVR is low in the fetus because of the relatively large ductus arteriosus and the placenta. Blood enters the descending aorta and supplies the lower fetal body, returning to the placenta via the iliac veins to the umbilical arteries.

### 2. What physiologic changes occur at birth?

When the neonate is delivered, the first breaths expand the lungs with air, and alveolar $pO_2$ increases. These changes lead to a dramatic decrease in PVR, although not to the normal adult values. At the same time, the umbilical cord is clamped, and the low-resistance placenta is removed from the circulation; this results in an abrupt increase in SVR. These changes lead to the following:

- Functional closure of the patent foramen ovale because the pressure on the left side of the heart (SVR) is greater than the pressure on the right side (PVR)
- Functional closure of the ductus arteriosus because of an increase in arterial $pO_2$; the ductus arteriosus becomes the ligamentum arteriosum
- Functional closure of the ductus venosus because of removal of the placenta

This pattern of circulation closely resembles the adult circulation. However, it is referred to as the transitional circulation because of the reversibility of the above-mentioned changes during adverse events, such as hypoxia or acidosis. Any insult that increases pulmonary vascular resistance results in reopening of the functionally closed fetal shunts. Factors that adversely affect PVR are hypoxia, hypercarbia, acidosis, hypothermia, and sympathetic stimulation. It is imperative in the initial management of the neonate in the delivery room to pay meticulous attention to ensuring adequate oxygenation, ventilation, and maintenance of normothermia. Reversion to fetal circulation is referred to as persistent pulmonary hypertension of the newborn.

### 3. How is neonatal resuscitation managed in the delivery room?

As soon as the newborn is delivered, a rapid assessment should be performed to determine the need for resuscitation (Figure 82-2). This rapid assessment answers the following three questions:

- Is the newborn full term?
- Is the newborn crying or breathing?
- Is the muscle tone good?

If the answer to all three questions is yes, resuscitation is not necessary, and the newborn can remain with the

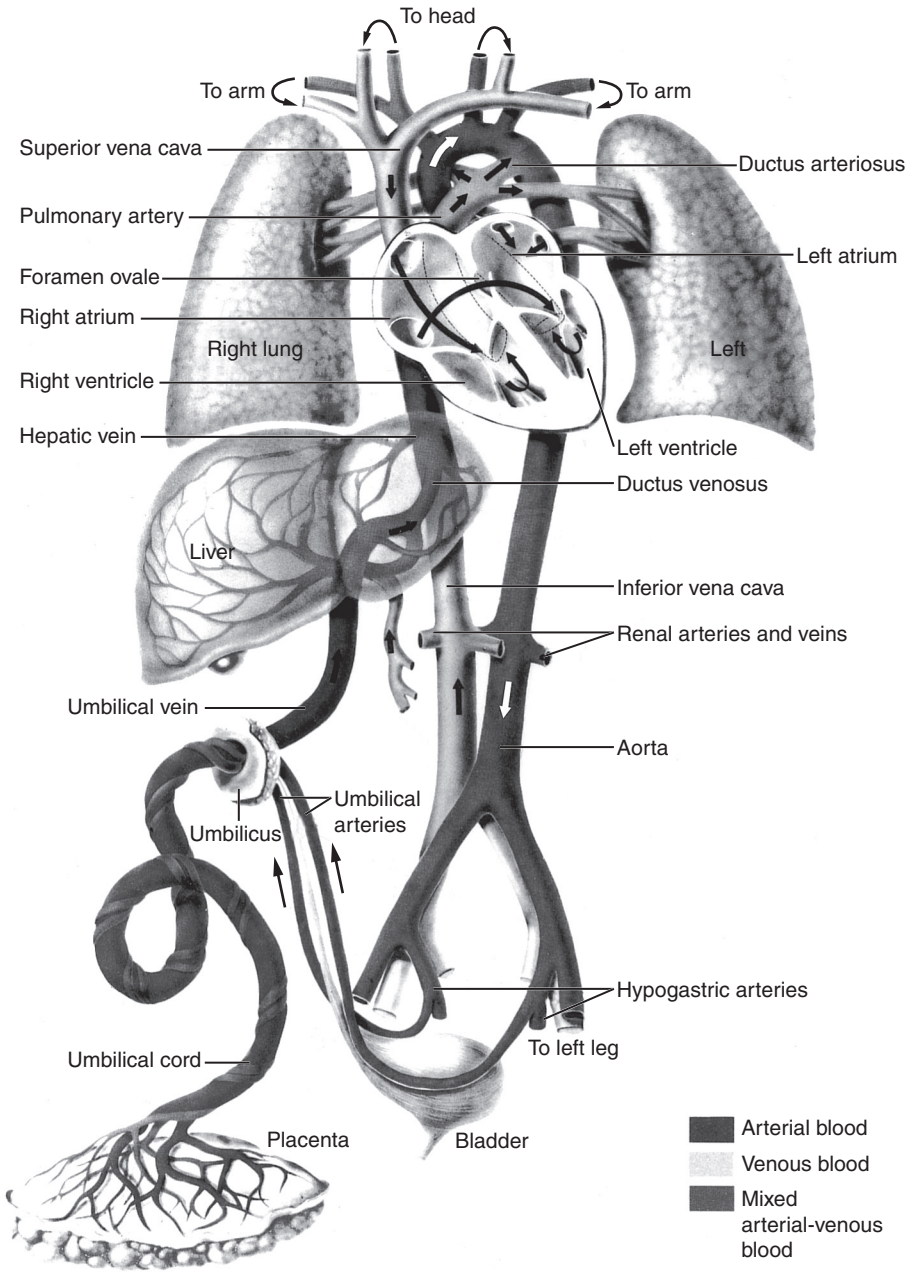


**FIGURE 82-1 ■ Fetal circulation.** (From Miller RD, Cucchiare RF, Miller ED, editors.: Anesthesia, 5th ed. Philadelphia: Churchill Livingstone; 2000. p. 1807.)

mother. If the answer to any of these questions is no, resuscitation should be initiated in the following order:

- Initial steps
  - Warm by radiant heat source
  - Clear the airway if needed
  - Dry the newborn
  - Stimulate breathing
- Ventilation
- Chest compressions
- Administration of epinephrine or volume expansion or both

In the first 60 seconds, known as the "golden minute," the following should be completed: the initial steps; reassessment of the respiratory status and heart rate (Box 82-1); and, if needed, administration of supplemental oxygen or positive pressure ventilation. Positive pressure ventilation should be at a rate of 40–60 breaths per minute, and the minimal inflation pressure to achieve a heart rate >100 beats per minute should be applied. Heart rate is assessed by auscultation of the precordium or palpation of the umbilical artery. When supplemental oxygen or positive pressure ventilation or both are begun, the assessment now consists of evaluation of respirations, heart rate, and oxygenation (see Box 82-1). Oxygenation is ideally monitored by pulse oximetry. However, it may take 1–2 minutes before pulse oximetry is functional, and in low-flow states it may not work at all. During every intervention, success is measured by an increase in heart rate.

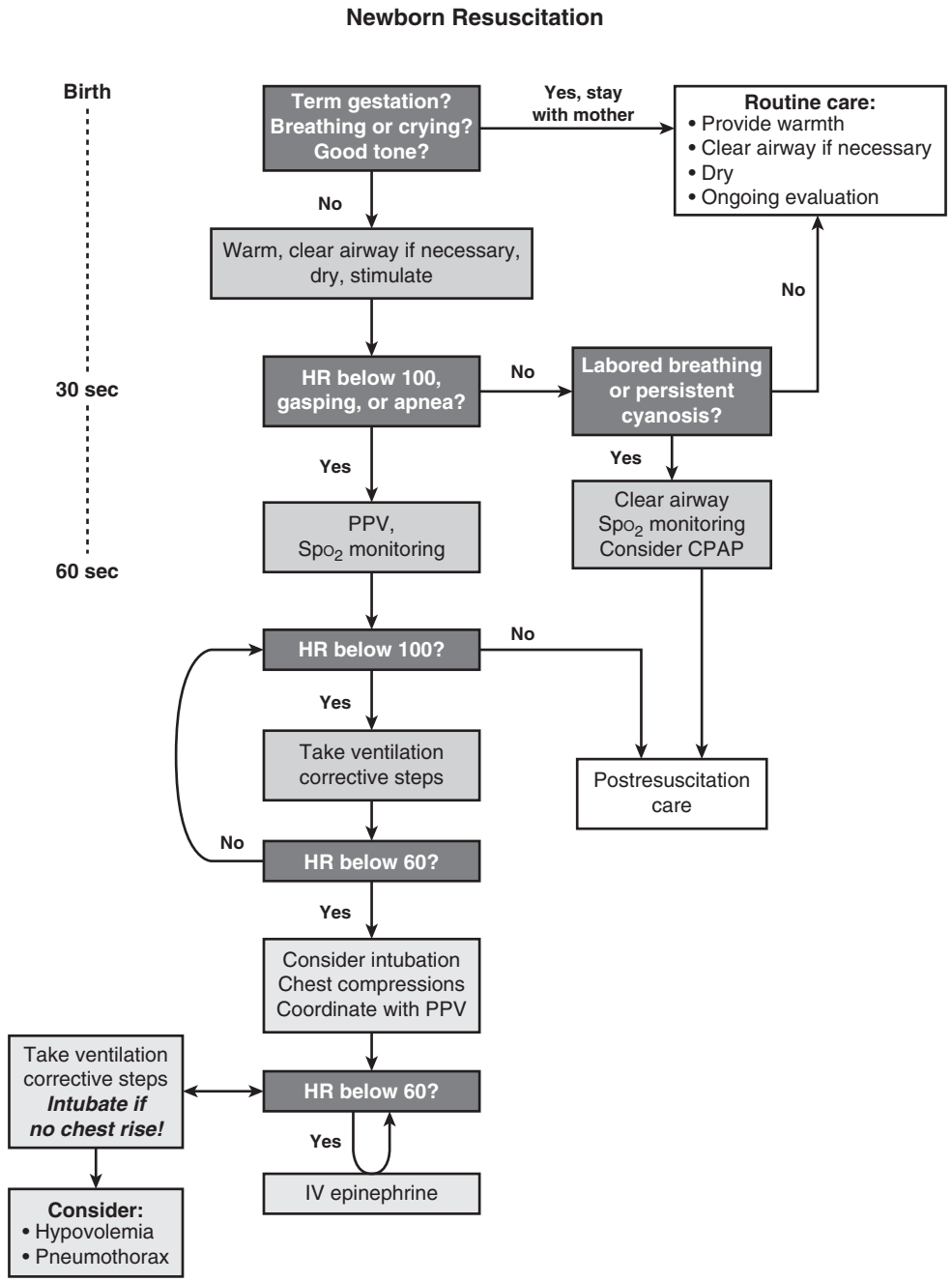


**FIGURE 82-2** ■ **Neonatal resuscitation in the delivery room.** (Adapted from Kattwinkel J, Perlman JM, Aziz K, et al.: Part 15. Neonatal resuscitation: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 122(Suppl 3):S909, 2010.)

**BOX 82-1 Assessment Parameters for Respirations and Heart Rate**

- Respirations
  - Apnea
  - Gasping
  - Labored or unlabored breathing
- Heart rate
  - > or < 100 beats per minute
- Oxygenation
  - Appropriate preductal oxygen saturation by age

Endotracheal intubation should be considered in the following circumstances:

- Nonvigorous newborn with meconium staining
- Prolonged or ineffective bag and mask ventilation
- Chest compressions are performed
- Special circumstances, such as congenital diaphragmatic hernia, "micropreemie"

Correct placement of the endotracheal tube should result in an increase in heart rate. An exhaled carbon dioxide detector is the recommended method to confirm correct endotracheal tube placement. However, if there is little

or no pulmonary blood flow, there may be a false-negative result. In the event that mask ventilation and endotracheal intubation are unsuccessful, the placement of a laryngeal mask airway has been shown to be effective for newborns ≥34 weeks gestation or weighing >2000 g.

Chest compressions should be started if the heart rate is <60 beats per minute after 30 seconds of adequate positive pressure ventilation with oxygen. Ventilation is the most important aspect of neonatal resuscitation; it is important to ensure that adequate ventilation is performed before chest compressions. Chest compressions can be accomplished in two ways:

- Place both thumbs on the lower third of the sternum while the other fingers encircle the neonate supporting the back.
- Place two fingers of one hand on the lower third of the sternum while the other hand supports the back.

The first method is preferred. Chest compressions should be about one third of the depth of the chest. There should be a 3:1 ratio of compressions to ventilations. In 1 minute, 90 chest compressions and 30 ventilations should be performed. Chest compressions and ventilations should not occur simultaneously. Respirations, heart rate, and oxygenation should be reassessed at regular intervals. Resuscitation efforts should continue until the heart rate is >60 beats per minute.

If the heart rate remains <60 beats per minute after adequate positive pressure ventilation and chest compressions, epinephrine 1:10,000 at a dose of 0.01–0.03 mg/kg should be given intravenously. Endotracheal epinephrine is no longer recommended because animal studies have shown that the intravenous dose given endotracheally is ineffective, and the higher doses necessary for a positive effect have not been evaluated for safety and efficacy. If endotracheal administration is considered because of lack of intravenous access, the dose is 0.5–0.1 mg/kg of epinephrine 1:10,000.

Additional resuscitative measures include volume expansion with an isotonic crystalloid solution or colloids for a hypovolemic infant. Hypovolemia should be suspected if an infant is not responding to the usual resuscitative measures or if the physical examination is consistent with shock. The initial dose of fluid is 10 mL/kg as a bolus. Additional fluid management should be based on clinical assessment. In a preterm infant, rapid infusion of large volumes should be avoided because preterm infants are susceptible to intraventricular hemorrhage. Naloxone, sodium bicarbonate, and vasopressors are not recommended during the initial resuscitation of a newborn in the delivery room.

It is important that all the equipment and pharmacologic agents necessary for resuscitation efforts are available and of the appropriate size (Box 82-2).

**BOX 82-2 Emergency Equipment for Neonatal Resuscitation**

- Airway
  - Oxygen source with blender, flowmeter, and tubing
  - Neonatal resuscitation bag with pressure relief valve
  - Facemasks—premature and newborn
  - Oropharyngeal airways
  - Laryngoscope handle with extra batteries
  - Laryngoscope blades—Miller 0 and 1, extra bulbs
  - Endotracheal tubes—2.5–4.0 mm ID
  - Stylet
  - Bulb syringe
  - Suction apparatus and catheters—6F to 10F
  - Meconium suction device
  - Carbon dioxide detector
  - Laryngeal mask airway (optional)
- Medications
  - Epinephrine 1:10,000
- Intravenous access and fluids
  - Isotonic crystalloid
  - 24-gauge and 22-gauge angiocatheters
  - Umbilical catheters—3.5F, 5F
  - Alcohol pads
  - Syringes and needles
- Miscellaneous
  - Gloves
  - Radiant warmer
  - Stethoscope
  - Electrocardiogram
  - Pulse oximeter

## 4. How is oxygen administration optimally managed during neonatal resuscitation?

Skin color in a newborn is a poor indicator of oxygen saturation. The lack of cyanosis in a newborn does not indicate that oxygenation is adequate. Studies have shown that both insufficient and excessive oxygenation can be harmful to a newborn. A meta-analysis of studies comparing neonatal resuscitation with 100% oxygen or room air showed that there was increased survival when air was used initially. To achieve adequate oxygenation without administering unnecessarily high oxygen concentrations, pulse oximetry is recommended when supplemental oxygen or positive pressure ventilation is necessary. Because oxygen saturation varies by age, a table of targeted preductal oxygen saturations is provided as part of the neonatal resuscitation algorithm (Table 82-1). The current recommendation is that the initial oxygen concentration used may be air or blended oxygen, and the oxygen concentration is titrated to the target oxygen saturation for age. If the heart rate remains <60 beats per minute after

TABLE 82-1 **Targeted Preductal Oxygen Saturation by Pulse Oximetry in the Newborn**

| Minutes after Birth | Oxygen Saturation by Pulse Oximetry (%) |
|---|---|
| 1 | 60–65 |
| 2 | 65–70 |
| 3 | 70–75 |
| 4 | 75–80 |
| 5 | 80–85 |
| 10 | 85–95 |

From Kattwinkel J, Perlman JM, Aziz K, et al.: Part 15. Neonatal resuscitation: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 122(Suppl 3):S909, 2010.

TABLE 82-2 **Apgar Score**

| | 0 | 1 | 2 |
|---|---|---|---|
| Heart rate | Absent | <60 | >60 |
| Respiratory effort | Absent | Poor | Vigorous |
| Muscle tone | Limp | Minimal flexion | Active movement |
| Reflex irritability | Absent | Grimace | Cry |
| Color | Extremities blue | Pink | Blue |

60 seconds of adequate ventilation, the oxygen concentration should be increased to 100%.

### 5. How is a newborn managed when meconium is present?

Meconium aspiration syndrome (MAS) occurs when meconium is aspirated in utero, at delivery, or during resuscitation. Previously, the recommendation consisted of suctioning the oropharynx after delivery of the shoulders, but subsequent studies have shown this to be of no value. Elective intubation and suctioning of the trachea in meconium-stained vigorous newborns were found to be of no value; in addition, complications associated with tracheal suctioning, such as laryngeal trauma, may occur. Although MAS is more likely to occur in nonvigorous meconium-stained newborns, elective intubation and tracheal suctioning have not been associated with a decreased incidence of MAS. However, there are not enough randomized controlled trials to change current practice recommendations of tracheal suctioning of meconium-stained nonvigorous newborns. During this maneuver, an assistant should monitor the heart rate continuously. If there is persistent bradycardia, this maneuver should be abandoned, and resuscitation should be initiated.

### 6. What is the Apgar score?

Apgar, an anesthesiologist, devised a scoring system to assess newborns for their clinical condition and need for medical intervention. The Apgar score (Table 82-2) consists of five parameters that are assessed at 1 minute and 5 minutes after birth: heart rate, respiratory effort, muscle tone, reflex irritability, and color. A score of 0, 1, or 2 is assigned to each parameter. A score of 8–10 is normal and requires no additional treatment. A score of 5–7 indicates moderate impairment; supplemental oxygen and tactile stimulation may be needed. A score of 0–4 indicates the need for immediate resuscitation. The 1-minute score is said to be inversely proportional to the risk of infant mortality, whereas the 5-minute score may relate to the degree of future neurologic impairment.

The Apgar score, although still widely performed, is not used to guide resuscitation efforts in the delivery room. One should not wait until 1 minute after birth to begin resuscitative efforts.

## SUGGESTED READINGS

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CASE 83

# Pediatric Cardiopulmonary Resuscitation

**Cheryl K. Gooden, MD, FAAP**

## QUESTIONS



A 6-year-old, obese boy with genu valgum underwent an uneventful anesthetic for removal of bilateral lower extremity hardware. While in the postanesthesia care unit, he received intravenous fentanyl and shortly thereafter became unresponsive with ensuing respiratory arrest. He developed pulseless ventricular tachycardia (VT) that deteriorated quickly to ventricular fibrillation (VF).

### 1. What is the etiology of cardiac arrest in children?

Most cardiac arrest events in infants and children are precipitated by respiratory failure or shock. Sudden cardiac arrest may be observed less frequently. Typically, sudden cardiac arrest is the result of an arrhythmia, such as pulseless VT or VF. Genetic mutations resulting in channelopathies have been linked to sudden cardiac arrest, such as in sudden infant death syndrome and sudden death in children. Channelopathies are a group of diseases that are characterized by abnormal myocyte ion channels or the proteins that regulate them resulting in fatal arrhythmias.

Primary factors that may lead to cardiac arrest in pediatric patients are respiratory failure, shock, and sudden arrhythmias (pulseless VT or VF). Secondary factors that may contribute to cardiac arrest and should be considered when managing arrest victims are listed in Box 83-1.

### 2. How do survival rates from cardiac arrest differ when comparing in-hospital with out-of-hospital settings?

Infants and children who experience in-hospital cardiac arrest are more likely to survive the event than infants and children in the out-of-hospital setting. However, overall there remains room for improvement in this area. For the most part, the numbers are low for infants and children who survive to discharge from the hospital after in-hospital (33%) or out-of-hospital (4%–13%) cardiac arrest. The American Heart Association (AHA) maintains an ongoing focus on early recognition and rapid intervention of respiratory failure or shock to prevents progression to cardiac arrest. When cardiac arrest occurs, early recognition and high-quality cardiopulmonary resuscitation (CPR) are important to improve survival.

### 3. What changes occurred to pediatric chest compression depth and compression/ventilation ratios with the 2010 American Heart Association guidelines?

A major change in the 2010 AHA Guidelines is to begin CPR with chest compressions as opposed to providing breaths. With this in mind, the initial "look, listen, and feel for breathing," was eliminated. For many of us who

**BOX 83-1 Factors Contributing to Cardiac Arrest**

**Primary Factors**

Respiratory failure
Shock
Sudden arrhythmias (pulseless VT or VF)

**Secondary Factors ("H's and T's")**

Hypoxia
Hypovolemia
Hydrogen ions (acidosis)
Hypoglycemia
Hypokalemia/hyperkalemia
Hypothermia
Thrombosis—coronary or pulmonary
Tamponade—cardiac
Tension pneumothorax
Toxins
Trauma

*VT*, ventricular tachycardia; *VF*, ventricular fibrillation.

learned the phrase "airway, breathing, and circulation (A-B-C)," it now has become "circulation, airway, and breathing (C-A-B)." The reason for this change was to prevent delayed chest compressions even though the most common origin of cardiac arrest in pediatrics is of a respiratory nature. The impetus for this change is multifactorial, as follows:

- Because high-quality chest compressions are the basis for effective CPR, time to initiation of chest compressions is important to survival. The time to deliver two breaths, particularly by nonskilled providers, delays chest compressions for a greater period of time (>18 seconds) than would the delay to first breath (≤18 seconds) if chest compressions are performed initially. Even though respiratory causes of cardiac arrest are more likely in pediatric populations, the time to first breath would not be significantly delayed.
- A bystander who is not a skilled health care provider may be more inclined to initiate CPR with chest compressions than rescue breaths. Because of this, the AHA has advocated for a number of years "hands-only" (chest compression–only) CPR for the bystander who is reluctant to perform rescue breathing. A bystander providing only chest compressions is better than not performing CPR at all.
- For the ease of learning CPR, especially for unskilled providers, the C-A-B sequence, although better suited for adult victims, is taught for both adult and pediatric resuscitation.

The 2010 recommendation for chest compression depth ("push hard") is approximately one third of the anterior-posterior diameter of the chest wall. This correlates with approximately 1.5 inches (4 cm) for an infant and 2 inches (5 cm) for a child (Table 83-1). Full chest recoil should occur between chest compressions.

During cardiac arrest, it is crucial that chest compressions are performed early and effectively without frequent or prolonged interruptions to generate a better cardiac output. To some extent, the cardiac output provides essential organs with much needed blood flow to restore baseline circulation as close as possible. Cycles of CPR should continue uninterrupted for 2 minutes before checking for a rhythm and pulse and should resume within 10 seconds. The number of compressions per minute changed from 100 to at *least* 100 compressions per minute ("push fast"). During resuscitation by more than one health care provider, the person doing chest compressions should change after each 2-minute cycle because fatigue is associated with lower quality chest compressions.

## 4. What are the recommendations for the delivery of breaths with and without an advanced airway?

Without an advanced airway (e.g., endotracheal tube, laryngeal mask airway), breaths should be synchronized with chest compressions. Two breaths are given after 30 compressions (30:2) with one rescuer and after 15 chest compressions (15:2) with two rescuers. Each breath

TABLE 83-1 **Pediatric Compression/Ventilation Parameters**

| | |
|---|---|
| Chest compressions/ventilation ratio | |
| Advanced airway not present | 1 provider or 2 unskilled providers, 30:2; 2 skilled providers, 15:2 |
| Advanced airway present | Asynchronous chest compressions and ventilation |
| Number of chest compressions ("push fast") | At least 100 compressions/minute |
| Depth of compressions ("push hard") | Infant - 1.5 inches (4 cm) |
| | Child - 2 inches (5 cm) |
| Ventilation | |
| Advanced airway not present | Each breath over 1 second, just until see chest rise |
| Advanced airway present | Breath every 6–8 seconds, just until see chest rise |

should not last >1 second and should be terminated when chest rise is detected (see Table 83-1). Excessive ventilation interferes with cardiac output and coronary artery perfusion. Excessive ventilation also could cause gastric distention, which would increase the risk of aspiration.

With an advanced airway, breaths and chest compressions are asynchronous. One breath is given every 6–8 seconds (i.e., 8–10 breaths per minute). Care must be taken to avoid excessive ventilation by terminating inflation when chest rise is achieved.

When an endotracheal tube is placed during resuscitation, capnography should be used to confirm placement. If possible, continuous monitoring of end-tidal carbon dioxide ($ETCO_2$) should be used during CPR as an indirect measure of the quality of chest compressions. An $ETCO_2$ of at least 10–15 mm Hg is associated with effective cardiac compressions. Return of spontaneous circulation (ROSC) is associated with increased $ETCO_2$, usually to >40 mm Hg.

## 5. What are the latest recommendations for automated external defibrillators or manual defibrillators in infants?

Defibrillation with an automated external defibrillator (AED) or manual defibrillator is reserved for shockable rhythms (i.e., VF, pulseless VT). Ideally, defibrillation should be provided early during resuscitation. However, CPR should not be delayed while awaiting an AED or manual defibrillator.

AEDs have become ubiquitous in most public settings. The 2010 AHA Guidelines include recommendations for its use in infants. Before these guidelines, AEDs were not recommended for infants.

As the name implies, an AED with pads applied to the patient's chest determines whether a shockable rhythm exists, charges to the manufacturer's set dose, and advises the user when to administer a shock. Many AEDs are capable of providing an energy dose that is appropriate for infants or children <8 years old. If the AED is not equipped with this capability, it can still be used in infants and children.

Many manual defibrillators are equipped with infant paddles. If not, adult paddles may be used. When available, a manual defibrillator is preferable to an AED for use in infants. However, defibrillation with an AED is a better option than no defibrillation at all (Table 83-2). The recommended initial dose is 2–4 J/kg. If a second shock is necessary, following a cycle (approximately 2 minutes) of CPR, a dose of 4 J/kg is recommended. If additional shocks are necessary, the minimum dose is 4 J/kg and may increase to 10 J/kg.

## 6. Is intraosseous access an acceptable form of vascular access during pediatric advanced life support?

Intraosseous (IO) cannulation is considered an excellent alternative option for vascular access. It can be obtained quickly, particularly in the setting of resuscitation, and is acceptable in patients of any age. Similar to intravenous (IV) access, medications, crystalloids, colloids, and blood products can be administered through an IO access. Additionally, the IO route is better for administering medications than through an endotracheal tube because uptake of medications through the endotracheal tube route tends to be unpredictable.

Several locations exist for placement of IO access in children. The most commonly used site is the proximal tibia. Additional locations include the anterior-superior iliac spine, distal femur, and distal tibia. Contraindications to IO placement are listed in Box 83-2.

There are various techniques for IO placement. IO or bone marrow needles are most commonly used for IO access. IO drills have appeared on the market more recently, and their use is becoming quite popular. If these are unavailable, spinal needles, hypodermic needles, and even butterfly needles may be used.

## 7. Are calcium and vasopressin recommended for routine use during pediatric cardiopulmonary arrest?

Compared with the 2005 AHA Guidelines, the 2010 guidelines deemphasize calcium administration during resuscitation because it does not offer any known advantages. The indications for calcium administration are documented hypocalcemia or hyperkalemia. It can be considered for the treatment of hypermagnesemia or calcium-channel blocker overdose.

Either calcium chloride (20 mg/kg) or calcium gluconate (60 mg/kg) may be administered. In an arrest situation,

TABLE 83-2 **Manual Defibrillator versus Automated External Defibrillator (AED)**

| | <10 kg; <1 year old | <25 kg; <8 years old | ≥25 kg; ≥8 years old |
|---|---|---|---|
| Manual defibrillator | Preferable to AED<br>Use infant paddles<br>Can use adult paddles if infant paddles unavailable | Use adult paddles | Use adult paddles |
| AED | Use only if manual defibrillator unavailable<br>Use attenuated dose<br>May use adult dose if attenuated dose unavailable | Use attenuated dose<br>May use adult dose if attenuated dose unavailable | Adult dosing |

**BOX 83-2 Contraindications to Intraosseous Placement**

Fracture or other injury to surrounding bone at the site
Osteogenesis imperfecta
Infection at the site
Prior intraosseous attempts at the same site

calcium is administered as a bolus. In a non–cardiac arrest situation, it should be infused over 30–60 minutes.

There is much discussion regarding the use of vasopressin during pediatric cardiac arrest. There is no consensus at the present time to support or refute inclusion of vasopressin in pediatric cardiac arrest algorithms. In certain situations where other medications have been unsuccessful (e.g., lack of response to epinephrine) during pediatric cardiac arrest, there may be a role for vasopressin. However, some reports show a worse outcome when vasopressin is used.

## 8. What are the cardiopulmonary resuscitation recommendations for infants and children with congenital heart disease?

For the first time, treatment considerations during cardiac arrest in infants and children with a single ventricle, Fontan or hemi-Fontan/bidirectional Glenn, or pulmonary hypertension are included in the 2010 AHA Guidelines. It is recognized that this patient population might dictate treatment options that vary from the pediatric patient without congenital heart disease. Specifically, consideration should be given to early intervention with extracorporeal membrane oxygenation in this patient population.

## 9. How is symptomatic bradycardia treated?

In pediatric patients, bradycardia is age related (Table 83-3). It is normal to observe a slower heart rate in a pediatric patient while at rest. However, bradycardia may be premonitory for cardiac arrest. Generally, symptomatic bradycardia is defined as a heart rate <60 beats per minute in the presence of cardiopulmonary impairment (i.e., hypotension, acutely altered mental status, shock).

The initial management of symptomatic bradycardia is to ensure that oxygenation and ventilation are satisfactory. If symptomatic bradycardia persists despite adequate oxygenation and ventilation, CPR is initiated. When there is no improvement in symptomatic bradycardia, epinephrine (0.1 mg/kg of 1:10,000) is administered. Atropine (20 μg/kg) should be reserved for cases of heightened vagal-mediated activity (e.g., suctioning, laryngoscopy), cholinergic overdose, Mobitz I and II blocks, and third-degree atrioventricular block. Cardiac pacing should be performed if bradycardia does not respond to epinephrine or atropine or if bradycardia occurs in patients with heart transplants. Treatable secondary factors should be considered (see Box 83-1).

## 10. How is pulseless electrical activity treated?

Pulseless electrical activity (PEA) is a nonshockable rhythm that can be observed in children during cardiac arrest, particularly from infancy to preadolescence. As the term PEA implies, there is no appreciable pulse on physical examination despite electrical activity on the electrocardiogram (ECG). The rhythm and rate observed with PEA may vary. For example, in PEA, some of the aberrant rhythms affect QRS complexes, T waves, atrioventricular dissociation, P–R intervals, or Q–T intervals. The rate associated with PEA ranges from slow to rapid.

The immediate treatment of PEA begins with CPR. Tracheal intubation does not have to be part of initial PEA management. When IV/IO access is obtained, epinephrine (0.1 mg/kg 1:10,000) is administered every 3–5 minutes until ROSC. After each 2-minute cycle of CPR, rhythm and pulse checks are performed to determine if the rhythm converted to a shockable one, if the rhythm remains PEA, or there is ROSC.

TABLE 83-3 **Normal Vital Signs According to Age**

| Age | Heart Rate (beats per minute) | Blood Pressure (mm Hg) | Respiratory Rate (breaths per minute) |
|---|---|---|---|
| Premature | 120–170 | 55–75/35–45 | 40–70 |
| 0–3 months | 100–150 | 65–85/45–55 | 35–55 |
| 3–6 months | 90–120 | 70–90/50–65 | 30–45 |
| 6–12 months | 80–120 | 80–100/55–65 | 25–40 |
| 1–3 years | 70–110 | 90–105/55–70 | 20–30 |
| 3–6 years | 65–110 | 95–110/60–75 | 20–25 |
| 6–12 years | 60–95 | 100–120/60–75 | 14–22 |
| >12 years | 55–85 | 110–135/65–85 | 12–18 |

From Hartman M, Cheifetz I: Pediatric emergencies and resuscitation. In Kliegman R, Stanton B, Gemell, et al. (eds.): Nelson Textbook of Pediatrics, 19th edition. Saunders, Philadelphia, 2011.

**TABLE 83-4 Sinus Tachycardia versus Narrow Complex Supraventricular Tachycardia**

| | Sinus Tachycardia | Narrow Complex Supraventricular Tachycardia |
|---|---|---|
| History | Consistent with underlying cause (e.g., dehydration, fever) | Vague, nonspecific, abrupt onset |
| P wave | Present, normal | Absent, abnormal |
| R–R interval | Variable | Constant |
| Rate | | |
| Infants | <220 beats per minute | ≥220 beats per minute |
| Children | <180 beats per minute | ≥180 beats per minute |

During the resuscitation, underlying causative factors for cardiac arrest should be sought and treated (see Box 83-1).

### 11. How is ventricular fibrillation or pulseless ventricular tachycardia treated?

There should be no hesitation to begin CPR for the treatment of VF or pulseless VT. VF and pulseless VT are shockable rhythms. The most important measure in managing these rhythms is defibrillation, with either a manual defibrillator or AED (see Question 5).

IV/IO epinephrine is the mainstay of drug therapy for VF or pulseless VT. The first dose of epinephrine (0.1 mg/kg of 1:10,000) is indicated after the second delivered shock, while the next cycle of CPR is in progress. Epinephrine is delayed until this time because defibrillation alone may result in a life sustainable rhythm.

During resuscitation, the endotracheal route has been used for delivering certain medications (e.g., epinephrine, atropine, lidocaine, naloxone) when the IV/IO route was unavailable. However, this route has been strongly discouraged for the following reasons:

- Blood levels attained with the endotracheal route are less than the blood levels attained by the IV/IO routes
- Evidence indicates that epinephrine administered through the endotracheal route can result in overriding β-adrenergic effects
- Chest compressions must be stopped

Amiodarone (5 mg/kg) for VF or pulseless VT is a second-line drug therapy. Lidocaine (1 mg/kg) also may be considered for use in VF or pulseless VT when amiodarone is unavailable. Secondary factors should be investigated for treatable causes (see Box 83-1).

### 12. How is supraventricular tachycardia treated?

The treatment of supraventricular tachycardia (SVT) depends on the width and appearance of the QRS complex and whether hemodynamic instability is present. The first step is to differentiate narrow complex tachycardia (QRS width <0.09 second) from wide complex tachycardia (QRS width >0.09 second). Treatment options for narrow complex tachycardia pivots on distinguishing sinus tachycardia from SVT (Table 83-4). Treatment of sinus tachycardia requires identification of an underlying cause (e.g., dehydration, fever). Controlling SVT begins with vagal maneuvers (Box 83-3) while obtaining IV/IO access. When IV/IO access is secured, adenosine should be administered as a rapid bolus and immediately followed by a saline flush. SVT that is unresponsive to vagal maneuvers and adenosine is treated with synchronized cardioversion (Table 83-5). When it is clinically acceptable, sedation may be provided before synchronized cardioversion.

The treatment of wide complex SVT depends on whether cardiopulmonary compromise (i.e., hypotension, acutely altered mental status, shock) is present. If cardiopulmonary compromise is present, synchronized cardioversion should be performed immediately. In the absence of cardiopulmonary compromise, a cardiology consultation should be obtained. Adenosine may be administered if the rate is regular and the QRS complex is monomorphic. Further management includes administration of either amiodarone (5 mg/kg) or procainamide (15 mg/kg). Verapamil may be considered as a treatment option in SVT in an older child. Verapamil is not the drug of choice for the treatment of SVT in infants and young children. Consultation with a

**BOX 83-3 Vagal Maneuvers**

**Infant/Younger Child**

Place a small ice pack on the face

**Older Child**

Carotid sinus massage
Valsalva maneuvers (i.e., forceful breaths through a straw)

TABLE 83-5 **Treatment Strategies for Supraventricular Tachycardia**

| | | |
|---|---|---|
| **Pharmacologic** | | |
| Adenosine | Initial dose: 0.1 mg/kg | Rapid bolus with flush; maximum 6 mg |
| | Next dose: 0.2 mg/kg | Rapid bolus with flush; maximum 12 mg |
| Amiodarone | 5 mg/kg | Infuse over 20–60 minutes; do not administer with procainamide |
| Procainamide | 15 mg/kg | Infuse over 30–60 minutes; do not administer with amiodarone |
| Verapamil | 0.1–0.3 mg/kg | Use only in older children; cardiology consultation |
| **Electrical** | | |
| Synchronized cardioversion | Initial shock: 0.5–1 J/kg | |
| | Next shock: 2 J/kg | If initial shock ineffective |

cardiologist is suggested if the use of verapamil becomes necessary in these patients (see Table 83-5).

### 13. What are the recommendations for supplemental oxygen use after return of spontaneous circulation?

A major concern after resuscitation from cardiac arrest is the amount of oxidative injury associated with ischemia and the ensuing reperfusion state. The literature suggests that oxidative injury is worse in the presence of hyperoxemia. Supplemental oxygen should be titrated in the post–cardiac arrest phase such that arterial oxyhemoglobin saturation is maintained between 94% and 99%.

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CASE 84

# Cardiopulmonary Resuscitation

**Amanda J. Rhee, MD • David L. Reich, MD • Yaakov Beilin, MD**

## QUESTIONS



An 86-year-old woman with congestive heart failure, coronary artery disease, and syncopal episodes presented for elective permanent pacemaker insertion. A recent 24-hour ambulatory electrocardiogram (ECG) demonstrated multiple episodes of severe sinus bradycardia associated with presyncopal symptoms. Monitored anesthesia care was requested because of the patient's advanced age and associated medical conditions. Infiltration of local anesthesia and isolation of the cephalic vein in the left deltopectoral groove proceeded uneventfully. During placement of the ventricular pacing lead, ventricular ectopy occurred. As the lead was repositioned, ventricular tachycardia was induced and rapidly deteriorated into ventricular fibrillation.

### 1. What is the initial response to a witnessed cardiac arrest?

In 2010, the American Heart Association (AHA) published updated Guidelines for Cardiopulmonary Arrest and Emergency Cardiovascular Care. The guidelines differ for lay rescuers and health care providers. This review focuses only on the recommendations for health care providers. The following major changes were made:

- Elimination of "look, listen, and feel"
- Deemphasis on pulse check
- Sequence of resuscitation is circulation, airway, breathing (C-A-B)
  - Changed from airway, breathing, circulation (A-B-C)
- Continued focus of ensuring high-quality chest compressions

Basic life support (BLS) protocol (Figure 84-1) is followed during the initial phase of cardiac arrest. Although these steps are described in sequence, they may occur simultaneously in the hospital setting. The initial response to a witnessed cardiac arrest is to confirm that the patient is unresponsive and apneic or has abnormal breathing (i.e., gasping). The health care provider immediately calls for assistance and a defibrillator. The recommendation to call for assistance before initiating chest compressions was established to decrease the time from cardiac arrest to first defibrillation, if appropriate. This recommendation is important because the highest survival rates are in patients who experience a witnessed cardiac arrest and have ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT) and who receive early chest compressions and defibrillation.

The next step is to check for a pulse (carotid artery) for no longer than 10 seconds before initiating cardiopulmonary resuscitation (CPR). One starts with high quality chest compressions. The essential element in treating cardiac arrest is beginning high-quality chest compressions without delay, to provide oxygenated blood to the heart and brain while advanced cardiopulmonary life support (ACLS) protocols are initiated. Components of high-quality chest compressions are as follows:

- "Push hard and push fast"
  - Adequate rate (at *least* 100 compressions per minute)
  - Adequate depth (2 inches)
- Full chest recoil between chest compressions

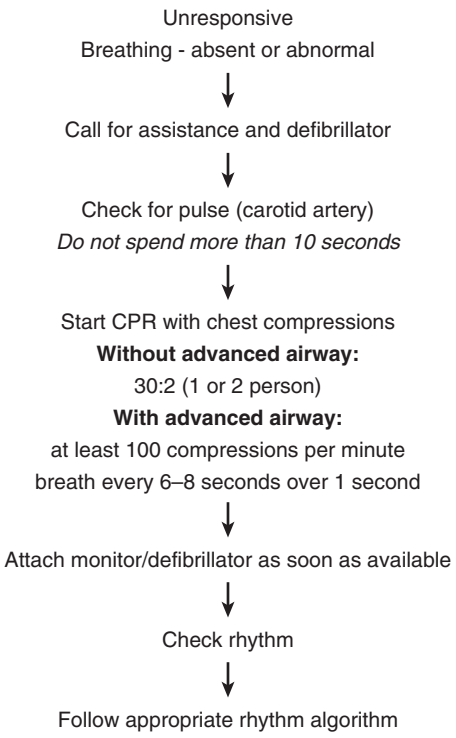


**FIGURE 84-1** ■ Components of basic life support.

- Minimize number (continuous for 2 minutes) and duration (<10 seconds) of interruptions in chest compressions
- Avoid excessive ventilation

To ensure that rescuer fatigue does not affect the quality of chest compressions, compressors should rotate every 2 minutes when five cycles of chest compressions and ventilations are completed. Additionally, chest compressions should resume immediately after defibrillation without checking for a pulse or rhythm.

If intraarterial blood pressure monitoring is available, a diastolic blood pressure >20 mm Hg indicates adequate chest compressions (i.e., adequate cardiac output). However, diastolic blood pressures <20 mm Hg indicate inadequate cardiac output, and efforts should be focused on improving the quality of chest compressions.

When there is no advanced airway in place, two breaths are given after 30 chest compressions are completed. A breath large enough to see chest wall rise (i.e., 6–7 mL/kg) over a 1-second interval is sufficient to provide adequate oxygenation and ventilation. This compression-to-ventilation ratio of 30:2 applies to single and two-person rescuers and is repeated for five cycles (over 2 minutes) before checking for a pulse or rhythm. The only exception is when the defibrillator first becomes available because early defibrillation (and early chest compressions) is associated with a higher survival rate.

If an advanced airway is in place, chest compressions are no longer synchronized with ventilation. Chest compressions are continuous while one breath is given every 6–8 seconds (8–10 breaths per minute). With or without an advanced airway, care should be taken to avoid excessive ventilation because it results in the following:

- Increased intrathoracic pressure that impedes venous return and ultimately decreases cardiac output during chest compressions
- Increased gastric inflation that may result in regurgitation and aspiration

Placement of an advanced airway should interfere minimally with chest compressions because chest compressions are critical to improved outcomes.

When capnography is available, an end-tidal carbon dioxide ($ETCO_2$) of at least 10–20 mm Hg is indicative of adequate chest compressions. $ETCO_2$ levels <10 mm Hg should prompt efforts to improve the quality of chest compressions.

When a defibrillator is available, a rhythm check should be performed. Further management depends on the rhythm identified.

A precordial thump may be considered for a witnessed cardiac arrest in a monitored patient with unstable or pulseless VT if a defibrillator is not immediately available. Defibrillation and the start of CPR should not be delayed to perform a precordial thump.

The best results (survival of approximately 40%) after cardiac arrest are achieved in patients receiving BLS within 4 minutes and ACLS within 8 minutes of cardiac arrest. Survival rates are <6% when both BLS and ACLS are started after 9 minutes. Patients most likely to be resuscitated include patients outside the hospital with a witnessed cardiac arrest secondary to VF, hospitalized patients with VF secondary to ischemic heart disease, patients with cardiac arrests not associated with coexisting life-threatening conditions, and patients who are hypothermic or intoxicated. Patients with severe multisystem disease, metastatic cancer, or oliguria do not often survive resuscitation efforts.

## 2. How do chest compressions produce a cardiac output?

It used to be assumed that chest compressions produced a cardiac output by directly compressing the ventricles against the vertebral column. This compression was thought to produce systole, with forward flow out of the aorta and pulmonary artery and backward flow prevented by closure of the atrioventricular (AV) valves. This explanation is flawed. Echocardiographic images during cardiac arrest show that the AV valves are not closed during chest compressions.

There are reports of patients who during episodes of monitored VF have developed systolic pressures capable of maintaining consciousness by coughing. Chest compressions per se are unnecessary to maintain a cardiac output. CPR is frequently ineffective in patients with flail chest until chest stabilization is achieved. If direct compression was the etiology of blood circulation in CPR, flail chest would be an advantage by increasing the efficiency of the "direct" compression. These observations have led to the proposal of the "thoracic pump" theory of CPR.

The "thoracic pump" theory proposes that forward blood flow is achieved because of phasic changes in intrathoracic pressure produced by chest compressions.

During the downward phase of compression, positive intrathoracic pressure propels blood out of the chest into extrathoracic vessels that have a lower pressure. Competent valves in the venous system prevent blood from flowing backward. During the upward phase of compression, blood flows from the periphery into the thorax because of negative intrathoracic pressure created by release of the compression. With properly performed cardiac compressions, systolic arterial blood pressures of 60–80 mm Hg can be achieved but with much lower diastolic pressures. Mean arterial pressures are usually <40 mm Hg. These pressures provide cerebral blood flows of only approximately 30% and myocardial blood flows of only about 10% compared with values before cardiac arrest.

### 3. What is the optimal airway management during cardiopulmonary resuscitation?

Optimal airway management during CPR depends on the experience of the rescuer. When unskilled providers attempted to place endotracheal tubes (ETT), the following complications occurred:

- Trauma to the oropharynx
- Unacceptably long periods of interrupted chest compressions and ventilation
- Hypoxemia
- Failure to recognize misplacement or dislodgment

Tracheal intubation, particularly by unskilled providers, is no longer considered the optimal way to manage the airway. In these circumstances, bag and mask ventilation or the use of alternative airways is preferable.

Bag and mask ventilation is performed initially in the nonintubated patient but risks gastric inflation, regurgitation, and aspiration. Despite these risks, the routine application of cricoid pressure during CPR is not recommended. In certain circumstances where regurgitation is of particular concern, cricoid pressure may be used. However, if effective ventilation is impeded, the pressure should be relaxed, adjusted, or ultimately released.

There is no specific recommendation regarding the timing of tracheal intubation. Whenever the decision is made to perform tracheal intubation, the following concepts apply:

- CPR should not be interrupted for >10 seconds.
- The compressor should be prepared to resume chest compressions as soon as the ETT is passed through the vocal cords.
- Confirmation of ETT placement should consist of:
  - Visualization of bilateral chest rise
  - Auscultation over the epigastrium and bilateral lung fields
  - Detection of $ETCO_2$
    - Continuous waveform capnography
    - Colorimetric or nonwaveform

Absence of $ETCO_2$ does not always indicate misplacement of the ETT (Box 84-1). In situations in which $ETCO_2$ is absent, a second method of confirmation should include either direct visualization of the ETT passing through the vocal cords or an esophageal detector device.

Supraglottic devices, such as laryngeal mask airways, are acceptable alternatives to bag and mask ventilation and tracheal intubation. Laryngeal mask airways and other supraglottic devices are not fully protective against aspiration of gastric contents.

**BOX 84-1 Conditions Associated with Proper Endotracheal Tube Placement without End-Tidal Carbon Dioxide Detection**

Inadequate chest compressions
Pulmonary embolus
Contamination of detector device by gastric contents or acidic drug (e.g., endotracheal epinephrine)
Severe airway obstruction (e.g., status asthmaticus)
Pulmonary edema

### 4. What are the complications of cardiopulmonary resuscitation?

Complications of CPR include skeletal (especially rib fractures), visceral, airway, and skin and integument (skin, teeth, lips) injuries. Some of these complications may require therapy and prolong hospitalization. Examples include rib and sternal fractures, myocardial and pulmonary contusions, pneumothorax, pericardial hematoma, tracheal and laryngeal injuries, liver and spleen ruptures, and gastric perforation and dilation. Of these complications, <0.5% are considered life-threatening. Serious harm occurring to patients while performing CPR is uncommon and should not dissuade bystanders from performing CPR.

### 5. What is the optimal dose of epinephrine?

Epinephrine is the therapy of choice for VF, pulseless VT, asystole, and pulseless electrical activity (PEA). Vasoconstriction caused by the α-adrenergic effects of epinephrine during CPR increases arterial pressure and improves myocardial and cerebral perfusion pressure. This is most likely a dose-dependent phenomenon.

The presence of coronary artery disease in many patients limits coronary artery blood flow even in the presence of higher aortic diastolic pressures. The β-adrenergic effects of epinephrine may actually worsen the outcome by increasing myocardial oxygen requirements.

Animal models have shown better outcomes from experimental cardiac arrest using 0.1–0.2 mg/kg of epinephrine, compared with the present recommended dose of 0.01 mg/kg. However, two more recent large multicenter investigations did not demonstrate survival differences in patients treated with larger doses of epinephrine. This lack of clinical efficacy may be related to the increased time that elapsed before the initial dose of epinephrine in clinical situations versus the animal studies. Until further studies clarify this issue, the current recommendation is 1 mg administered intravenously or intraosseously of a 1:10,000 epinephrine solution every 3–5 minutes. Higher doses (up to 0.2 mg/kg) are not recommended and may be harmful.

### 6. What is the indication for vasopressin in cardiopulmoanry resuscitation?

Vasopressin, also known as antidiuretic hormone, is a potent vasoconstrictor. The vasoconstrictive effect of vasopressin increases blood flow to the brain and heart during CPR. The vasoconstrictive effect is mediated via V1 receptors and is independent of the adrenergic receptor–mediated effect of epinephrine. Vasopressin appears to lack the β-adrenergic–mediated adverse effects of epinephrine, such as increased myocardial oxygen demand and tachycardia.

Studies comparing outcomes after cardiac arrest showed no difference whether vasopressin or epinephrine was administered. Repeated doses of vasopressin during resuscitation did not result in improved survival rates compared with repeated doses of epinephrine. Based on these studies, the current recommendation is that 40 units of vasopressin administered intravenously or intraosseously may be substituted for the first or second dose of epinephrine in all the algorithms. Because of the longer half-life of vasopressin (10–20 minutes) compared with epinephrine (3–5 minutes) and lack of supportive evidence in human trials, repeated doses are not recommended at this time.

### 7. What are the indications for sodium bicarbonate administration?

Sodium bicarbonate ($NaHCO_3$) previously was used routinely during CPR, even without knowledge of the acid-base status. Although acidosis inhibits myocardial contractility and catecholamine efficacy, this does not appear clinically significant in the range of pH commonly encountered and the catecholamine doses administered during resuscitation.

The detrimental effects of $NaHCO_3$ are as follows:

- Hypernatremia leads to hyperosmolarity. Hyperosmolarity may cause decreased aortic pressures leading to a reduction in coronary perfusion pressure.
- Intracellular acidosis develops. As is apparent from the equilibrium equation, every 50 mEq of bicarbonate administered produces large amounts of carbon dioxide ($CO_2$) gas that freely diffuses across cellular membranes and causes a paradoxical exacerbation of intracellular acidosis. Intracellular $CO_2$ tensions >300 mm Hg and pH values <6.1 have been recorded.

$$[HCO_3^-] + [H^+] \rightleftharpoons [H_2CO_3] \rightleftharpoons [CO_2] + [H_2O]$$

- Extracellular alkalosis shifts the oxyhemoglobin dissociation curve to the left impairing oxygen delivery.

The routine use of $NaHCO_3$ is not recommended. Special circumstances when $NaHCO_3$ administration is desirable include preexisting metabolic acidosis, hyperkalemia, or tricyclic antidepressant overdose. Otherwise, $NaHCO_3$ should be administered only based on laboratory findings of a low bicarbonate concentration or calculated base deficit. Calculation of the base deficit is as follows:

$$\text{Patient's weight (kg)} \times \text{base deficit} \times 0.3$$

To minimize the risk of iatrogenic alkalosis, the full calculated correction dose should not be administered. Most clinicians administer half the calculated dose and recheck the base deficit before any further administration of $NaHCO_3$.

### 8. What are the indications for calcium administration during cardiopulmonary resuscitation?

Routine administration of calcium during CPR is not recommended. Specific indications for calcium therapy during CPR include hyperkalemia, documented hypocalcemia, and calcium-channel blocker overdose.

### 9. How are ventricular fibrillation and pulseless ventricular tachycardia managed?

After CPR has been initiated and the underlying rhythm recognized as VF and pulseless VT, immediate defibrillation is indicated. Depending on whether the defibrillator is monophasic or biphasic, the shock current is set to 360 J or 120–200 J. The 2010 guidelines recommend one shock followed immediately by five cycles (2 minutes) of CPR without checking the rhythm or feeling for a pulse. After 2 minutes of CPR, the rhythm is checked, and if it is a shockable rhythm, defibrillation is repeated. Either epinephrine or vasopressin should be administered at this time. If during the next rhythm check (after 2 minutes of CPR) pulseless VT and VF still exist, another shock should be delivered. A dose of epinephrine or vasopressin (depending on what the first drug administered was) should be administered if 3 minutes has elapsed since the previous dose. If repeated defibrillation, epinephrine and vasopressin administration, and appropriately administered CPR are ineffective (i.e., refractory VF or VT), amiodarone should be administered as a 300-mg intravenous bolus, after the third shock (Table 84-1). This can be followed by a second dose of 150 mg intravenously. If hypomagnesemia is suspected or polymorphic VT with long QT syndrome (e.g., torsades de pointes) is present, magnesium sulfate, 1–2 mg intravenously, should be given.

### 10. What is the management of asystole and pulseless electrical activity?

Asystole, the absence of cardiac electrical activity, and PEA, cardiac electrical activity without a detectable pulse,

**TABLE 84-1 Therapy for Ventricular Fibrillation and Pulseless Ventricular Tachycardia**

| | |
|---|---|
| Defibrillation | |
| Monophasic | 360 J |
| Biphasic | 120–200 J (as recommended by manufacturer, if known use highest energy level) |
| Epinephrine | 1 mg 1:10,000 IV every 3–5 minutes |
| Vasopressin | 40 units IV (instead of first or second dose of epinephrine) |
| Amiodarone | 300 mg IV, may be repeated as 150 mg |
| Magnesium sulfate | 1–2 g IV (polymorphic VT with long QT interval, torsades de pointes) |

*IV,* Intravenously; *VT,* ventricular tachycardia.

are managed in the same way. Once cardiac arrest is identified, help should be called for, and CPR should immediately be performed until monitoring or a defibrillator is attached to the patient. The rhythm should be checked, and if asystole or PEA is identified, CPR should continue for 2 minutes while intravenous access is established (if not already present), epinephrine 1 mg intravenously is administered (repeated every 3–5 minutes during resuscitation), and placement of an advanced airway with capnography monitoring is considered. Vasopressin, 40 U intravenously, can be administered once instead of the first or second dose of epinephrine. If the rhythm remains the same after 2 minutes of CPR, reversible causes should be investigated (Box 84-2). Further treatment should be customized to the suspected underlying cause. After every 2 minutes of CPR, the rhythm should be checked, and further management is determined by the current rhythm identified. For example, if VF is identified during a rhythm check, the algorithm for VF management should be followed (i.e., defibrillation).

## 11. How is symptomatic bradycardia managed?

Bradycardia is defined as a heart rate <60 beats per minute. Clinically significant bradycardia is defined as bradycardia inappropriate for the clinical condition. Most patients do not become symptomatic until the heart rate is <50 beats per minute. Because the most common cause of bradycardia is hypoxia, the initial management of symptomatic bradycardia is directed at evaluation of the respiratory system. Patency of the airway, signs of increased work of breathing, and oxygen saturation should be determined. Supplemental oxygen should be administered if the patient is hypoxic, and electrocardiogram (ECG) monitoring and intravenous access should be established. Immediate treatment is indicated if further assessment determines the presence of any of the following:

- Hypotension
- Altered mental status
- Heart failure
- Shock
- Angina

The first-line treatment is atropine, 0.5 mg intravenously, repeated every 3–5 minutes to a maximum of 3 mg. If poor perfusion is present, external pacing should not be delayed by administration of atropine. Atropine should be given with caution in the presence of acute coronary syndrome or myocardial infarction because it may exacerbate ischemia or increase infarct size. Atropine may be ineffective in the heart transplant patient. If the bradycardia is due to type II second-degree or third-degree heart block, atropine is unlikely to be effective. Transcutaneous pacing or β-adrenergic therapy is warranted until transvenous pacing can be established. If atropine is ineffective, transcutaneous pacing, dopamine infusion (2–10 μg/kg per minute), or epinephrine infusion (2–10 μg per minute) is indicated (Table 84-2).

**BOX 84-2 Treatable Causes (5 H's and 5 T's) of Asystole and Pulseless Electrical Activity**

| | |
|---|---|
| Hypovolemia | Tension pneumothorax |
| Hypoxia | Tamponade (cardiac) |
| Hydrogen ion (acidosis) | Toxins |
| Hypokalemia or hyperkalemia | Thrombosis (coronary) |
| Hypothermia | Thrombosis (pulmonary) |

## 12. How are supraventricular tachyarrhythmias managed?

Tachycardia is defined as a heart rate >100 beats per minute. However, clinically significant tachycardia does not usually occur until the heart rate is >150 beats per minute. The most important initial step in the management of tachyarrhythmias is to evaluate whether the patient is stable or unstable. If the patient is unstable (i.e., presence of hypotension, signs of shock, acutely altered mental status, acute heart failure, or ischemic chest discomfort), immediate synchronized electrical cardioversion should be performed (Table 84-3). Wide irregular complexes should be managed the same as pulseless VT and VF with unsynchronized shocks (i.e., 360 J monophasic, 120–200 J biphasic).

If the patient is stable, the next treatment (Table 84-4) decision is based on the width of the QRS complex. If the width of the QRS complex is <0.12 second (narrow complex), preferred management consists of vagal maneuvers and adenosine (if regular rhythm). Adenosine is given as a rapid bolus of 6 mg intravenously that is repeated in

**TABLE 84-2 Therapy for Symptomatic Bradycardia**

| | |
|---|---|
| Atropine | 0.5 mg IV, every 3–5 minutes, maximum 3 mg<br>Caution in presence of ACS or MI<br>May be ineffective in presence of heart transplant or type II second-degree and third-degree heart block |
| Transcutaneous pacing | |
| Dopamine | 2–10 μg/kg/min |
| Epinephrine | 2–10 μg/min |

*ACS,* Acute coronary syndrome; *IV,* intravenously; *MI,* myocardial infarction.

**TABLE 84-3 Therapy for Unstable Supraventricular Tachycardia**

| | |
|---|---|
| **Synchronized Electrical Cardioversion** | |
| Narrow complex | 50–100 J |
| Narrow irregular | 200 J monophasic<br>100–200 J biphasic |
| Wide regular | 100 J |
| **Unsynchronized Shocks** | |
| Wide irregular | 360 J monophasic<br>120–200 J biphasic |

TABLE 84-4 **Therapy for Stable Supraventricular Tachycardia**

| | |
|---|---|
| **Narrow Complex (QRS <0.12 Second)** | |
| Vagal maneuvers | Valsalva, carotid sinus massage |
| Adenosine | 6 mg IV, repeat in 2 minutes 12 mg IV; regular rhythm only |
| β-adrenergic blocker | |
| Atenolol | 5 mg IV over 5 minutes, repeat in 10 minutes |
| Esmolol | 0.5 mg/kg intravenous loading dose followed by infusion 50 μg/kg/min; if ineffective, repeat loading dose and increase infusion to 100 μg/kg/min, repeat to maximum 300 μg/kg/min |
| Metoprolol | 5 mg IV every 5 minutes to maximum 15 mg |
| Propranolol | 0.5–1 mg IV, repeated to maximum 0.1 mg/kg |
| Calcium-channel blocker | |
| Diltiazem | 15–20 mg (0.25 mg/kg) IV over 2 minutes, 20–25 mg (0.35 mg/kg) IV in 15 minutes; maintenance 5–15 mg per hour |
| Verapamil | 2.5–5 mg IV over 2 minutes, repeat 5–10 mg every 15–30 minutes to maximum dose 20–30 mg; contraindications include CHF, impaired ventricular function, wide complex tachycardia |
| **Wide Complex (QRS >0.12 Second)** | |
| Adenosine | 6 mg IV, repeated in 2 minutes 12 mg IV; regular rhythm only, contraindicated in WPW |
| Procainamide | 20–50 mg/min or 100 mg every 5 minutes until arrhythmia suppressed, hypotension, QRS duration increased by 50%; maximum 17 mg/kg; maintenance 1–4 mg/min; avoid if QT interval prolonged or CHF |
| Amiodarone | 150 mg IV over 10 minutes, repeat if recurs; maintenance 1 mg/min for first 6 hours then 0.5 mg/min for 18 hours |
| Sotalol | 100 mg IV (1.5 mg/kg) over 5 minutes; avoid if QT interval prolonged |

*CHF,* Congestive heart failure; *IV,* intravenously; *WPW,* Wolff-Parkinson-White.

2 minutes as 12 mg intravenously if the rhythm does not convert. Sometimes vagal maneuvers or adenosine may be diagnostic in that the true underlying arrhythmia is revealed when the rate is slowed (e.g., atrial fibrillation, atrial flutter). If these treatments do not convert the rhythm, the rhythm recurs, or they disclose a different type of tachyarrhythmia, β-adrenergic blocker or calcium-channel blocker therapy should be instituted.

If the width of the QRS is >0.12 second (wide complex), adenosine should be administered only if the rhythm is regular and the complexes are monomorphic. If administered when the rhythm is irregular or the complexes polymorphic, adenosine may precipitate VF. Other treatment options include antiarrhythmic infusions of procainamide, amiodarone, or sotalol.

If atrial fibrillation/flutter is suspected as the underlying rhythm, it is imperative to evaluate the patient before further management is initiated. If possible, the patient's cardiac function should be assessed, Wolff-Parkinson-White syndrome should be ruled out, and the time of onset of atrial fibrillation should be determined (i.e., <48 hours or >48 hours). The goals are to treat unstable patients urgently to control the rate, convert the rhythm, and provide anticoagulation. Patients with an onset of symptoms >48 hours should be evaluated for thrombi in the atria using transesophageal echocardiography before electrical cardioversion is attempted.

Wolff-Parkinson-White syndrome is preferably treated with electrical cardioversion or amiodarone. Adenosine, β-adrenergic blockers, calcium-channel blockers, and digoxin are contraindicated because they can lead to an increased ventricular response or may precipitate VF by selectively blocking the AV node in the presence of coexisting accessory conduction pathways.

When the diagnosis of atrial fibrillation/flutter is confirmed, treatment usually consists of electrical cardioversion, β-adrenergic blockers, calcium-channel blockers (e.g., diltiazem), or digoxin. Amiodarone is preferred in unstable patients or patients with impaired ventricular function.

### 13. What are the indications for magnesium therapy?

Magnesium deficiency is associated with ventricular ectopy, sudden cardiac death, and congestive heart failure. It can also precipitate refractory VF and impede correction of hypokalemia. Hypomagnesemia should be corrected in cases of refractory VT or VF. Magnesium sulfate is the treatment of choice for polymorphic wide-complex tachycardia associated with congenital or acquired long QT syndrome (e.g., torsades de pointes). Magnesium supplementation may also reduce the incidence of ventricular arrhythmias after myocardial infarction.

### 14. What are the indications for a pacemaker?

Electrical pacing is generally ineffective, and no studies have observed a survival benefit when pacemakers are used during cardiac arrest. The use of transcutaneous or transvenous pacemakers in ACLS is indicated in patients with symptomatic bradyarrhythmias (i.e., myocardial ischemia, hypotension, mental status changes, pulmonary edema), in patients with high-degree AV block when intravenous access is unavailable, and for overdrive pacing in patients with refractory tachyarrhythmias. It is reasonable to initiate transcutaneous or transvenous pacing in unstable patients who are unresponsive to atropine.

### 15. Why is it important to monitor serum glucose?

Serum glucose levels may affect neurologic function after cardiac arrest. Animal studies have shown poorer functional brain recovery after normothermic cerebral ischemia in hyperglycemic animals. The mechanism probably relates to increased lactic acid production. It is unclear what levels of glucose should be treated, but it is reasonable to treat hyperglycemia that is >180 mg/dL. Severe hypoglycemia, as a result of overtreatment of hyperglycemia, causes neuronal injury and should be avoided.

### 16. What are the indications for open cardiac massage?

There are insufficient data to support or refute the use of open chest CPR; however, open cardiac massage may be beneficial for postoperative cardiac surgical patients (in case of pericardial tamponade), for patients in the operating room if the heart is accessible, for patients with severely deformed thoracic cages, and in some cases for patients with penetrating chest trauma. It has not been found to be of value in patients who have had prolonged closed chest CPR. Open cardiac massage can be considered in patients with critical aortic stenosis who are not responding to closed chest compressions.

### 17. What is the role for therapeutic hypothermia?

There may be a benefit to hypothermia after return to spontaneous circulation from out-of-hospital VF cardiac arrest or in-hospital cardiac arrest. More recent reports suggest improved outcomes in post–cardiac arrest patients treated with therapeutic hypothermia despite adverse initial neurologic or neurophysiologic risk factors. Typically, the patient is cooled to 32°–34° C for 12–24 hours. This can be achieved by a rapid infusion of 30 mL/kg of cold intravenous fluids followed by a cooling blanket or application of ice packs to maintain hypothermia. Percutaneous coronary interventions during therapeutic hypothermia may be associated with an improved outcome.

### 18. What are the special considerations for cardiopulmonary resuscitation in a pregnant patient?

The incidence of cardiac arrest in parturients is approximately 1:30,000 pregnancies. Treatment should be guided by the physiology of pregnancy. Possible causes of cardiopulmonary arrest during pregnancy include venous thromboembolism, preeclampsia, sepsis, amniotic fluid embolism, hemorrhage, trauma, cardiomyopathy, and congenital or acquired cardiac disease. The protocols for ACLS, including selection of medications, doses, indications for defibrillation, and selection of energy (joules), are the same for pregnant patient as for nonpregnant patients, with some specific considerations.

Because of the elevated diaphragm and abdominal contents by the gravid uterus, chest compressions should be performed slightly higher on the sternum. The uterus accounts for 10%–15% of the cardiac output, and this shunting of blood limits the effectiveness of CPR. Also, when in the supine position, the uterus compresses the aorta and vena cava resulting in impaired venous return to the heart. Left uterine displacement should be considered using a 30-degree leftward tilt. However, in a tilted patient, chest compressions are less effective because chest compressions in a nonsupine patient provide only 80% of the transmitted external force. After initiation of CPR in the supine position, manual left uterine displacement and left lateral tilt may be considered if CPR is ineffective in the supine position. Owing to uterine diversion of cardiac output and aortocaval compression, the AHA recommends cesarean delivery if CPR has not been successful within 4 minutes. Delivering the fetus within 5 minutes after maternal cardiac arrest provides the best chance of survival for both the mother and the fetus.

## SUGGESTED READINGS

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CASE 85

# Do Not Resuscitate

**Leila Hosseinian, MD**

## QUESTIONS

1. Does the American Society of Anesthesiologists have guidelines for do not resuscitate orders or other directives that limit treatment in the operating room?
2. What options regarding resuscitation efforts in the operating room should be discussed with the patient or patient's surrogate before administration of anesthesia?
3. What course of action can be taken if the anesthesiologist and the patient or surgeon cannot come to an agreement?
4. How long should the agreed on adjustments to do not resuscitate status be continued?
5. How would you counsel this patient on her do not resuscitate or intubate status before proceeding with surgery?

A 64-year-old woman presented for right hip replacement. She had a history of myasthenia gravis, unresponsive to therapy. When healthy, her exercise tolerance was equal to 4 METS; however, exacerbations precipitated by minor illness confined her to bed. She has refused cardiopulmonary resuscitation ("do not resuscitate" [DNR]) or intubation ("do not intubate" [DNI]) in the event of an emergency. You informed the patient you would like to discuss her DNR/DNI orders, and the patient did not understand why because the procedure was going to be done under spinal anesthesia.

### 1. Does the American Society of Anesthesiologists have guidelines for do not resuscitate orders or other directives that limit treatment?

The American Society of Anesthesiologists (ASA) last affirmed ethical guidelines for the anesthesia care of patients with DNR orders or other directives that limit treatment in 2008. The ASA guidelines apply to competent patients and incompetent patients who previously expressed their preferences. Before the early 1990s, when the guidelines were first written, it was assumed that DNR orders were automatically revoked while a patient was in the operating room because anesthesia and surgery were deemed to be a temporary altered state. Also, many procedures and drugs used routinely in the operating room can be considered as resuscitative. Guidelines recommending automatic suspension violate patients' rights of self-determination in a responsible and ethical manner. Instead, communication between the physician and the patient is an essential element of the preoperative preparation to determine goals of care.

### 2. What options regarding resuscitation efforts in the operating room should be discussed with the patient or the patient's surrogate before administration of anesthesia?

Because administration of anesthesia and surgery involve procedures and practices that overlap with resuscitation, the anesthesiologist can provide the following alternatives to full dismissal of DNR status:

- *Full attempt at resuscitation:* Because the period of time under anesthesia and in the immediate postoperative period is an alternate state, the patient or surrogate may request full suspension of existing directives during this time. All resuscitative efforts can then be brought to bear.
- *Limited attempt at resuscitation defined with regard to specific procedures:* The patient or surrogate may choose to refuse specific resuscitation procedures. The anesthesiologist discusses with the patient or surrogate the procedures that may need to be performed, highlighting which procedures are essential for the success of anesthesia and surgery versus the procedures that are not essential and can be refused. Procedures that are frequently discussed include chest compressions, defibrillation, tracheal intubation, administration of resuscitative medications, use of supplemental oxygen, placement of central lines, invasive monitoring, and use of bag and mask ventilation. The procedure-related DNR approach requires anticipation of the most likely problems that may occur and limits the physician when an unexpected situation arises. However, this approach does make it easier to implement DNR orders successfully when multiple caregivers are

involved. There is a concern that when faced with limited treatment options, the anesthesiologist may provide a "light" anesthetic to decrease the likelihood of needing any form of resuscitation, ultimately resulting in inadequate anesthesia.

- *Limited attempt at resuscitation defined with regard to the patient's goals and values:* The patient or surrogate may allow the anesthesiologist to make decisions regarding acceptable treatments based on the patient's goals and values rather than on individual procedures. Some patients may find certain treatments acceptable if the clinical event is temporary and quickly reversible but would want treatment withheld if the condition is or becomes irreversible or would result in permanent damage. Patients are often less concerned with the technical details of resuscitation and more concerned with issues such as the potential for pain and long-term outcomes of resuscitation. This approach allows for treatment of unexpected cardiac or respiratory events as long as that treatment complies with the patient's care goals. However, some anesthesiologists may be uncomfortable with the goal-directed DNR approach. They may have legal and ethical concerns regarding their decisions based on their best judgment during the time of the critical event. This method works only if the team caring for the patient throughout the case maintains consistency. There is too great a risk of misinterpretation of patient's goals if they are passed on from one anesthesiologist to another. Ideally, the individuals taking care of the patient should have first-hand knowledge of the patient and were involved in the discussion of the patient's goals. Most physicians prefer the adaptability and flexibility of this approach, but it does require a high degree of trust between the patient and physicians, which is not always possible. Documentation of the goal-directed DNR approach should include a narrative that summarizes the discussions that occurred between the patient and physicians.

### 3. What course of action can be taken if the anesthesiologist and the patient or surgeon cannot come to an agreement?

When the anesthesiologist finds the patient's or surgeon's limitation of interventions to conflict with his or her moral views, withdrawal from the case is appropriate after obtaining a replacement to provide care. If the limitation of interventions is in conflict with generally accepted standards of care, the anesthesiologist should voice these concerns to the appropriate hospital committee (e.g., ethics committee). For example, an anesthesiologist can refuse to comply with a patient declining intubation for an exploratory laparoscopy. (In the United States, it is not common practice to substitute supraglottic devices for tracheal intubation during laparoscopy). If surgery is urgent or emergent and an alternative anesthesiologist is unavailable in an appropriate time frame, the original anesthesiologist must proceed with reasonable adherence to the patient's directives.

### 4. How long should the agreed on adjustments to do not resuscitate status be continued?

Reinstitution of the prior DNR/DNI status needs to be discussed with patients during the preoperative evaluation. Some patients prefer to reinstitute full DNR/DNI status on arrival to the postanesthesia care unit; others agree on extending the limited DNR/DNI status to cover the perioperative period.

### 5. How would you counsel this patient on her do not resuscitate or intubate status before proceeding with surgery?

Although the patient is having hip replacement surgery under regional anesthesia, it is important to explain to the patient the risk of a high spinal anesthetic. The ability to intubate or mask ventilate for a defined period is necessary for resuscitation, even though this is a rare event. Also, hypotension may occur requiring the use of vasopressor medications. The approach to this discussion can be as follows:

- *Full resuscitation:* The DNR/DNI order is fully rescinded during the operative and postanesthesia care unit period.
- *Procedure-related:* Anesthesia-related procedures that overlap with resuscitative efforts should be discussed. An explanation of these procedures and their expected time course is helpful for patients to understand them. A definitive end time needs to be established as well. For example, the patient may agree to intubation in the event of a high spinal but only for the duration of the spinal.
- *Goal-related:* The patient's goals of care need to be understood. If the patient rejects machines or drugs to maintain cardiac function, an agreement may allow treatment if the condition is considered to be temporary and due to the surgery. It is important that all parties involved agree on what is considered temporary.

If the patient refuses any alteration in status, the anesthesiologist either can agree to proceed after explaining the risks to limiting care or can refuse to care for the patient if another anesthesiologist is available.

## SUGGESTED READINGS

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CASE 86

# Acute Respiratory Distress Syndrome

**Leila Hosseinian, MD**

## QUESTIONS

1. Define acute respiratory distress syndrome.
2. What are the common causes of acute respiratory distress syndrome?
3. Explain the pathophysiology of acute respiratory distress syndrome.
4. Describe the ventilatory strategies for acute respiratory distress syndrome.
5. What role does permissive hypercapnia have in current lung protective strategies?
6. Can prone positioning help improve oxygenation in patients with acute respiratory distress syndrome?
7. Can recruitment maneuvers improve oxygenation in patients with acute respiratory distress syndrome?
8. Is extracorporeal membrane oxygenation an evidence-based treatment for acute respiratory distress syndrome?
9. Is high-frequency jet ventilation an effective ventilation mode for patients with acute respiratory distress syndrome?
10. Do inhaled nitric oxide and other vasodilators improve ventilation/perfusion mismatch?
11. Can the antiinflammatory property of steroids inhibit progression of inflammation contributing to acute respiratory distress syndrome?
12. Does fluid restriction help lung function?

A 52-year-old man presented for exploratory laparotomy. He complained of fever, severe abdominal pain, and vomiting for 3 days. Past medical history was significant for Crohn's disease, hypertension, and multiple bowel resections, the last of which was done 1 week ago. He weighed 176 pounds (80 kg) and stood 5 feet 9 inches (175 cm) tall. Clinically significant vital signs included heart rate, 123 beats per minute, blood pressure, 90/65 mm Hg, and respiratory rate, 29 breaths per minute. Laboratory findings included hematocrit of 46% and white blood cell count of 23,000/$mm^3$. Sodium and creatinine were mildly elevated. Intraoperatively, the patient was hemodynamically unstable. Postoperatively, he remained intubated and ventilated in the intensive care unit. Overnight he became more difficult to ventilate with elevated peak airway pressures and increasing fraction of inspired oxygen ($FiO_2$) requirements.

### 1. Define acute respiratory distress syndrome.

Acute respiratory distress syndrome (ARDS) is characterized by inflammation of the lung parenchyma leading to impaired gas exchange, hypoxemia, and nonhydrostatic pulmonary edema. The incidence of ARDS in the intensive care unit (ICU) ranges from 4%–9%, with a mortality rate of approximating 40%–45%. ARDS was first described in 1967 by Ashbaugh et al. in 12 patients, who had cyanosis refractory to oxygen therapy, decreased lung compliance, and diffuse infiltrates on chest radiograph. By 1994, a new definition was established by the American-European Consensus Conference Committee (AECC) as follows:

- Acute onset
- Bilateral infiltrates on chest radiograph
- Pulmonary capillary wedge pressure (PCWP) ≤18 mm Hg or absence of clinical evidence of left atrial hypertension
- Acute lung injury considered to be present if $PaO_2/FiO_2$ ratio ≤300
- Acute respiratory distress considered to be present if $PaO_2/FiO_2$ ratio ≤200

There has been some criticism regarding the AECC oxygenation criteria because they do not account for variations in the $PaO_2/FiO_2$ ratio in response to varying levels of positive end expiratory pressure (PEEP). With the current definition, a patient with a $PaO_2/FiO_2$ ratio <200 on a PEEP of 12 cm $H_2O$ is considered equivalent to a patient with a similar $PaO_2/FiO_2$ ratio on a PEEP of 5 cm $H_2O$. Investigators have advocated that a standardized $PEEP/FiO_2$ assessment is necessary to classify ARDS severity accurately. The $PaO_2/FiO_2$ ratio has failed to predict ARDS outcomes consistently in epidemiologic studies. This failing is likely due to ignoring PEEP in their evaluation.

In a study from Spain by Cortes et al. (2012), one third of patients who died with a clinical diagnosis of ARDS did not have histologic evidence of diffuse alveolar damage on autopsy. This finding questions the current clinical criteria used for diagnosis of ARDS. With regard to the AECC chest radiograph definition of ARDS, there is

some controversy regarding the lack of acknowledgment of the severity or distribution of infiltrates. Furthermore, the distribution of infiltrates seen on chest radiographs and computed tomography (CT) scans often disagree, questioning the use of chest radiograph rather than CT scan findings to diagnose ARDS. Finally, the criteria requiring PCWP <18 mm Hg is not easy to assess noninvasively and is flawed by interobserver measurement variability. Some authors have argued for the use of echocardiography; however, it is also dependent on interpretation and availability.

## 2. What are the common causes of acute respiratory distress syndrome?

ARDS is most often part of a systemic inflammatory process. Sepsis is associated with the highest risk of progression to ARDS. Various precipitating events can either directly or indirectly result in lung injury and eventually ARDS (Table 86-1).

The inciting cause can be used to predict progression and prognosis of ARDS. For example, ARDS associated with trauma has a better prognosis compared with non–trauma-related injury. In terms of disease progression, pulmonary infections are associated with a higher risk of ARDS progression compared with nonpulmonary infections.

## 3. Explain the pathophysiology of acute respiratory distress syndrome.

ARDS develops when inflammatory cytokines injure the epithelium and endothelium of the lungs. In early phases, alveolar macrophages release proinflammatory cytokines such as tumor necrosis factors (TNF) and interleukin (IL)-1, IL-6, and IL-8. These cytokines attract neutrophils to the lungs, where they release a wide variety of substances (e.g., reactive oxygen species, proteases). These substrates injure alveolar epithelium and endothelium, leading to increased capillary permeability, which is the hallmark of ARDS. This results in leakage of protein-rich edema into the interstitium and air spaces. Protein-rich edema fluid in the alveolus inactivates surfactant and creates diffuse alveolar damage. ARDS may resolve completely in some patients, after the acute phase. In others, the disease progresses to persistent reduced lung compliance with increased alveolar dead space and interstitial fibrosis. For most patients who survive, pulmonary function returns to normal within 6–12 months. Most deaths are due to sepsis or multiorgan failure and not hypoxia.

TABLE 86-1 **Causes of Acute Respiratory Distress Syndrome**

| | Direct Lung Injury | Indirect Lung Injury |
|---|---|---|
| Common | Pneumonia<br>Aspiration | Sepsis<br>Severe trauma<br>Multiple blood transfusions |
| Less common | Inhalational injury<br>Air embolism<br>Fat embolism<br>Near drowning | Acute pancreatitis<br>Drug overdose<br>Post–cardiopulmonary bypass |

## 4. Describe the ventilatory strategies for acute respiratory distress syndrome.

ARDS is treated with mechanical ventilation to correct hypoxemia and hypercapnia (Box 86-1). The goals are to maintain acceptable gas exchange, minimize ventilator-induced lung injury, and treat underlying causes of illness. Although mechanical ventilation is the modality keeping these patients alive, it can also extend inflammation in response to cyclic tidal alveolar hyperinflation. Cyclic overdistention produced by excessive transpulmonary pressure is a determinant of ventilator-induced lung

**BOX 86-1 National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome Clinical Network Mechanical Ventilation Protocol Summary**

1. Calculate PBW
   A. Males = 50 + 2.3 (height inches − 60)
   B. Females = 45.5 + 2.3 (height inches − 60)
2. Set any ventilatory mode
3. Set ventilator to achieve initial $V_T$ = 8 mL/kg PBW
4. Reduce $V_T$ by 1 mL/kg until $V_T$ = 6 mL/kg PBW
5. Adjust $V_T$ and RR to achieve
   A. pH goal of 7.3–7.45
   B. $P_{plat}$ goal ≤30 cm $H_2O$
6. Maintain $PaO_2$ 55–80 mm Hg or oxygen saturation 88%–95% using
   A. Minimum PEEP of 5 cm $H_2O$
   B. Minimum $FiO_2$
   C. Use incremental increases in PEEP and $FiO_2$ to achieve goals
7. $P_{plat}$ goal ≤30 cm $H_2O$
   A. If $P_{plat}$ >30 cm $H_2O$
      i. Decrease $V_T$ by 1 mL/kg PBW at a time (minimum 4 mL/kg PBW)
   B. If $P_{plat}$ <25 cm $H_2O$ and $V_T$ <6 mL/kg PBW
      i. Increase $V_T$ by 1 mL/kg PBW until
         a. $P_{plat}$ >25 cm $H_2O$ or
         b. $V_T$ = 6 mL/kg PBW
8. pH goal 7.3–7.45
9. Acidosis management (pH <7.3)
   A. pH 7.15–7.3
      i. Increase RR until pH >7.3 or $PaCO_2$ <25 (maximum RR = 35)
   B. pH <7.15
      i. $V_T$ may be increased by 1 mL/kg PBW increments until pH >7.15
         a. $P_{plat}$ may exceed 30 cm $H_2O$
   C. May give sodium bicarbonate
10. Alkalosis management (pH >7.45)
    A. Decrease RR if possible

*$FiO_2$*, Fraction of inspired oxygen; *PBW*, predicted body weight; *PEEP*, positive end expiratory pressure; *Pplat*, plateau pressure; *RR*, respiratory rate; *$V_T$*, tidal volume.

injury (VILI). Dreyfuss et al. (1988) studied rat lungs to determine whether VILI resulted from a pressure-mediated or lung volume (stretch)–mediated injury. These investigators subjected rats to incremental peak inspiratory pressure, and the tidal volume was restricted in one group using a thoracoabdominal binder to limit chest wall excursion. High tidal volume ventilation, independent of airway pressure, produced severe lung injury, otherwise known as volutrauma. The investigators also found PEEP to be protective, preventing pulmonary epithelial damage and alveolar edema. The ARDS Clinical Network (ARDSnet) completed a landmark trial in 2000 with 861 patients with ARDS (Acute Respiratory Distress Syndrome Network, 2000). Improved mortality was seen when a tidal volume of 6 mL/kg based on predicted body weight (PBW) was used compared with the traditional value of 12 mL/kg based on PBW. The group with tidal volume 6 mL/kg was restricted to a plateau pressure ≤30 cm $H_2O$, and the group with tidal volume 12 mL/kg was restricted to a much higher plateau pressure of ≤50 cm $H_2O$ (Table 86-2). The low tidal volume group was found to have reduced levels of inflammatory mediators, which reflect less severe lung injury.

No particular ventilator mode has improved ARDS mortality. The ARDSnet trial used volume control mode, and PEEP was used to improve oxygenation. There are three types of alveoli in ARDS:

- Normal—always inflated and participating in gas exchange
- Flooded—unable to participate in gas exchange
- Atelectatic or partially flooded—with the right amount of PEEP can be recruited to participate in gas exchange

The goal of "lung protective" ventilation (i.e., reduced tidal volumes) is to avoid excessive pulmonary stress and strain; higher PEEP prevents regional excessive stress and strain by avoiding alveolar collapse and reopening during mechanical ventilation. However, the optimal level of PEEP remains unclear. Several randomized controlled trials comparing higher versus lower levels of PEEP in patients with ARDS showed improved oxygenation with higher levels of PEEP without significant differences in mortality rates.

## 5. What role does permissive hypercapnia have in current lung protective strategies?

Reduced tidal volume avoids stretch-induced lung injury and provides lung protective ventilation; however, it generally leads to elevations in $PaCO_2$. This increase has been an accepted approach termed "permissive hypercapnia." There is some evidence that hypercapnic acidosis may contribute to the benefits seen with protective lung ventilation. However, it can be detrimental in patients with elevations in intracranial pressure or pulmonary vascular resistance.

## 6. Can prone positioning help improve oxygenation in patients with acute respiratory distress syndrome?

The distribution of pulmonary infiltrates is not uniform in ARDS. Consequently, positioning a patient prone could improve oxygenation by relieving atelectasis, enhance ventilation/perfusion matching, increase end expiratory lung volume, and more uniformly distribute lung stress and strain with tidal cycling. Although oxygenation in patients with ARDS can be improved with prone positioning, there is no evidence of decreased mortality. A meta-analysis pooling patient populations with the most severe ARDS suggested that prone positioning should be considered as a rescue regimen for patients with intractable hypoxemia. The potential risks of prone positioning are primarily related to physical injury and tube dislodgment during turning maneuvers.

## 7. Can recruitment maneuvers improve oxygenation in patients with acute respiratory distress syndrome?

Recruitment maneuvers are transient increases in transpulmonary pressure intended to promote reopening of collapsed alveoli. The maneuver is accomplished by increasing continuous positive airway pressure to 35–50 cm $H_2O$ for 30 seconds. Several studies have shown improved gas exchange and decreased hypoxia after recruitment maneuvers; however, there are no randomized controlled trials to show benefit on ARDS mortality. In addition, patients can become hypotensive with recruitment maneuvers because they decrease cardiac preload.

## 8. Is extracorporeal membrane oxygenation an evidence-based treatment for acute respiratory distress syndrome?

Extracorporeal membrane oxygenation (ECMO) was first applied to patients with ARDS in 1972. ECMO is the optimal method for oxygenating blood while maintaining total lung protection. However, the risks of ECMO (bleeding from anticoagulation and infection from intravascular catheters) mitigate its potential benefit. At this point, ECMO should be applied only in experienced institutions and should be reserved for patients for whom safe mechanical ventilation is impossible.

## 9. Is high-frequency jet ventilation an effective ventilation mode for patients with acute respiratory distress syndrome?

High-frequency jet ventilation (HFJV) is a mode of mechanical ventilation that uses rapid respiratory rates (100–200 breaths per minute) and small tidal volumes (2–5 mL/kg). Although tidal volumes are often smaller than traditional estimates of both anatomic and physiologic dead space, adequate oxygenation and ventilation can be achieved. HFJV administers oxygen under high pressure through a small-bore aperture into an endotracheal tube. Valves control the intermittent delivery of gas jets. Smaller tidal volumes help avoid injury from excessive end inspiratory lung volumes. The disadvantages include hypercapnia with respiratory acidosis and associated circulatory depression, auto-PEEP, increased cerebral blood flow, elevated intracranial pressures, and enhanced requirements for sedation and neuromuscular blockade. A mortality benefit from HFJV has not been

shown; however, oxygenation can be improved within the first 24 hours of therapy.

### 10. Do inhaled nitric oxide and other vasodilators improve ventilation/perfusion mismatch?

Nitric oxide is a potent vasodilator that is delivered to the pulmonary vasculature by inhalation, without causing systemic vasodilation. It has been shown to protect type II pneumocytes from stretch injury and may be protective of endothelial tissue by decreasing platelet and leukocyte adhesion to endothelium. Inhaled nitric oxide (iNO) also vasodilates the microcirculation, which allows for increased perfusion of tissue beds and improved ventilation/perfusion matching, resulting in better oxygenation. More recent trials have shown no effect on either mortality or the duration of mechanical ventilation when using iNO for patients with ARDS. It may be useful as a rescue therapy in patients with refractory hypoxia, but the benefit of improved oxygenation is temporary. Treatment with less selective vasodilators (sodium nitroprusside, epoprostenol, and alprostadil) has also not been proven to be beneficial.

### 11. Can the antiinflammatory property of steroids inhibit progression of inflammation contributing to acute respiratory distress syndrome?

Patients with ARDS have persistent elevations in plasma levels of inflammatory cytokines (TNF-α, IL-1β, and IL-6). Theoretically, suppression of these substances could reverse the inflammatory component of ARDS. In a more recent study, although treatment with methylprednisolone increased the number of ventilator-free days, shock-free days, and ICU-free days, it did not change the mortality rate from ARDS.

### 12. Does fluid restriction help lung function?

One consequence of ARDS is increased pulmonary capillary permeability resulting in pulmonary edema. The Fluid and Catheter Therapy Trial (FACTT), published in the *New England Journal of Medicine* in 2006, evaluated whether fluid restriction would improve outcomes in patients with acute lung injury. The conservative fluid strategy group (average loss of 136 mL over 7 days) showed better lung injury scores, oxygenation indices, increased number of ventilator-free and ICU-free days, and lower plateau pressures and PEEP versus the liberal fluid management group (average net gain of almost 7 L over the first 7 days). There was no difference in the development of shock or the need for renal replacement therapy between the two groups. However, mortality rates were not significantly different between the two groups.

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CASE 87

# Respiratory Failure

**Andrew B. Leibowitz, MD**

## QUESTIONS

1. What is postoperative respiratory failure?
2. Describe the two main types of acute respiratory failure.
3. What are the indications for tracheal intubation in a patient with dyspnea?
4. When should noninvasive ventilation be considered, and how is it prescribed?
5. What are the four primary causes of hypoxemia, how are they distinguished, and which is most likely in this patient?
6. How would you treat this patient?
7. What are the most common ventilatory modes?
8. How does pulmonary embolism manifest, and how is it diagnosed and treated?
9. What criteria are used to determine if extubation should be performed?

A 59-year-old woman with carcinoma underwent a left hemicolectomy. She had a history of chronic obstructive pulmonary disease (COPD) secondary to long-standing tobacco use and type 2 diabetes mellitus. Surgery was complicated by aspiration after extubation and reintubation. Arterial blood gas (ABG) values are pH 7.35, carbon dioxide tension ($PaCO_2$) 37 mm Hg, and oxygen tension ($PaO_2$) 54 mm Hg on controlled mechanical ventilation (CMV) with a rate of 12 breaths per minute, tidal volume of 650 mL, fraction of inspired oxygen ($FiO_2$) of 0.5, and positive end expiratory pressure (PEEP) of 5 cm $H_2O$. Peak inspiratory pressures are 26 cm $H_2O$. After several days in the intensive care unit (ICU), the patient's respiratory status improved.

### 1. What is postoperative respiratory failure?

Postoperative respiratory failure is the postoperative need for continued mechanical ventilation or the need for reintubation and mechanical ventilation after extubation in the early postoperative period (i.e., 24–48 hours).

### 2. Describe the two main types of acute respiratory failure.

The two main types of acute respiratory failure are as follows:

- Type I—hypoxemic
- Type II—hypercapnic

Occasionally both types may coexist.

Hypoxemic acute respiratory failure is discussed in detail in Question 5. Hypercapnic acute respiratory failure occurs when a patient develops acute respiratory acidosis, usually with a $PaCO_2$ >50 mmHg. It is caused by either ineffective minute ventilation or, much less commonly, excessive carbon dioxide ($CO_2$) production (e.g., malignant hyperthermia, thyroid storm). Ineffective minute ventilation has three main clinical causes, as follows:

- Decreased respiratory rate (e.g., secondary to opioids, brainstem lesions)
- Decreased tidal volume (e.g., residual neuromuscular blockade, myasthenia gravis, splinting)
- Increased physiologic dead space (e.g., COPD, later stages of acute respiratory distress syndrome [ARDS], shock)

Hypercapnia can also result in hypoxemia, as is discussed in Question 5.

### 3. What are the indications for tracheal intubation in a patient with dyspnea?

Clinical indications include patient fatigue, accessory muscle use, paradoxical breathing pattern, and inability to protect the airway. $PaO_2$ ≤60 mm Hg (i.e., oxygen saturation <90%), $FiO_2$ ≥0.5, and increasing $PaCO_2$ (e.g., 10 mm Hg above baseline or ≥50 mm Hg) are ABG abnormalities that alone, and especially in combination with any of the clinical indications, support the need to intubate and initiate mechanical ventilation.

### 4. When should noninvasive ventilation be considered, and how is it prescribed?

Noninvasive ventilation may be effective in place of tracheal intubation when respiratory distress is expected to be short-lived (e.g., ideally <24 hours), and the patient can cooperate with the requisite mask fitting and protect the airway. Mild to moderate pulmonary edema responding to medical therapy, COPD exacerbation, and perhaps splinting are reasonable postoperative conditions for

consideration of noninvasive ventilatory support. Generally, noninvasive ventilation is set with inspiratory pressure support (PS) and continuous positive airway pressure (CPAP), which together are termed BPAP (bilevel positive airway pressure). A common initial setting is 10 cm $H_2O$/5 cm $H_2O$ (PS/CPAP) adjusted by appearance, respiratory rate, oxygen saturation by pulse oximetry ($SpO_2$), and measured $PaCO_2$. The success rate for avoidance of eventual tracheal intubation is highly dependent on respiratory care team effort and patient selection. Extreme care must be taken to avoid the unobserved need to progress to tracheal intubation.

## 5. What are the four primary causes of hypoxemia, how are they distinguished, and which is most likely in this patient?

The four primary causes of hypoxemia are hypoventilation (i.e., hypercapnia), shunt, ventilation/perfusion ($\dot{V}/\dot{Q}$) mismatch, and diffusion impairment. Low $FiO_2$ and low barometric pressure can cause hypoxemia but do not warrant consideration in this context.

Hypoventilation is a reduction in gas flow to the alveoli. This reduction occurs whenever there is ineffective minute ventilation (see Question 2). The hallmark feature is an increased $PaCO_2$. Two basic equations relate to this condition.

The first equation demonstrates the relationship between $PaCO_2$ and alveolar ventilation:

$$PaCO_2 = \frac{\dot{V}CO_2}{V_A} \times K$$

where $\dot{V}CO_2$ is the $CO_2$ produced, $V_A$ is the alveolar ventilation, and K is a constant equal to 0.863. This equation demonstrates that if the alveolar ventilation is halved, $PaCO_2$ doubles, and vice versa.

The second equation is the alveolar gas equation:

$$P_AO_2 = FiO_2 \left(P_{atm} - P_{H_2O}\right) - \frac{PaCO_2}{RQ}$$

where $P_AO_2$ is the alveolar partial pressure of oxygen, $P_{atm}$ is the atmospheric pressure (760 mm Hg at sea level), $P_{H_2O}$ is the saturated pressure of water at 37° C (47), and RQ is the respiratory quotient (approximately 0.8). This equation predicts that although hypoventilation causes a decrease in $P_AO_2$, this may be overcome by administration of an increased $FiO_2$. Postoperative patients with respiratory depression receiving supplemental oxygen may have a delayed diagnosis of hypoventilation (e.g., $SpO_2$ >90% and $PaCO_2$ >60 mm Hg). For this patient, the $P_AO_2$ calculates to 310 mm Hg.

Shunt occurs when blood passes from the venous circulation to the arterial circulation without exposure to ventilated alveoli. Ventricular septal defects and extrapulmonary shunts sometimes allow significant amounts of venous blood to pass to the arterial side without oxygenating. Such physiology creates large right-to-left shunts. This is the most glaring example of a shunt, but less obvious intrapulmonary shunting, involving the vasculature of the lung, is common in respiratory diseases. The primary feature of significant shunting is the failure of $PaO_2$ to increase in response to increasing $FiO_2$. The degree of shunting is calculated by the shunt equation, as follows:

$$\frac{\dot{Q}_S}{\dot{Q}_T} = \frac{(CcO_2 - CaO_2)}{CcO_2 - C\bar{v}O_2)}$$

where $\dot{Q}_S$ and $\dot{Q}_T$ refer to the shunt and total pulmonary blood flows, and $CcO_2$, $CaO_2$, and $C\bar{v}O_2$ refer to the oxygen content of pulmonary end-capillary, arterial, and mixed venous blood.

Arterial oxygen content is calculated as follows:

$$CaO_2 = \left(Hgb \times 1.34 \times SaO_2\right) + 0.003 \times PaO_2$$

where Hgb is the hemoglobin concentration in g/dL, $SaO_2$ is the arterial oxygen saturation of Hgb, and $PaO_2$ is the arterial oxygen tension. Hemoglobin concentration and $SaO_2$ are the main determinants of blood oxygen content, with $PaO_2$ playing a comparatively small role except in special situations such as severe anemia or hyperbaric oxygen therapy.

Ventilation/perfusion ($\dot{V}/\dot{Q}$) mismatch is the most common cause of hypoxemia and the hardest to understand. In this condition, there is inefficient and incomplete transfer of gas from the alveoli to the capillary because of mismatching of blood flow and ventilation. Mismatching varies in different areas of the lungs at any point in time. Elements of shunt and hypoventilation may exist. Hypercapnia is not prominent unless mismatching is severe. Essentially, when hypoventilation, shunt, and diffusion impairment (see later) are excluded as primary causes of an increased alveolar to arterial (A-a) gradient, $\dot{V}/\dot{Q}$ mismatch is the cause.

Diffusion impairment is the result of incomplete equilibrium between alveolar gas and capillary blood because of an abnormality in the thin-walled and easily crossed alveolar-capillary barrier. This condition may occur in a variety of chronic lung diseases such as interstitial fibrosis, asbestosis, and sarcoidosis but is not commonly seen in acute respiratory failure. Although diffusion capacity may be measured in a pulmonary function laboratory using carbon monoxide, bedside quantification of diffusion-limited hypoxemia using standard laboratory tests is impossible.

In this patient, the A-a gradient is 256, whereas the $PaO_2/FiO_2$ ratio is 108 (diagnostic for ARDS). $\dot{V}/\dot{Q}$ mismatch and shunt are the most likely pathophysiologic explanations and are commonly seen in ARDS. $PaCO_2$ is normal, which excludes hypoventilation, and diffusion abnormality is uncommon in acute situations. Significant shunt can be excluded if an increase in $FiO_2$ is associated with a commensurate increase in $PaO_2$.

## 6. How would you treat this patient?

The first measure should focus on improving the A-a gradient. Manual recruitment maneuvers help to minimize atelectasis and open up new lung units. These maneuvers require the administration of several supraphysiologic tidal volumes (e.g., >20 mL/kg). Increasing PEEP increases

the functional residual capacity and allows a greater portion of ventilation to occur in opened alveoli during each breath. Incrementally increasing PEEP to 15 cm $H_2O$ may be required.

Maintenance of $PaO_2$ >60 mm Hg with $FiO_2$ ≤0.6 is a short-term goal because hypoxemia can be injurious, and $FiO_2$ >0.6 may cause oxygen toxicity and result in ARDS. $FiO_2$ of 1.0 is almost always toxic within 24–48 hours, so reduction of $FiO_2$ toward 0.6 is a good short-term (i.e., in <12–24 hours) goal. When shunt is a significant issue, reduction in high $FiO_2$ levels frequently results in little change in $PaO_2$, so frequent ventilatory changes with vigilant $SpO_2$ and ABG monitoring are necessary.

Shortly after achieving adequate oxygenation, a low tidal volume strategy as outlined in the ARDS Network investigation (i.e., 6 mL/kg of lean body weight with peak inflation pressure <30 cm $H_2O$) should be instituted. Another ARDS-specific treatment is maintenance of a relatively "dry" state versus liberal fluid administration. Other general intensive care unit (ICU) measures include gastrointestinal bleeding prophylaxis, deep vein thrombosis prevention, early enteral feeding, and daily sedation breaks.

## 7. What are the most common ventilatory modes?

A complete overview of mechanical ventilation is beyond the scope of this chapter. The most commonly used ventilatory modes are outlined in Table 87-1.

Generally, mechanical ventilation is required to assist a patient who is:

- Unable to contribute any respiratory effort (e.g., CMV, assist controlled [AC], and pressure controlled [PC] mode)
- Able to contribute only some effort (e.g., synchronized intermittent mechanical ventilation [SIMV] and SIMV/PS mode)
- Able to contribute significant effort (e.g., PS mode)

"Trigger" refers to the event that initiates a breath. The trigger can be either of the following:

- Time—the set respiratory rate determines when a breath will be delivered This is the most common intraoperative method. If the rate is set at 12 breaths per minute, a breath is delivered every 5 seconds.
- Patient—the ventilator detects an inspiratory effort generated by the patient. The inspiratory effort can be detected by the generation of either negative pressure (AC mode) or inspiratory flow (PS mode).

"Breath goal" refers to the set desired breath; generally, this is either a volume or a pressure delivered by the ventilator. In the case of SIMV, the patient-generated breaths are entirely determined by patient effort. Type of breath delivered is ventilator setting derived (CMV, AC, PC modes), entirely patient derived (intermittent breaths taken in SIMV mode), or patient assisted (PS mode).

CMV is used only in the operating room setting. The respiratory rate and tidal volume are set, and the patient cannot take any spontaneous breaths. It is an appropriate mode only under general anesthesia.

AC ventilation allows a patient to receive a preset number of ventilator breaths per minute and detects additional inspiratory efforts by the patient and delivers a ventilator breath with the same set tidal volume. PC ventilation delivers breaths determined by pressure, not volume. It is a mode used almost exclusively by intensivists in the management of ARDS but can be helpful whenever lung compliance is grossly abnormal (e.g., obese patients undergoing laparoscopic surgery). Improved oxygenation and ventilation occur in this mode because the pressure-time curve characteristics of each breath are associated with better alveolar ventilation. Tidal volume is completely determined by the pressure set and lung compliance, so extra vigilance needs to be maintained by observing the delivered tidal volume, $SpO_2$, and either end-tidal $CO_2$ or $PaCO_2$.

SIMV combines ventilator breaths at a set rate synchronized not to interfere with spontaneous breaths that the patient takes.

PS ventilation is used to assist spontaneous breaths. The ventilator detects an inspiratory effort by the patient and maintains a preset pressure until the inspiratory flow decreases, usually to 25% of the peak flow. A PS of 5–10 cm $H_2O$ should be equivalent to breathing spontaneously without a tracheal tube and associated ventilator hoses and valves because it compensates for the resistance contributed by these items. A higher PS provides additional support.

Combinations of these modes are also frequently used, especially SIMV with PS in which the patient-generated breaths given between the ventilator-generated breaths are supported with a PS mode. This combination may be

TABLE 87-1 **Commonly Used Ventilatory Modes**

| Patient Contribution | Mode | Trigger | Breath Goal | Delivered Breath |
|---|---|---|---|---|
| None | CMV | Time | Set tidal volume | Ventilator set |
| None or minimal | AC | Time and patient | Set tidal volume | Ventilator set |
| None or minimal | PC | Time | Set pressure | Ventilator set and tidal volume variable |
| Minimal to significant | SIMV | Time and patient | Set tidal volume and patient-generated tidal volume | Ventilator set and patient |
| Moderate to nearly complete | PS | Patient | Set pressure | Assist of patient and tidal volume variable |

*AC,* Assist controlled; *CMV,* controlled mechanical ventilation; *PC,* pressure controlled; *PS,* pressure support; *SIMV,* synchronized intermittent mandatory ventilation.

more comfortable for a patient transitioning from a fully supported mode (AC or PC) to a minimally supported mode (PS alone) than SIMV alone. Newer ventilators provide AC modes with the ability to regulate pressure over the course of the respiratory cycle (i.e., pressure regulated volume control), which provides some of the same benefits of PC ventilation but without the need for deep sedation or paralysis.

### 8. How does pulmonary embolism manifest, and how is it diagnosed and treated?

Pulmonary embolism usually manifest as an acute decrease in $PaO_2$ without infiltrate on radiograph. Common alternative causes for an acute decrease in $PaO_2$ are asthma (even in the absence of wheezing) that is also associated with no infiltrate on radiograph, and pneumonia, usually associated with a new infiltrate on radiograph. In pulmonary embolus, the patient usually is tachycardic. The patient usually is tachycardic and dyspneic and might develop a new supraventricular arrhythmia. Presentation in critically ill ventilated patients is variable, and the diagnosis is usually made by computed tomography angiogram, although lower extremity duplex, ventilation/perfusion scanning, and occasionally pulmonary angiogram may be performed. Treatment consists of anticoagulation. In this setting, intravenous heparinization, guided by partial thromboplastin time monitoring, or subcutaneous low-molecular-weight heparin may be administered. In patients whose risk of bleeding from anticoagulation is high, inferior vena cava filter placement should be considered.

### 9. What criteria are used to determine if extubation should be performed?

Several extubation criteria need to be met. They are best grouped into two categories, general and respiratory-specific.

General criteria are as follows:

1. Patients should be awake, alert, and cooperative with the ability to protect the airway.
2. Patients should be hemodynamically stable with minimal or no vasopressor requirement.
3. Patients should not have a high fever or gross manifestations of sepsis (e.g., rigors).
4. Patients should not require tests (e.g., computed tomography scan or magnetic resonance imaging) or surgical interventions, especially if transportation out of the ICU will be required shortly after the planned extubation.

Respiratory-specific criteria are as follows:

1. Patients should maintain $SpO_2$ >90% on $FiO_2$ ≤0.4 and a minute ventilation requirement <10 L per minute while on mechanical ventilation.
2. Patients should undergo a spontaneous breathing trial for at least 30–60 minutes during which they are placed on a PS of 5–10 cm $H_2O$ or on a T-piece. A grossly successful trial is judged by absence of tachycardia, bradycardia, hypertension, hypotension, distress (e.g., respiratory, agitation), diaphoresis, accessory muscle use, paradoxical breathing, and $SpO_2$ ≤90%. More specifically, a rapid shallow breathing index (RSBI) should be calculated, as follows:

$$\text{RSBI} = \frac{\text{respiratory rate per minute}}{\text{tidal volume in liters}}$$

A value <100 is predictive of success.

An ABG is not required at the end of the spontaneous breathing trial, but it may be helpful, especially in borderline patients whose appearance and RSBI are not completely reassuring. Also, despite best efforts and adherence to these guidelines, approximately 10% of patients in ICUs require reintubation ≤24 hours after extubation.

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CASE 88

# Cardiovascular System

**Paula Trigo, MD • Gregory W. Fischer, MD**

## QUESTIONS

1. What are the etiology and pathophysiology of right ventricular failure?
2. What is the impact of chronic pulmonary arterial hypertension on right ventricular function?
3. How is right ventricular failure diagnosed?
4. Explain the treatment strategies for right ventricular failure.
5. What intraoperative monitoring is recommended for patients with right ventricular failure?
6. What is the prognosis of patients with right ventricular failure?

A 74-year-old woman was admitted for elective mitral valve repair. Her past medical history was significant for hypertension, diabetes, and hyperlipidemia. After an uneventful induction of general anesthesia, a pulmonary artery catheter (PAC) was placed via the right internal jugular vein. Her baseline pulmonary artery pressures were elevated (45/20 mm Hg). All other clinical and laboratory parameters were within normal limits. A transesophageal echocardiogram (TEE) obtained before cardiopulmonary bypass showed prolapse of the posterior mitral valve leaflet (P2 segment) with severe mitral regurgitation and a dilated left ventricle with normal ejection fraction. The right ventricle was mildly dilated and showed mild impairment of function. There was mild tricuspid regurgitation.

After successful surgical repair of the mitral valve, the patient was weaned off cardiopulmonary bypass on moderate inotropic support (epinephrine 0.1 μg/kg per minute). The left ventricular ejection fraction was 40%. There was now moderate right ventricular (RV) dysfunction accompanied by moderate tricuspid regurgitation (Figure 88-1). The pulmonary artery pressures remained elevated (50/22 mm Hg), and central venous pressure was within normal limits (10–12 mm Hg). Cardiac index was 2.0 L/min/m$^2$, and mixed venous saturation was 72%. The patient was transferred to the cardiothoracic intensive care unit (CTICU) for further postoperative management.

The patient was initially stable in the CTICU with good hemodynamic function. The epinephrine infusion was progressively weaned. However, during the first postoperative night, she received large amounts of intravenous fluids in an attempt to improve borderline systemic blood pressure. As a result, the patient's central venous pressure increased from 10 mm Hg to 20 mm Hg, without improvement in systemic blood pressure (85/45 mm Hg). Despite increasing vasoactive support, the clinical status continued to deteriorate, showing signs of progressive low cardiac output and beginning multiorgan failure. The patient's cardiac index and mixed venous oxygen saturation declined to 1.5 L/min/m$^2$ and 45%, respectively. Lactate values progressively increased reaching a maximum of 8 mmol/L. TEE performed on the morning of postoperative day 1 showed a severely depressed right ventricle and severe tricuspid regurgitation. Left ventricular ejection fraction was 50%.

The decision was made to return to the operating room for emergent implantation of a right ventricular assist device (RVAD) (Thoratec Centrimag; Thoratec, Pleasanton, CA). The procedure was uneventful, and the patient returned to the CTICU for further management. Over the course of the next 12 hours, the patient showed a dramatic improvement in hemodynamic status. The signs of early multiorgan failure (i.e., low urine output, elevated transaminases) were reversed. Over the course of the next few days, the RVAD could be progressively weaned, and the patient was taken back to the operating room on postoperative day 7 for RVAD explantation, which proceeded without difficulty. Her trachea was extubated 3 days after RVAD explantation, and she was subsequently weaned off all vasoactive support. The patient was discharged home on postoperative day 37.

### 1. What are the etiology and pathophysiology of right ventricular failure?

RV failure results from any structural or functional disorder that makes the right ventricle unable to eject blood into the pulmonary circulation. The most common etiologies of RV failure are listed in Table 88-1. RV failure is also a prominent feature of various forms of congenital heart disease, such as tetralogy of Fallot, transposition of the great arteries, Ebstein anomaly, and Eisenmenger syndrome. Acute RV failure can also be seen in patients with sickle cell disease during acute chest syndrome.

The pathophysiology of RV failure is complex. It develops from functional impairment of the underlying free wall and interventricular septum. Myocyte fiber orientation is the key to RV performance. The septum is composed of oblique and transverse fibers. This specific

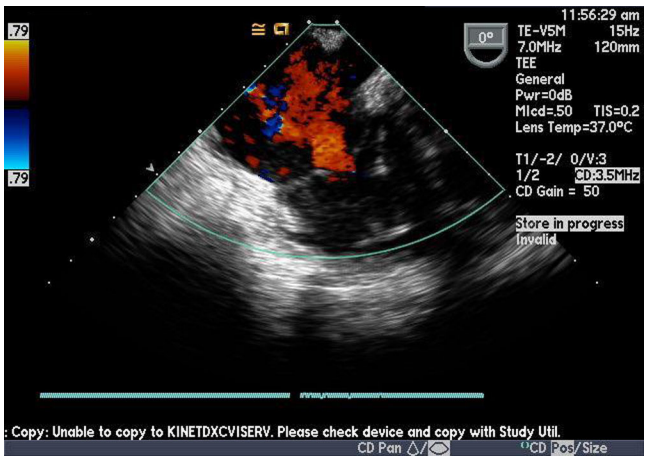


**FIGURE 88-1** ■ Moderate tricuspid regurgitation.

TABLE 88-1 **Etiologies of Right Ventricular Failure**

| |
|---|
| Left ventricular failure |
| Right ventricular ischemia |
| Intrinsic myocardial disease |
| Pressure overload<br>Pulmonary valve stenosis<br>Chronic pulmonary hypertension from any cause |
| Acute pulmonary hypertension<br>Severe left ventricular dysfunction<br>Protamine reaction<br>Hypoxemia<br>Acidosis<br>Tension pneumothorax<br>Acute pulmonary embolism<br>Transfusion-related acute lung injury |
| Sepsis |
| Cardiac tamponade |
| Post–cardiothoracic surgery states<br>Inadequate myocardial protection<br>Myocardial stunning<br>Coronary air embolism |

orientation of fibers is essential for ventricular function and determines the ejection fraction. The concept of the septum as the "biventricular motor" is useful to understand the interdependence of both ventricles. The central role of the septum in RV function provides the basis of treatment for RV infarction and RV dysfunction after cardiac surgery.

In the case presented, the etiology of RV failure is multifactorial. On the one hand, the patient had pulmonary arterial hypertension (PAH) preoperatively. This chronic increase in afterload leads to increased wall tension, which produces increased metabolic demand. Consequently, the ischemic state of the heart during intraoperative cross-clamping is less well tolerated. On the other hand, the function of the left ventricle is frequently depressed immediately after mitral valve repair. The ischemic period and the increased afterload against which the left ventricle now has to function are the main culprits in the reduction of ejection fraction commonly encountered in this patient population.

Weaning the epinephrine, in conjunction with the large amounts of intravenous fluids administered in the CTICU, resulted in acute volume overload, tricuspid annular dilation, and severe tricuspid regurgitation. Once this spiral of RV dilation, severe tricuspid regurgitation, and RV failure was initiated, it could be broken only by rapid implementation of mechanical support.

## 2. What is the impact of chronic pulmonary arterial hypertension on right ventricular function?

In chronic PAH, the right ventricle adapts to increased afterload with concentric hypertrophy and flattening of the interventricular septum; this decreases compliance of the left ventricle leading to diastolic dysfunction. Consequently, diastolic dysfunction is commonly seen in patients with chronic PAH. Plasma levels of brain natriuretic peptide and troponin T correlate well with pulmonary vascular resistance (PVR), and increases in these parameters are associated with increased mortality in patients who have idiopathic PAH.

If PAH remains untreated, and the right ventricle continues to eject blood into a high pulmonary pressure system, the hypertrophied right ventricle deteriorates to dilation and ultimately failure, with a decrease in cardiac output and end-organ perfusion. This reduced perfusion, along with increased myocardial oxygen demand, can result in RV ischemia even in the absence of significant coronary atherosclerotic disease.

## 3. How is right ventricular failure diagnosed?

The clinical presentation of RV failure is fluid retention (i.e., peripheral edema, ascites, and anasarca), low cardiac output that may lead to exercise intolerance or fatigue, and arrhythmias. Cardiac magnetic resonance imaging (MRI) is a useful tool to assess RV structure and function. Some studies show that MRI is the most accurate method of measuring right ventricular ejection fraction (RVEF). Radionuclide-based techniques provide independent assessments of RV function. Cardiac catheterization can measure hemodynamic data and accurately assess PVR. Another test to provide anatomic and functional characteristics is pulmonary angiography.

The most reliable, versatile, and available method to assess RV structure and performance is echocardiography. In two-dimensional echocardiography, RVEF can be measured with Simpson's rule and the area-length method. RV fractional area change is measured in the four-chamber view. In end-stage pulmonary disease, RVEF and RV fractional area change are well correlated. Tricuspid annular plane systolic excursion is another quantitative assessment of RV function, and it is usually

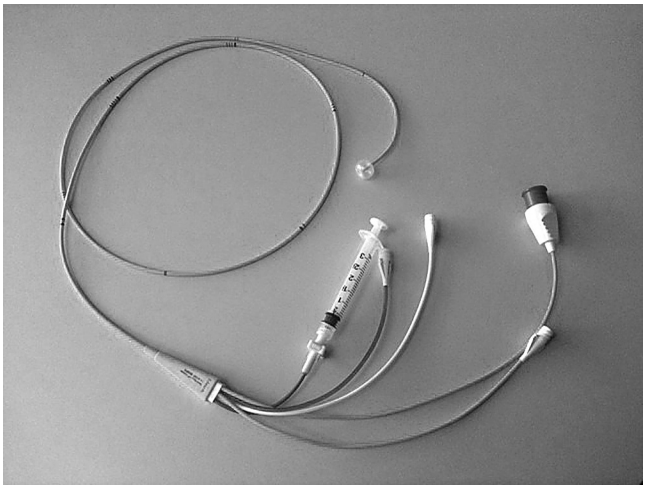

**FIGURE 88-2** ■ Pulmonary Artery Catheter (PAC).

measured with M-mode imaging in the four-chamber view. Tissue Doppler imaging allows quantitative assessment of RV systolic function and measures myocardial velocities. RV myocardial performance index is a useful parameter to assess patients with congenital heart disease and pulmonary hypertension, and it usually increases with RV dysfunction.

PACs in the operating room are a valuable tool to assess hemodynamic status, intravascular volume, and venous oxygen saturation (Figure 88-2). TEE is an alternative monitor to assess cardiac function in the perating room.

## 4. Explain the treatment strategies for right ventricular failure.

The goals for treating RV failure are optimizing preload, decreasing RV afterload, ensuring atrioventricular conduction, and supporting both right and left ventricular contractility. Because bowing of the RV septum toward the left ventricle further compromises left ventricular function, overdistention of the right ventricle needs to be avoided, with a balanced approach of optimizing preload and minimizing RV afterload. Pharmacologic therapy, such as inotropic support with catecholamines, should be the first-line treatment preceding mechanical support by intraaortic balloon pump or RVAD. RV preload must be managed with caution, providing volume but avoiding overdistention of the right ventricle. Normal atrioventricular conduction is essential.

Ventilatory support should be adjusted to ensure adequate oxygenation, avoid hypercarbia and acidosis, and minimize peak inspiratory pressures. Additionally, hypothermia has been associated with increased PVR and should be avoided.

Use of pulmonary vasodilator therapy can be utilized to further decrease PVR. Consequently, pharmacologic agents that reduce pulmonary artery pressures, such as phosphodiesterase inhibitors (e.g., milrinone, inamrinone [previously known as amrinone]), pulmonary vasodilators such as nesiritide and prostaglandin $E_1$ and its analogues (e.g., epoprostenol, iloprost), and nitric oxide, represent good choices. If RV dysfunction persists despite maximal medical therapy, implementation of mechanical support should be considered, such as intraaortic balloon pump or RVAD.

## 5. What intraoperative monitoring is recommended for patients with right ventricular failure?

Placement of a PAC is useful to obtain cardiac outputs by thermodilution and to monitor right-sided (central venous pressure) and left-sided (pulmonary artery diastolic pressure or pulmonary capillary wedge pressure) filling pressures (Table 88-2). After hemodynamic pressures and cardiac outputs are obtained, the clinician can use integrated software to calculate vascular resistances and ventricular stroke work quickly (Table 88-3). These parameters can be used to guide pharmacologic support of the patient (i.e., inotrope vs. vasoconstrictor). Measurement of mixed venous oxygen saturation can be obtained from the pulmonary artery port.

The use of PACs is not exempt from complications, such as arrhythmias, heart block in patients with previous bifascicular block, pneumothorax, air embolism, and endocardial and valvular damage. Very serious complications such as pulmonary infarction, pulmonary artery perforation, and hemorrhage have been reported. A study conducted by Schwann et al. (2011) showed higher morbidity and mortality in patients undergoing coronary artery bypass grafting who received PACs. Multiple investigations in general surgical and intensive care unit patients have failed to show any advantage in using PACs when compared to central venous lines alone. With TEE becoming even more readily available in the general surgical setting, it would not be surprising to see the PAC eventually become extinct in perioperative medicine, making way for TEE-guided fluid, inotropic, or vasopressor therapy.

TABLE 88-2 **Normal Intracardiac Pressures**

| Anatomic Site | Mean (mm Hg) | Range (mm Hg) |
|---|---|---|
| Right atrial pressure | 6 | 1–12 |
| Right ventricle | 25/5 | 15–30/2–8 |
| Systolic PA pressure | 20 | 15–30 |
| Diastolic PA pressure | 10 | 5–15 |
| Mean PA pressure | 15 | 10–20 |
| PCWP | 10 | 5–15 |
| Left atrial pressure | 10 | 4–15 |
| LVEDP | 10 | 4–15 |
| Left ventricular systolic pressure | 120 | 90–140 |

*LVEDP,* Left ventricular end diastolic pressure; *PA,* pulmonary artery; *PCWP,* pulmonary capillary wedge pressure.

TABLE 88-3 **Pulmonary Artery Catheter–Derived Hemodynamic Parameters**

| | |
|---|---|
| Cardiac output (CO) | 4–6 L/min |
| Cardiac index (CI) = CO/BSA | 2.8–4.2 L/min/$m^2$ |
| Stroke volume (SV) | 50–100 mL |
| Stroke index (SI = SV/BSA) | 30–65 mL/$m^2$ |
| **Left ventricular stroke work index (LVSWI)** LVSWI = 1.36 × (MAP − PCWP) × SI/100 | 45–60 g-m/$m^2$ |
| **Right ventricular stroke work index (RVSWI)** RVSWI = 1.36 × (MPAP − CVP) × SI/100 | 5–10 g-m/$m^2$ |
| **Systemic vascular resistance (SVR)** SVR = (MAP − CVP) × 80/CO | 900–1400 dyne•sec•$cm^{-5}$ |
| **Systemic vascular resistance index (SVRI)** SVRI = (MAP − CVP) × 80/CI | 1500–2400 dyne•sec•$cm^{-5}$/$m^2$ |
| **Pulmonary vascular resistance (PVR)** PVR = (MPAP − PCWP) × 80/CO | 150–250 dyne•sec•$cm^{-5}$ |
| **Pulmonary vascular resistance index (PVRI)** PVRI = (MPAP − PCWP) × 80/CI | 250–400 dyne•sec•$cm^{-5}$/$m^2$ |

*BSA,* Body surface area; *CI,* cardiac index; *CO,* cardiac output; *CVP,* central venous pressure; *LVSWI,* left ventricular stroke work index; *MAP,* mean arterial pressure; *MPAP,* mean pulmonary arterial pressure; *PCWP,* pulmonary capillary wedge pressure; *PVR,* pulmonary vascular resistance; *PVRI,* pulmonary vascular resistance index; *RVSWI,* right ventricular stroke work index; *SI,* stroke index; *SV,* stroke volume; *SVR,* systemic vascular resistance; *SVRI,* systemic vascular resistance index.

## 6. What is the prognosis of patients with right ventricular failure?

RV failure is associated with increased morbidity and mortality. There are select markers of RV failure associated with prognosis, such as hemodynamics (e.g., right atrial pressure, cardiac index), systolic performance indices (e.g., RVEF, RV fractional area change, tricuspid annular plane systolic excursion), and diastolic filling profiles. However, most patients who have an initial hemodynamic insult and subsequently survive have spontaneous early hemodynamic recovery and late normalization of RV function. More recent strategies aimed at using long-term ventricular assist devices either as primary therapy or as bridge to recovery have significantly improved survival rates.

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CASE 89

# Sepsis and Multisystem Organ Dysfunction Syndrome

**Jordan Brand, MD**

QUESTIONS

1. Distinguish among systemic inflammatory response syndrome, sepsis, severe sepsis, septic shock, and multisystem organ dysfunction syndrome.
2. What are the pathophysiology and manifestations of sepsis-related organ dysfunction?
3. How are sepsis and multisystem organ dysfunction syndrome treated?
4. How is catheter-related sepsis evaluated, managed, and prevented?
5. What patient subgroups may require different therapeutic approaches?

A 57-year-old man with a history of diabetes mellitus and *Helicobacter pylori* infection is admitted to the intensive care unit after exploratory laparotomy for perforated duodenal ulcer. Vital signs are heart rate of 113 beats per minute, blood pressure of 83/40 mm Hg, respiratory rate of 18 breaths per minute, temperature of 38.9° C, and oxygen saturation by pulse oximetry ($SpO_2$) of 98%. He subsequently remains hypotensive despite fluid resuscitation and develops oliguria and coagulopathy.

## 1. Distinguish among systemic inflammatory response syndrome, sepsis, severe sepsis, septic shock, and multisystem organ dysfunction syndrome.

Sepsis has been recognized as a clinical syndrome for many years. Systemic inflammatory response syndrome (SIRS) is a more recent development, defined by the American College of Chest Physicians in 1992. Both conditions are recognized as part of a continuum of disease processes that involve similar pathophysiologic mechanisms. SIRS is defined by four cardinal criteria that are indicators of inflammation (Table 89-1).

Although SIRS is frequently associated with infection, it can be caused by many noninfectious etiologies, such as pancreatitis, trauma, surgery, cardiopulmonary bypass, burns, anaphylaxis, drugs, or aortic dissection. If SIRS is associated with positive blood cultures or other conclusive indicators of infection, it is referred to as sepsis. Severe sepsis indicates that the patient has developed organ dysfunction secondary to sepsis. In septic shock, a closely related entity, sepsis results in hypoperfusion or arterial hypotension or both. Multisystem organ dysfunction syndrome (MODS) indicates the dysfunction of two or more systems such that intervention is needed to maintain homeostasis. MODS can result from sepsis but can also be due to other conditions, such as noninfectious SIRS or cardiogenic shock. Although these conditions share many features, recent years have seen an effort to standardize and clarify their nomenclature.

## 2. What are the pathophysiology and manifestations of sepsis-related organ dysfunction?

Numerous theories have been proposed to explain the cascade of events that results in sepsis. Most of these theories share the general concept that sepsis is the result of an initial infectious insult. The infection results in immune activation, with subsequent detrimental hyperactivity of the immune system. The initial insult is most commonly a localized or blood-borne bacterial infection. The cell membranes of gram-negative bacteria contain various elements that may initiate strong immune responses, such as lipopolysaccharide, thought to be the main factor in gram-negative sepsis. Gram-positive bacteria do not contain lipopolysaccharides, and much of their pathogenicity is thought to be due to exotoxins, which are immunogenic toxins secreted by bacteria.

Numerous proinflammatory cytokines are released in response to these stimuli, such as interleukin (IL)-1, IL-2, IL-6, and IL-10; interferon-γ, and tumor necrosis factor (TNF)-α. TNF-α creates a positive feedback loop, in which it acts to increase its own production and the production of other inflammatory mediators. This process is initially beneficial as a response to bacterial invasion but can become deleterious. Cytokine production results in activation of immune cells as well as complement, which can cause apoptosis and endothelial cell dysfunction. Activated endothelial cells express molecules, such as tissue factor, that are prothrombotic. The result is microvascular thrombosis and ischemia that is thought to underlie the development of organ dysfunction. In addition, endothelial cells produce increased levels of nitric oxide

**TABLE 89-1 Diagnostic Criteria for Systemic Inflammatory Response Syndrome**

| Heart Rate | Ventilation | Temperature | WBC |
|---|---|---|---|
| >90 bpm | RR>20 bpm *or* $pCO_2$ <30 mm Hg | >38° C *or* <36° C | >12,000 *or* <4000 *or* >10% bands |

*bpm,* beats per minute; *$pCO_2$,* Carbon oxide tension; *RR*, respiratory rate; *WBC,* white blood cells.

(NO), which functions as a vasodilator, resulting in hypotension.

Almost any infection can result in a septic state. In some cases, it is thought that if a patient's gastrointestinal mucosa is disrupted via hypoperfusion or other trauma, endogenous gut flora may cross the mucosal barrier and cause bacteremia and sepsis. This is known as the gut translocation theory of sepsis. It may be a particular problem in patients who are already immunocompromised, as well as patients who are hypotensive from shock and patients with gastrointestinal pathology, such as intestinal obstruction or cancer. Although the process of translocation occurs in many situations outside critical illness and may be part of normal immune surveillance, it has been suggested by numerous studies that such translocation increases septic mortality. It is likely that after an initial infection or other injury that causes decreased visceral perfusion, bacteria from the gut may cause a second insult, which then results in worse outcomes. Enteral nutrition has been advocated as a way of maintaining mucosal integrity and preventing translocation; however, this has not been conclusively proven.

Organ dysfunction can take many forms. Myocardial dysfunction is common, especially after the initial cytokine storm. It appears to be due to circulating myocardial depressant factors rather than ischemia. In the initial septic period, decreased systemic vascular resistance (SVR) and venodilation produce a hyperdynamic, high-output state. During the first few days of a septic episode, this hyperdynamic state may transition to both systolic and diastolic dysfunction. Pulmonary hypertension secondary to lung injury may exacerbate right heart failure.

Most septic states are characterized by vasodilatation and lack of appropriate response to vasoconstrictors owing to multiple factors, including activation of adenosine triphosphate–sensitive potassium channels in smooth muscle, increased production of NO, and deficiency of arginine vasopressin (AVP). This deficiency is part of the rationale for administration of exogenous AVP in septic shock. Acidosis can decrease the responsiveness of vasculature to vasopressors, exacerbating the problem.

The lung is one of the most frequently injured organs in sepsis. Under the influence of cytokines, endothelial cells in the lung upregulate adhesion molecules and chemoattractants, resulting in infiltration of lung parenchyma and alveolar spaces by activated neutrophils. These neutrophils release various inflammatory mediators that damage pneumocytes and allow leakage of fluid and proteinaceous debris into alveolar spaces. This series of events inactivates residual surfactant, causing impaired gas diffusion, atelectasis, and ventilation-perfusion mismatch. The process is termed acute lung injury (ALI) or acute respiratory distress syndrome (ARDS) when more severe (Table 89-2). High inspired oxygen concentrations and ventilator pressures necessary to maintain oxygenation may perpetuate inflammation. This injury can affect the pulmonary vasculature and cause pulmonary hypertension, which may persist after hypoxia has resolved.

Renal injury secondary to sepsis is also quite common. Systemic vasodilatation and hypotension can result in direct renal ischemia. In the presence of volume depletion owing to vasodilation, the kidney tries to maintain the glomerular filtration rate (GFR) by releasing substances that stimulate intrarenal vasoconstriction, particularly constriction of the efferent arteriole. Eventually, these compensatory mechanisms may fail, resulting in decreased GFR. Endothelial injury can also cause intrarenal microvascular dysfunction and thrombosis. Patients with renal dysfunction of sepsis can exhibit normal urine output, oliguria, or anuria and may have different degrees of impaired solute filtration. One well-validated framework for quantifying acute kidney injury in sepsis comprises the RIFLE criteria (Table 89-3).

The liver may exhibit several abnormalities in sepsis. Liver macrophages, known as Kupffer cells, can participate in the cytokine response to an inflammatory stimulus. Liver endothelium is also susceptible to involvement in the overall physiologic state. Hepatocytes decrease production of some proteins, such as prealbumin and albumin, and may increase production of proinflammatory proteins, such as C-reactive protein. Hypotension may result in "shock liver," which is characterized by elevations in transaminases and decreased synthetic function, with resultant hypoalbuminemia and coagulopathy. As the initial insult resolves, increases in alkaline phosphatase and bilirubin are frequently seen. Even without this shock state, sepsis can result in biliary stasis, sometimes with consequent biliary sludging and acalculous cholecystitis.

**TABLE 89-2 Clinical Criteria for Acute Lung Injury and Acute Respiratory Distress Syndrome**

| Syndrome | ALI | ARDS |
|---|---|---|
| Pulmonary infiltrates | Bilateral and heterogeneous | Bilateral and heterogeneous |
| PAOP | <18 mm Hg | <18 mm Hg |
| $PaO_2$:$FiO_2$ ratio | <300 | <200 |

*ALI,* Acute lung injury; *ARDS,* acute respiratory distress syndrome; *$PaO_2$:$FiO_2$,* arterial oxygen tension:fraction of inspired oxygen; *PAOP,* pulmonary arterial occlusion pressure.

TABLE 89-3 **RIFLE Classification of Acute Kidney Injury**

| CLASS | Glomecular Filtration Rate | Urine Output |
|---|---|---|
| **R**isk | Decreased by ≥25%<br>*or*<br>Baseline SCr increased × 1.5 | <0.5 mL/kg/hour for ≥6 hours |
| **I**njury | Decreased by ≥50%<br>*or*<br>Baseline SCr increased ×2 | <0.5 mL/kg/hour for ≥12 hours |
| **F**ailure | Decreased ≥75%<br>*or*<br>Baseline SCr increased ×3<br>*or*<br>SCr >4 mg/dL with acute increase of 0.5 mg/dL | <0.3 mL/kg/hour for ≥24 hours<br>*or*<br>Anuria for ≥12 hours |
| **L**oss | Complete loss of kidney function >4 weeks | |
| **E**SRD | Complete loss of kidney function >3 months | |

*ESRD*, End-stage renal disease; *SCr,* serum creatinine.

Derangements of the hematologic system from sepsis include direct bone marrow suppression as well as effects of microvascular thrombosis and consumptive coagulopathy. The most extreme form of consumptive coagulopathy is disseminated intravascular coagulation (DIC). DIC frequently results in diffuse thrombosis, hypofibrinogenemia, coagulopathy, increased levels of fibrin degradation products, and concurrent abnormal thrombosis and bleeding. Changes in iron metabolism can cause inadequate hematopoiesis and anemia of chronic disease. Microvascular thrombosis may cause hemolysis of red blood cells, resulting in microangiopathic hemolytic anemia. White blood cell count may be high or low, depending on the adequacy of bone marrow function. Leukopenia is thought to be a negative prognostic sign. Thrombocytopenia may result from bone marrow suppression as well as abnormal platelet activation and adhesion.

Both the central nervous system (CNS) and the peripheral nervous system are frequently dysfunctional in sepsis. CNS abnormalities may include encephalopathy, which is typically recognized by altered level of consciousness and a symmetric neurologic examination. In contrast to other metabolic encephalopathies, asterixis, tremor, and myoclonus may be absent. Septic encephalopathy can manifest as delirium, which is very common and is an independent predictor of poor outcome. Involvement of the peripheral nervous system owing to hypoperfusion, cytokines, and deconditioning causes partial denervation and myoneuropathy, which results in prolonged weakness, ventilator dependence, and substantial morbidity in survivors of sepsis.

## 3. How are sepsis and multisystem organ dysfunction syndrome treated?

There are four primary components to treatment of sepsis and MODS.

### *Control the Initiating Infection*

Infection control consists of both source control and antimicrobial therapy. If the source of infection is unclear, a standard work-up should include cultures of blood, urine, and sputum; a chest x-ray; and possibly a computed tomography scan. Source control may consist of abscess drainage, débridement of infected tissue, or removal of infected implants or hardware. Although it can be desirable to perform surgery as early as possible, in some cases, definitive therapy may be delayed based on the patient's acute instability. Percutaneous drainage or other nonsurgical therapies may be selected initially to reduce the stress of the procedure on an already compromised patient. Definitive surgical management, when necessary, can be delayed until the patient's condition has improved.

In addition to source control, appropriate antimicrobial therapy is essential to limiting morbidity and mortality. Although blood cultures (as well as other appropriate cultures) should be collected before administering antibiotics, administration of antibiotics should never be delayed to fulfill this goal. Early treatment of infection facilitates termination of the immune response before it grows out of control. Patients in whom antibiotic administration is delayed have higher mortality rates, and these delays appear to be one of the most important predictors of mortality in critically ill patients. Appropriate antibiotics should have broad gram-positive and gram-negative coverage and should be tailored to cover any known or suspected source of infection.

### *Appropriate Resuscitation and Maintenance of Organ Perfusion*

Early aggressive resuscitation to minimize organ dysfunction is one of the best-accepted therapies for sepsis. Early resuscitation with specific goals for central venous oxygen saturation, blood transfusions, inotropes, sedation, and mechanical ventilation can significantly decrease mortality in early sepsis compared with an approach based solely on vital signs and urine output. Although this specific approach is not universally accepted, many influential groups, such as the Surviving Sepsis Campaign, recommend it. Most critical care clinicians agree that early use of targeted resuscitation to maintain organ perfusion can be a helpful approach. Much debate centers on which measurements and targets should be used. Arterial pulse pressure analysis, echocardiography, and esophageal Doppler may be more accurate than older hemodynamic indicators such as central venous pressure (CVP).

Regardless of the method chosen, the central question to be answered is whether a patient's cardiac output and perfusion are adequate, and, if not, whether the patient would benefit from volume loading, inotropes, or both. If a patient is judged to be volume-depleted (or volume-responsive, depending on the measurements used), the first step is usually fluid resuscitation. Colloid or crystalloid may be used; colloid is more expensive, and there is little conclusive evidence that it is better than crystalloid.

If the patient remains malperfused but is no longer volume-responsive, inotropes are indicated. Traditionally, dopamine and dobutamine have been used, although epinephrine and milrinone may be desirable in certain circumstances.

Patients with septic shock may remain hypotensive even after circulating volume and cardiac output are restored. Certain tissue beds, such as the brain and kidney, tend to be more pressure-dependent and may experience ischemia in this circumstance. It may be necessary to administer vasopressor agents to maintain arterial pressure. Phenylephrine may be used, especially if the patient has no central access, because it is less likely to cause tissue ischemia if it extravasates. If central access is available, norepinephrine is considered first-line therapy because it is a more potent vasoconstrictor and has some β-adrenergic activity, making it a more "physiologic" choice. More recently, vasopressin has become popular because many septic patients quickly become AVP-depleted and are expected to benefit from "hormone replacement." AVP may also have some benefits over norepinephrine because it seems to increase urine output and may lead to improved outcomes in patients with less severe sepsis. Although dopamine traditionally has been a first-line pressor and inotrope in sepsis and other shock states, it can cause tachyarrhythmias. Although dopamine is believed by many to preserve renal function in shock, a large body of literature refutes this idea.

### *Prophylaxis to Prevent Complications*

Many patients with sepsis die of complications that can be avoided with appropriate prophylactic measures. Because of hypotension and gut hypoperfusion, endogenous defenses against gastric acidity may fail resulting in peptic ulcers and upper gastrointestinal bleeding. Histamine-2 blockers and proton pump inhibitors are preventive measures. Sepsis is a hypercoagulable state, and even patients with mild thrombocytopenia and coagulopathy may be prone to thrombosis, primarily venous thrombosis. Thromboprophylaxis with subcutaneous unfractionated or low-molecular-weight heparin and sequential compression devices may prevent morbidity and mortality. Despite the lifesaving nature of mechanical ventilation, it can leave patients vulnerable to ventilator-associated pneumonia (VAP), worsen hemodynamics, and may necessitate additional sedation. Placing patients in a semirecumbent position, which reduces microaspiration and incidence of VAP, and routine use of spontaneous breathing trials and sedation interruption, which can lessen the duration of mechanical ventilation, may reduce these risks. Much evidence suggests that prevention of severe hyperglycemia using insulin infusions prevents infectious and neuromuscular complications. However, it is unclear how tight glycemic control must be to benefit patients; this is an area of much ongoing research.

### *Support and Replacement of Organ Function*

Despite all efforts to prevent it, many patients go on to develop organ dysfunction as a result of sepsis. Besides the aforementioned techniques to maintain organ perfusion and reduce complications, support or replacement of organ function is sometimes necessary. Most commonly, this support takes the form of mechanical ventilation or renal replacement therapy (RRT). If mechanical ventilation is necessary, the aforementioned prophylactic measures should be taken to reduce VAP and decrease time spent on the ventilator. In patients developing ALI/ARDS, a ventilation strategy using lower tidal volumes (6 mL/kg of ideal body weight) has been shown to reduce mortality. Use of higher levels of positive end expiratory pressure and recruitment maneuvers to prevent atelectasis may also be beneficial. Early use of neuromuscular blocking agents has been shown more recently to reduce mortality in ARDS, but because these drugs can have significant undesirable effects (i.e., myopathies, neuropathies, alterations of the neuromuscular junction), it may be too early to adopt this treatment broadly.

RRT can be lifesaving in cases of refractory hyperkalemia or other electrolyte abnormalities. It is also useful to treat severe acidosis, volume overload, uremia, or drug intoxication. Despite some enthusiasm for its use to modulate cytokine response and alter the course of sepsis, trials for this purpose have been disappointing. RRT may be performed continuously or intermittently. Both approaches provide comparable outcomes, although continuous therapies seem to be associated with slightly better hemodynamic stability in critically ill patients. However, intermittent therapy has benefits in terms of catheter maintenance and resource use. With continuous therapy, hemofiltration or hemodialysis may be selected; this decision frequently depends on local standards.

Replacement of other vital organ functions is not easily accomplished. Blood products and growth factors are available to replace inadequate erythropoiesis, thrombopoiesis, and leukocyte production. However, there are negative effects of blood transfusions, such as immunosuppression, transfusion reactions, and transfusion-associated lung injury. Although there have been some successes with liver replacement therapies for acute liver failure, there is little experience with sepsis-related liver failure. Critically ill patients may exhibit relative adrenal insufficiency. Although many experts endorse corticosteroid therapy in these circumstances, it is still uncertain whether such therapy improves morbidity and mortality.

## 4. How is catheter-related sepsis evaluated, managed, and prevented?

One particular infectious process that bears special mention is central line–associated bloodstream infection (CLABSI). CLABSI is an important cause of morbidity and mortality in the intensive care unit and may be responsible for $2.3 billion per year in excess healthcare costs.

When an indwelling catheter is placed, bacteria can colonize the catheter tip via intraluminal or extraluminal routes. The extraluminal route seems to be more important in the initial period after placement, before the catheter tract can heal and reepithelialize. Conversely, the intraluminal route becomes more important the longer the catheter remains in place.

Catheter-related infection should be suspected in any patient with bacteremia or sepsis and an indwelling catheter. This is especially true if the catheter site appears indurated or purulent, although these are unreliable predictors of infection.

When a catheter-related bloodstream infection is suspected, blood cultures should be drawn from another (preferable peripheral) site to prove bacteremia definitively. If cultures are positive, the culprit line should be removed and, if necessary, replaced at another site. Bacteremia, despite appropriate antimicrobial therapy, is particularly suspicious for catheter-related infection. If suspicion is very high, a potentially infected line should be removed even in the absence of definitive culture evidence. Antimicrobial medications are indicated and should broadly cover common pathogens, such as staphylococci, enterococci, and gram-negative bacilli.

CLABSI is increasingly being documented as a sentinel event. Much research has focused on the best ways to prevent catheter colonization and infection. Several approaches have met with success (Box 89-1). Consequently, these practices are implemented widely throughout the health care system. Although catheter removal is a useful technique to prevent infection, the strategy of routine catheter exchange has repeatedly failed to decrease infection rates. This approach may lead to increased rates of mechanical complications, such as thrombosis and pneumothorax.

### 5. What patient subgroups may require different therapeutic approaches?

Any patient population that is not expected to respond to therapeutic measures in a predictable fashion may require special consideration. For example, the usual early goal-directed resuscitation for patients with sepsis gives specific targets for CVP to guide initial fluid loading. However, in patients with heart failure, particularly right heart failure with or without pulmonary hypertension, this may be a deleterious strategy. In a patient with right heart failure, this approach may lead to overdistention of the right ventricle, shifting the interventricular septum to the left, decreasing left ventricular preload and compliance, and resulting in impaired myocardial performance. Such patients may warrant a more balanced approach that includes earlier use of inotropes and the addition of pulmonary vasodilators such as inhaled NO. In extreme cases of combined septic shock and heart failure, the addition of short-term cardiac support, such as an intraaortic balloon pump, may be extremely helpful. Patients with renal failure may warrant more careful volume management and may require early dialysis. However, this does not mean that fluid resuscitation should be withheld.

Likewise, patients with impaired immune systems often warrant more careful consideration. They may not show the usual clinical indicators of infection, especially if they are receiving corticosteroids, and generally require broader antimicrobial coverage. The range of pathogens that may cause a severe systemic response in these individuals is much greater than in immunocompetent patients. Fungi, mycobacteria, and viruses must be considered as targets for therapy. Also, it may be desirable to minimize the use of indwelling catheters and other devices, even more than is the standard of care, because of the decreased ability of immunosuppressed patients to resist invasion by environmental microorganisms.

Lastly, in patients who have a poor prognosis, such as patients with advanced age or metastatic cancer, it may be inappropriate to proceed with aggressive care. In these cases, careful attention should be paid to the patient's wishes before falling ill. Depending on the patient's desires and the likelihood of recovery, it may be better to make a transition to palliative care rather than engage in interventions that are unlikely to improve length or quality of life. Such decisions should always be made with the participation of the patient's family members and, in select cases, a hospital ethics committee.

**BOX 89-1 Evidence-Based Practices to Reduce Catheter-Related Infection**

- Adherence to checklists and use of standard protocols
- Staff education and training
- Use of catheter materials and coatings that reduce bacterial adhesion and growth
- Preference for subclavian vein over other sites
- Good hand hygiene
- Use of chlorhexidine-alcohol preparation solution
- Removal of catheters when no longer needed

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CASE 90

# Renal System

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## QUESTIONS

1. How is acute kidney injury defined?
2. What are the incidence and outcome of acute kidney injury in the intensive care unit?
3. Explain the pathophysiology of acute kidney injury.
4. How is the etiology of acute kidney injury determined in the intensive care unit?
5. Discuss acid-base balance regulation, and identify acid-base disturbances resulting from acute kidney injury.
6. What is contrast-induced nephropathy?
7. Describe the pathogenesis of contrast-induced nephropathy.
8. Identify the risk factors for and probability of developing contrast-induced nephropathy.
9. What are the options for preventing contrast-induced nephropathy?
10. What are the indications for dialysis in the intensive care unit?
11. What are the options for renal replacement therapy?
12. Discuss problems encountered with renal replacement therapy.
13. How is the most appropriate renal replacement therapy selected?

A 62-year-old man presented for emergency repair of a type A dissecting ascending aortic aneurysm. He had a history of hypertension, diabetes, and hyperlipidemia. In the emergency department, he complained of acute onset of chest pain. The work-up included a computed tomography scan with intravenous contrast agent administration. On postoperative day 1 in the cardiothoracic intensive care unit, his creatinine level increased twofold, with a decrease in urine output and a metabolic acidosis.

### 1. How is acute renal injury defined?

Acute renal failure (ARF) is the sudden development of renal insufficiency that results in the retention of urea and other nitrogenous waste products as well as dysregulation of extracellular volume and electrolytes. It is also known as acute kidney injury (AKI). AKI encompasses the entire range of renal dysfunction, from minor to requiring renal replacement therapy. The measurement of serum creatinine, which measures glomerular filtration rate (GFR), has been used to evaluate kidney function loss. The Acute Dialysis Quality Initiative developed criteria for different stages of renal injury. The RIFLE criteria consist of three graded levels of risk, injury, and failure, which are based on the magnitude of elevation of serum creatinine and urine output (Table 90-1). There are also two outcome measures, loss of renal function and end-stage renal disease.

The RIFLE scoring system has some disadvantages. The RIFLE criteria do not have a time component for creatinine levels; this does not allow for analysis of renal function as a dynamic process. For example, a doubling of creatinine in 24 hours is more significant than if creatinine doubles in 3 days, but this is not reflected within the RIFLE criteria. Change in urine output is generally the most important criterion used in the intensive care unit (ICU) to determine renal dysfunction because it can more rapidly help identify risk.

The Acute Kidney Injury Network (AKIN), recognizing the importance of time course to kidney injury, modified the RIFLE criteria (Table 90-2). Their diagnostic criteria for AKI include an abrupt (≤48 hours) reduction in kidney function defined as one of the following:

- Absolute increase in serum creatinine of ≥0.3 mg/dL
- Increase in serum creatinine of ≥50% (1.5-fold from baseline)
- Reduction in urine output (documented urine output of <0.5 mL/kg/hour for ≥6 hours)

Risk from the RIFLE criteria is equivalent to stage 1 of the AKIN classification system, injury is equivalent to stage 2, and failure is equivalent to stage 3. Loss of renal function and end-stage renal disease were removed from the AKIN classification. Both criteria are based on creatinine as a marker for renal injury, which is a routine blood test. However, there are limitations to the usefulness of creatinine as a marker because many factors affect creatinine levels, including body size, catabolic state, rhabdomyolysis, dilutional effects, and drugs. Blood urea nitrogen (BUN) has also been used as a marker of renal function, but it too is affected by various factors, including excessive protein intake, protein catabolism, total parenteral nutrition, acute myocardial infarction, gastrointestinal bleeding, steroid administration, and dehydration.

New markers of AKI are under investigation. Cystatin C is an endogenous cysteine-proteinase inhibitor that is

TABLE 90-1 **RIFLE Classification System**

| Class | GFR | UO |
|---|---|---|
| **R**isk | Decreased by ≥25%<br>*or*<br>Baseline SCr increased × 1.5 | <0.5 mL/kg/hour ≥6 hours |
| **I**njury | Decreased by ≥50%<br>*or*<br>Baseline SCr increased × 2 | <0.5mL/kg/hour ≥12 hours |
| **F**ailure | Decreased by ≥75%<br>*or*<br>Baseline SCr × 3<br>*or*<br>SCr >4 mg/dL with acute increase of 0.5 mg/dL | <0.3 mL/kg/hour ≥24 hours<br>*or*<br>Anuria ≥12 hours |
| **L**oss | Complete loss of kidney function >4 weeks | |
| **E**SRD | Complete loss of kidney function >3 months | |

*ESRD,* End-stage renal disease; *GFR,* glomerular filtration rate; *SCr,* serum creatinine; *UO,* urine output.
Deterioration of renal function should be both sudden (within 1-7 days) and sustained (24 hours).

TABLE 90-2 **Acute Kidney Injury Network (AKIN) Classification or Staging System for Acute Kidney Injury**

| Stage | SCr | UO |
|---|---|---|
| 1 | Increase ≥0.3 mg/dL<br>*or*<br>Baseline increase ≥150% to 200% (1.5–2 fold) | <0.5 mL/kg/hour ≥6 hours |
| 2 | Baseline increase >200% to 300% (>2 to 3 fold) | <0.5 mL/kg/hour ≥12 hours |
| 3 | Baseline increase >300% (>3 fold)<br>*or*<br>≥4 mg/dL with acute increase of at least 0.5 mg/dL<br>*or*<br>Initiation of renal replacement therapy | <0.3 mL/kg/hour ≥24 hours<br>*or*<br>Anuria for ≥12 hours |

*SCr,* Serum creatinine; *UO,* urine output.
Deterioration of renal function must occur within 48 hours.

produced by all cells. In contrast to creatinine, cystatin C is filtered and not secreted across the glomerulus. It has been shown to increase faster than creatinine in patients with AKI. Another marker, urinary neutrophil gelatinase, has been shown to be one of the earliest proteins induced in the kidney after ischemic or nephrotoxic insult. More studies are needed to test the specificity and sensitivity of these markers.

## 2. What are the incidence and outcome of acute kidney injury in the intensive care unit?

AKI occurs with significant frequency in the hospital and especially in the ICU. The incidence of AKI ranges from 1%–36% of critically ill patients. Risk factors for AKI are well established and include age, sepsis, cardiac surgery, intravenous contrast media, diabetes, rhabdomyolysis, preexisting renal disease, hypovolemia, and shock. There are a few settings that are very closely associated with ICU-acquired renal failure (Table 90-3). Based on the RIFLE criteria, hospital mortality among ICU patients is as follows:

- 5%–10% in patients without renal dysfunction
- 9%–27% in patients at risk
- 11%–30% in patients with renal injury
- 26%–40% in patients with renal failure

TABLE 90-3 **Conditions Associated with Acquired Renal Failure in the Intensive Care Unit**

| Condition | Incidence (%) |
|---|---|
| Multiorgan failure | 30–75 |
| Sepsis | 30–50 |
| Drugs | 20–40 |
| Postoperative state | 15–30 |
| Impaired cardiac output/hypovolemia | 15–30 |

## 3. Explain the pathophysiology of acute kidney injury.

Blood is delivered to the kidneys and proceeds through the glomerulus, where it is filtered. The filtrate migrates to tubules where reabsorption and secretion take place and is eliminated as formed urine through the ureters, bladder, and urethra. The first steps to diagnosing renal failure come from determining if the etiology is prerenal (reduction in renal perfusion), renal (disorder of renal vasculature, glomeruli, interstitium, or tubules), or postrenal (obstruction of urine flow). In the ICU, renal failure is 17%–36% prerenal, 63%–81% renal, and 1%–4% postrenal. Many cases of renal failure have more than one cause, especially in critically ill patients.

Prerenal AKI is caused by extracellular fluid loss, extracellular fluid sequestration, or significantly reduced cardiac output. It is readily reversible if diagnosed and treated early. Kidneys compensate for reduced GFR by reabsorption of salt and water to increase circulating blood volume. Fluid resuscitation is the treatment of choice for AKI caused by renal hypoperfusion secondary to hypovolemia. Whether crystalloids or colloids are better for fluid resuscitation is still debatable. The essential principle is intravascular volume expansion to provide adequate preload and renal perfusion. Low cardiac output and hypotensive states resulting in prerenal AKI are treated with vasopressors and inotropes that help increase mean arterial pressure and cardiac output, ensuring optimal renal perfusion. Drugs that can cause prerenal AKI are norepinephrine, angiotensin II, endothelin, and prostaglandins that cause afferent arteriolar constriction, which reduces glomerular capillary hydrostatic pressure and glomerular ultrafiltrate. Diuretics cause depletion of

extracellular fluid volume. Nonsteroidal antiinflammatory drugs (NSAIDs) are cyclooxygenase inhibitors that impair renal vasodilation, resulting in increased renal vascular tone. This form of ARF is easily reversible if diagnosed and treated early. If treatment is not instituted early, NSAIDs can result in decreased renal perfusion to renal tubular epithelial cells causing acute tubular necrosis (ATN). Finally, angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) reduce renal perfusion pressure and dilate efferent arterioles. This combination of effects results in reduced glomerular capillary filtration pressure and causes ARF.

Postrenal azotemia is an unusual cause, especially in the ICU, and is easy to rule out using renal ultrasound. The most common etiology in men is bladder outlet obstruction from prostate disease. Obstruction to urine flow can occur within the kidneys when distal tubules become occluded with crystals (e.g., uric acid). Bilateral ureteral obstruction is rare but can be caused from extensive intraabdominal cancer or retroperitoneal fibrosis. Occluded Foley catheters can result in postrenal AKI. Blocked urine flow increases intratubular pressure so that net glomerular filtration pressure is decreased; this results in either severely reduced or stopped glomerular filtration.

Intrarenal renal failure is the likely diagnosis when prerenal and postrenal failures have been excluded. The most common renal cause of AKI is ATN. ATN is primarily due to renal ischemia secondary to renal hypoperfusion. The degree of ischemia required to cause ATN is variable. Ischemic ATN results in depletion of adenosine triphosphate (ATP) causing renal tubular cell death. Other causes of ATN include nephrotoxins and pigmenturia (hemoglobinuria, myoglobinuria). Two of the most commonly encountered nephrotoxins are aminoglycoside antibiotics and radiocontrast media. Pigmented induced AKI is caused by tubular obstruction, direct proximal tubular cell injury, and vasoconstriction. Protection from pigment-associated AKI includes maintenance of adequate extracellular fluid volume, renal perfusion, and urinary alkalization (increases solubility of hemoglobin and myoglobin to reduce cast formation).

Other renal causes of AKI that are less prevalent in the ICU include renal vascular disorders of both large and small vessels and acute glomerulonephritis. Vascular disorders include thrombotic occlusion, emboli, thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, and vasculitis. These disorders can reduce blood flow to the kidneys and their filtering unit.

## 4. How is the etiology of acute kidney injury determined in the intensive care unit?

Assessment of AKI and oliguria starts with placement of a urinary drainage catheter to trend hourly urine output. Cardiac hemodynamics and volume status are assessed for optimization of preload and renal perfusion. An echocardiogram may be considered to assess ventricular function. Nephrotoxic drugs (e.g., ACE inhibitors, ARBs, NSAIDs, certain antibiotics) are eliminated. Commonly administered antibiotics that can cause AKI include aminoglycosides, amphotericin B, β-lactams, penicillins, rifampin, and vancomycin. Laboratory studies including BUN, creatinine, electrolytes, and osmolality should be performed (Table 90-4). If diuretics are not taken, the fractional excretion of sodium should be measured. Examination of urinary sediment could be helpful. Tubular epithelial or granular casts are indicative of tubular injury, whereas hyaline casts are seen in low perfusion states.

TABLE 90-4 **Evaluation of the Etiology of Oliguria**

| Laboratory Test | Prerenal | Renal |
|---|---|---|
| BUN/Cr | >20:1 | <10:1 |
| Urine osmolality | >500 | <400 |
| Urine/plasma osmolality | >1.3 | <1.1 |
| Urine specific gravity | >1.016 | <1.010 |
| Urine $Na^+$ (mEq/L) | <20 | >40 |
| FENa | <1% | >2% |
| Urinary sediment | Hyaline casts | Tubular epithelial cells<br>Granular casts |

*BUN,* Blood urea nitrogen; *Cr,* creatinine; *FENa,* fractional excretion of sodium.

## 5. Discuss acid-base balance regulation, and identify acid-base disturbances resulting from acute kidney injury.

The largest amount of acid within the body is carbon dioxide ($CO_2$). It is controlled by chemoreceptors within the carotid bodies, aortic arch, and medulla. Alveolar ventilation is increased when the carotid bodies and aortic arch are exposed to increased $CO_2$ levels or when the medulla is exposed to decreased pH of cerebrospinal fluid. $CO_2$ is buffered by hemoglobin, where it binds with water ($H_2O$). The reaction is catalyzed by carbonic anhydrase to form carbonic acid ($H_2CO_3$). $H_2CO_3$ subsequently ionizes to hydrogen and bicarbonate.

$$HCO_3^- + H^+ \rightarrow H_2CO_3 \rightarrow CO_2 + H_2O$$

$$CO_2 + H_2O \xleftarrow{\text{Carbonic anhydrase}} H_2CO_2$$

When buffering capacity is overwhelmed, and compensation by increased alveolar ventilation is inadequate (i.e., respiratory failure), chloride ($Cl^-$) is excreted from the kidneys saving ammonium ($NH_4^+$) to maintain electrochemical balance. In addition to the primary role of the kidneys in excretion of nitrogenous waste products, bicarbonate is also absorbed.

In AKI, rapid loss of kidney function leads to subsequent retention of nitrogenous waste products and inability to reabsorb bicarbonate. Acidosis from AKI is a reflection of accumulated urea, ammonia, phosphate,

sulfate, formate, and strong ions (e.g., $Cl^-$) in addition to bicarbonate loss from inability to reabsorb bicarbonate. When the kidneys recover with improved GFRs (as reflected by creatinine levels), excretion of nitrogenous waste products coupled with $Cl^-$ leads to resolution of the metabolic acidosis.

## 6. What is contrast-induced nephropathy?

AKI from radiocontrast media is known as contrast-induced nephropathy (CIN), which is associated with significant morbidity and mortality. The diagnosis of CIN requires either an absolute increase of 0.5 mg/dL or a >25% increase of serum creatinine. CIN usually manifests within the first 24 hours after contrast agent administration as nonoliguric AKI. For most patients, CIN is mild and self-limited, although there is still a risk of AKI necessitating dialysis in certain high-risk patients.

## 7. Describe the pathogenesis of contrast-induced nephropathy.

Renal vasoconstriction and direct tubular injury are the major mediators of CIN. CIN is believed to be caused by contrast-induced release of vasoconstrictors (e.g., endothelin, adenosine) and cytotoxic effects of contrast agents, which have been correlated with the agent's osmolality.

## 8. Identify the risk factors for and probability of developing contrast-induced nephropathy.

The most recent generation of iodinated radiocontrast media is nonionic, classified as either low-osmolality agents or isoosmolar. Compared with the first-generation products, which were ionic monomers with high osmolality, the newer agents are associated with a significant reduction in the incidence of CIN. Mehran et al. published a simple risk score for prediction of CIN in percutaneous coronary interventions (Tables 90-5 and 90-6).

TABLE 90-5 **Point Assignment for Risk Score of Contrast-Induced Nephropathy**

| Points | Criteria |
|---|---|
| 1 | Per 100 mL contrast media used |
| 3 | Hematocrit<br>Male <39%<br>Female <35%<br>Diabetes |
| 4 | Age >75 years<br>Serum creatinine >1.5 g/dL |
| 5 | Systolic blood pressure <80 mm Hg<br>Intraaortic balloon pump<br>Congestive heart failure |

Adapted from Mehran et al.

TABLE 90-6 **Risk Score for Prediction of Contrast-Induced Nephropathy in Percutaneous Coronary Interventions**

| Cumulative Points | CIN Risk (%) | Dialysis Risk (%) |
|---|---|---|
| ≤5 | 7.5 | 0.04 |
| 6–10 | 14 | 0.12 |
| 11–16 | 26.1 | 1.09 |
| >16 | 57.3 | 12.8 |

*CIN,* Contrast-induced nephropathy.
Adapted from Mehran et al.

## 9. What are the options for preventing contrast-induced nephropathy?

The only treatment for CIN is supportive; much of the focus has been on preventive measures. Because CIN is believed to be caused by renal vasoconstriction and direct cytotoxic damage with oxygen free radical formation, most clinical studies have centered on volume expansion, diuretics, and vasodilators.

Several small studies have looked at the effect of pretreatment with mannitol and furosemide administered immediately before receiving iodinated radiocontrast material. These studies have shown that mannitol provides no benefit, whereas furosemide increased the risk of AKI even though volume depletion was not associated with diuretic therapy.

Likewise, inhibition of renal vasoconstriction by vasodilatory agents has not been promising. The CONTRAST trial looked at 315 patients with chronic kidney disease who were randomly assigned to receive fenoldopam or saline alone. The fenoldopam group had no reduction in CIN. Other drugs, such as theophylline and iloprost, showed a small absolute benefit in low-risk patients, whereas nonselective endothelin receptor antagonists showed an increase in the risk of CIN.

Acetylcysteine has been studied extensively in the prevention of CIN. Its protective mechanism is imparted by antioxidant and vasodilatory properties. Several large studies have led to inconsistent results. A dosage of 1200 mg twice daily was shown to have a small advantage in preventing CIN.

The most effective method of preventing CIN is volume expansion. A prospective randomized trial of 1620 patients resuscitated with 1 mL/kg/hour for 24 hours showed the superiority of 0.9% normal saline compared with 0.5% normal saline. To test whether or not alkalization can protect kidneys from free radical injury, sodium bicarbonate was studied as a resuscitation fluid. Compared with resuscitation with isotonic sodium bicarbonate, isotonic normal saline has had mixed results. In randomized trials and meta-analyses, isotonic normal saline was found to be either similar or inferior to isotonic sodium bicarbonate in the prevention of CIN.

Prophylactic hemofiltration and hemodialysis have not added any benefit compared with less invasive modalities. Atrial natriuretic peptide, statins, ascorbic

acid, and trimetazidine have not been shown to add any additional benefit; these agents have not been thoroughly studied to recommend routine use in the prophylactic treatment of CIN.

Reducing the risk of acquiring CIN requires a multifactorial approach. Issues for consideration include using nonionized, low-osmolar to isoosmolar contrast media and limiting the volume. All common nephrotoxic drugs, such as NSAIDs and metformin, should be discontinued before receiving radiocontrast. Isotonic sodium bicarbonate (add three 50-mL ampules of 1 mEq/mL sodium bicarbonate to 850 mL of sterile water) should be administered at 3 mL/kg 1 hour before the procedure, followed by 1 mL/kg for 6 hours after completion of the procedure. Acetylcysteine can also be administered (1200 mg twice daily orally) the day before and the day of radiocontrast injection.

## 10. What are the indications for dialysis in the intensive care unit?

ARF is marked by a swift decline in kidney function leading to azotemia and oliguria. There is no consensus regarding the optimal timing for dialysis therapy in a critically ill patient. Box 90-1 lists the most common reasons for dialysis in the ICU.

### *Renal Indications*

Hyperkalemia as a result of decreased renal excretion can be life-threatening in patients with ARF. Exogenous sources such as intravenous fluids, potassium replacement, and medications (e.g., ACE inhibitors) all need to be carefully regulated. Nonrenal causes of hyperkalemia, such as tumor lysis syndrome, rhabdomyolysis, or hematoma reabsorption, can also lead to life-threatening hyperkalemia by causing a rapid shift in potassium from the intracellular to the extracellular space.

When renal function is severely impaired, accumulation of acids can lead to a high anion gap acidosis. When severe acidosis (pH <7.20) occurs, treatment with exogenous sodium bicarbonate is often initiated. This treatment may be detrimental in patients at risk for volume overload and hypernatremia or in cases of concomitant respiratory acidosis. In these patients or in patients refractory to medical treatment, dialysis affords another option for clearance of acidic waste.

**BOX 90-1 Common Indications for Dialysis in the Intensive Care Unit**

**Renal**
- Hyperkalemia
- Uremia
- Acidosis
- Hypervolemia secondary to renal failure

**Nonrenal**
- Toxins
- Congestive heart failure
- Liver failure

Uremia typically results when GFR is decreased to <10 mL/min and BUN levels are >100 mg/dL. Common causes include excessive protein ingestion (parenteral or enteral), gastrointestinal bleeding, and corticosteroid use. Prompt initiation of dialysis is advised when patients develop encephalopathy, pericarditis, or hemorrhage.

Critically ill patients tend to be severely hypervolemic as a result of aggressive fluid resuscitation and reduction in filtered sodium load. Dialysis is indicated when aggressive diuretic therapy fails to achieve optimal volume status.

### *Nonrenal Indications*

Hemodialysis is indicated for the treatment of life-threatening toxic ingestions and any severe metabolic acidosis that occurs from ingestion. Volume overload from congestive heart failure is another common indication for renal replacement therapy. These patients often have low cardiac outputs and resultant renal hypoperfusion. They tend to retain sodium and fluid as a result of increased circulating levels of catecholamines and neurohormonal factors. When patients become refractory to treatment with diuretics and inotropic agents, dialysis ultrafiltration is often effective. Finally, patients with liver failure are predisposed to developing azotemia and hepatorenal syndrome. Renal replacement therapy is commonly used to assist with solute and fluid clearance.

## 11. What are the options for renal replacement therapy?

Options for renal replacement therapy include hemodialysis and continuous renal replacement therapies. Intermittent hemodialysis is the most common therapy for ARF in the ICU. A session typically lasts 4 hours and requires a dialysis machine and trained personnel. The dialysis machine is primarily diffusion dependent with a higher dialysate rate (>500 mL/min) compared with blood flow (300 mL/min). Blood flow runs countercurrent to the dialysate and produces a rapid decrease in plasma solute concentration.

Continuous renal replacement therapy (CRRT) includes multiple different modalities, and therapies are generally run continuously. They are better tolerated in patients who are hemodynamically unstable because they use a lower blood flow rate. The most commonly used are continuous arteriovenous hemofiltration (CAVH), continuous arteriovenous hemodialysis (CAVHD), continuous venovenous hemofiltration (CVVH), continuous venovenous hemodialysis (CVVHD), and slow continuous ultrafiltration (SCUF). CAVH and CAVHD use the patient's mean arterial pressure as the impetus for blood flow across the membrane. An arteriovenous circuit is used, which avoids the need for a blood pump, and solute removal occurs by convection. CAVHD includes dialysis allowing for the diffuse clearance of solute. Blood flow ranges from 50–100 mL/min. CVVH and CVVHD are similar to CAVH and CAVHD except that they require central venous access and connection to an extracorporeal blood pump to maintain the transmembrane pressure gradient. SCUF is similar to CAVH and CVVH but functions to remove fluid and not solute. SCUF is primarily used in patients with heart failure.

### 12. Discuss problems encountered with renal replacement therapy.

The most common complication of intermittent hemodialysis is hypotension, which typically occurs when a large amount of fluid is removed at a rapid rate in a patient with poor oncotic pressure (e.g., sepsis, heart failure). In addition, rapid removal of fluid can be associated with electrolyte depletion—potassium or calcium—leading to arrhythmias. Another potential complication of intermittent hemodialysis is dysequilibrium syndrome. Clinically, this syndrome manifests as seizures, headaches, or lethargy following dialysis. Dysequilibrium syndrome is believed to result from cerebral edema following rapid decrease in serum osmolality compared with the intracellular space, as solute is removed and water is drawn into the brain.

CRRT requires the presence of large-bore central venous access, placing the patient at risk for complications of central venous access such as infection and pneumothorax. In addition, patients whose only access is via the subclavian vein are at risk for developing subclavian stenosis, and the use of the ipsilateral arm for permanent dialysis can be impaired. CRRT also predisposes patients to hypothermia as large volumes of unwarmed ultrafiltrate are frequently replaced. Finally, patients with CRRT require anticoagulation because exposure of blood and plasma to the filter over a longer period of time at a slower flow rate leads to activation of clotting factors and filter failure. Heparin is often required to achieve anticoagulation and increase the life span of the filter but predisposes the patient to bleeding.

Patients can also have a reaction to the dialysis membrane. All membranes have varying degrees of biocompatibility and can release cytokines and complement activation as blood comes into contact with the membrane. Patients are predisposed to the possibility of systemic inflammatory response syndrome or anaphylaxis. Air embolism is also a possibility if a circuit disconnection occurs or if the pump is not sufficiently primed before connection to the patient.

### 13. How is the most appropriate renal replacement therapy selected?

The choice of renal replacement therapy depends on the indication for dialysis, available vascular access, existence of other organ dysfunction, estimated duration of therapy, technologic availability, and trained personnel. Limited data exist to support the benefit of CRRT over intermittent dialysis. Because most patients in the ICU have some component of hemodynamic instability, CRRT is typically better tolerated because it removes solutes and water at a slower rate over a longer period. However, CRRT also requires anticoagulation, which presents a problem in patients who have developed or are prone to bleeding. Intermittent hemodialysis may be more effective in a patient with refractory hyperkalemia or ingested toxins.

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CASE 91

# Central Nervous System

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## QUESTIONS



A 35-year-old man sustained injuries in a motor vehicle accident and was taken to the nearest emergency department. His vital signs, x-rays, and laboratory values were normal. As his wounds were sutured, he complained of the worst headache of his life. His mental status acutely deteriorated. He was diagnosed with subarachnoid hemorrhage (SAH) and increased intracranial pressure (ICP), which were treated. After an uneventful course in the intensive care unit (ICU), he was transferred to the floor, where he experienced a seizure. After the seizure, he remained confused and combative. Later, he sustained an unwitnessed cardiac arrest from which he had return of spontaneous circulation after 30 minutes. However, he never regained consciousness.

## 1. What is subarachnoid hemorrhage?

SAH is the extravasation of blood into the subarachnoid space, which is located between the pia and the arachnoid membrane. The most common cause of SAH is traumatic head injury. Traumatic SAH in elderly adults often occurs after falls and head injury, whereas the most common cause in young people is motor vehicle accidents.

Nontraumatic SAH is most commonly associated with intracranial aneurysm rupture (approximately 80%–90%). Approximately 5% of the population harbor an aneurysm, and 20%–30% of people with an aneurysm have multiple aneurysms; however, very few aneurysms rupture spontaneously. Although SAH is responsible for about 5% of all strokes, the incidence of spontaneous SAH is only 25 per 100,000 in the United States. The peak incidence of aneurysmal SAH is between 50 and 60 years of age, with a higher prevalence in women and African Americans. Other nontraumatic causes include vascular malformations, tumors, and infections.

Risk factors for aneurysmal SAH are multifold, consisting of both modifiable and genetic factors. In the United States, smoking, hypertension, alcohol abuse, and cocaine abuse (especially in young people) are independent risk factors for SAH. Genetic diseases such as polycystic kidney disease and connective tissue diseases (e.g., Marfan syndrome, Ehlers-Danlos syndrome) increase the risk of developing aneurysms. In certain populations, such as the Japanese and Finnish, a familial syndrome is associated with intracranial aneurysms. The strongest risk factor for SAH is a history of previous SAH. There appears to be a higher incidence of SAH in winter and spring months as well as an association between atmospheric pressure changes and number of SAHs per day; the reasons are unknown.

## 2. How is subarachnoid hemorrhage diagnosed?

The symptom classically associated with aneurysmal SAH is described as "the worst headache of my life" and is reported in nearly 80% of awake patients. Many patients also report a sentinel headache, which generally occurs 2–8 weeks before a major SAH. Other symptoms include nausea, vomiting, pain radiating to the legs (blood pooling in lumbar cistern), nuchal rigidity, meningeal signs, cranial nerve palsies, focal neurologic symptoms, loss of consciousness, and seizures. Death occurs in 12% of people before receiving treatment.

Timely diagnosis is essential for SAH because prompt treatment has a significant impact on outcome. SAH is misdiagnosed in 12% of patients, leading to delayed treatment and is associated with a fourfold higher risk of death or disability at 1 year. Although SAH accounts for only 1% of all patients with headaches presenting to the emergency department, approximately 20% of all patients with SAHs present with sentinel headaches before major SAH. When a patient presents to the emergency department with a headache, a high index of suspicion for possible leak (sentinel headache) could prevent rerupture and be lifesaving.

Noncontrast computed tomography (CT) scan of the head is the diagnostic test of choice for acute SAH. The probability of detecting SAH by CT scan is related

**TABLE 91-1 Modified Fisher Score**

| Grade | CT Scan Findings | Chance of Developing Vasospasm (%) |
|---|---|---|
| 0 | No SAH or IVH | NA |
| 1 | Thin SAH, no IVH | 24 |
| 2 | Thin SAH with IVH | 33 |
| 3 | Thick SAH, no IVH | 33 |
| 4 | Thick SAH with IVH | 40 |

*CT,* Computed tomography; *IVH,* intraventricular hemorrhage; *SAH,* subarachnoid hemorrhage.
For references, see Capes et al. (2001) and Champion et al. (2009).

to time from SAH and severity of bleeding. The sensitivity of CT scans is nearly 100% within the first 12 hours after bleeding; sensitivity decreases to 90% at 24 hours and 60%–80% by days 5 and 6. The modified Fisher score, based on CT scan findings, is used to predict the likelihood of vasospasm (Table 91-1). In patients with negative or inconclusive CT scan findings, examination of cerebrospinal fluid (CSF) with lumbar puncture for the presence of red blood cells or xanthochromia suggests the diagnosis of SAH. SAH is unlikely in patients with severe headache and a negative CT scan and lumbar puncture. Fluid attenuated inversion recovery (FLAIR) or proton density–weighted magnetic resonance imaging (MRI) can be used to diagnose SAH. However, because of cost, availability, and logistics of MRI, it is not widely used to diagnose acute SAH.

The "gold standard" for diagnosis of cerebral aneurysm as a cause of SAH is cerebral angiography. The advantages of cerebral angiography are better resolution of smaller aneurysms (<5 mm) and the ability to treat (coil) at the same time. Disadvantages of cerebral angiography are invasiveness requiring the proper facilities, skilled physicians, and large iodinated dye loads. CT angiography (CTA) is nearly as effective in diagnosing aneurysms that are >5 mm. For aneurysms <5 mm, the sensitivity is roughly 60%–80%. Magnetic resonance angiography (MRA) has been increasingly used to help diagnose the cause of SAH. However, MRA has major limitations including availability, cost, motion artifacts, and long duration making it unsuitable for unstable patients. Both CTA and MRA require interpretation by skilled radiologists and are diagnostic only.

### 3. How are patients with subarachnoid hemorrhage managed?

Evaluation of a patient with suspected SAH should start with the ABCs (airway, breathing, circulation) followed by a mental status examination. Although many patients with SAH present without airway compromise, the potential for neurologic deterioration from continued bleeding is significant. Continuous monitoring of mental status is extremely important because changes may herald loss of consciousness, inability to protect the airway, and respiratory failure requiring emergent intubation.

Examination for external signs of trauma helps differentiate traumatic versus nontraumatic causes of SAH. In the case of traumatic SAH, it is important to rule out other injuries that might require immediate treatment or that may complicate care (e.g., cervical spine injury, pneumothorax, tamponade, rupture of intraabdominal organs). A complete neurologic examination should also be performed.

Several clinical measurement scales have been used to estimate the severity and outcome of SAH. The Hunt and Hess grading scale, which is based on patients' clinical condition, is the most widely used. It classifies severity and estimated risk of mortality after SAH (Table 91-2).

When the diagnosis of a SAH is confirmed, further work-up is required to identify the etiology. Traumatic causes usually have a clear history of injury or are associated with stigmata such as scalp trauma or skull fracture. Nontraumatic SAHs are most likely due to cerebral aneurysms (approximately 80%–90%). Of aneurysms, 90% are located in the anterior circulation (Box 91-1), and 10% are located in the posterior circulation. Other causes include arteriovenous malformation, intracranial dissection with pseudoaneurysm rupture, endocarditis with mycotic aneurysm rupture, meningitis, encephalitis, cavernous malformations, and cerebral vasculopathies.

The cornerstone of treatment for SAH is securing the aneurysm to control bleeding and prevent rebleeding. Throughout the 1980s, open surgical clipping was the only treatment available. In the 1990s, endovascular coiling using platinum coils was introduced. Endovascular

**TABLE 91-2 Hunt and Hess Grading Scale for Subarachnoid Hemorrhage**

| Grade | Clinical Examination | Mortality (%) |
|---|---|---|
| 1 | Mild headache<br>Slight nuchal rigidity | 1 |
| 2 | Moderate-to-severe headache<br>Severe nuchal rigidity<br>Cranial nerve palsy | 5 |
| 3 | Mild focal deficit<br>Lethargy<br>Confusion | 19 |
| 4 | Stupor<br>Moderate-severe hemiparesis<br>Slight decerebrate rigidity | 40 |
| 5 | Coma<br>Decerebrate rigidity<br>Moribund | 77 |

**BOX 91-1 Aneurysms of the Cerebral Circulation**

| | |
|---|---|
| Anterior communicating artery | 30% |
| Posterior communicating artery | 25% |
| Middle cerebral artery bifurcation | 20% |
| Internal carotid artery bifurcation | 8% |
| Other anterior | 7% |
| Posterior circulation | 10% |

coiling excludes aneurysms from the circulation by filling the aneurysm with platinum coils, which results in clot formation, decreasing the potential for rebleeding.

There is still controversy at the present time regarding whether open surgical clipping or endovascular coiling is superior. The decision whether to coil or clip is determined on a patient-by-patient basis taking into account the size, shape, and location of each aneurysm, patient condition, and the experience of available physicians. The International Subarachnoid Aneurysm Trial (ISAT) showed a statistically significant improvement in disability and death at 1 year in patients who had endovascular coiling compared with surgical clipping (24% vs. 31%). At 7-year follow-up, the surgical cohort had significantly higher mortality and seizure rates. However, early rebleeding was higher in the endovascular group. Although endovascular coiling has become more common and widely available, preference among centers is largely related to the culture, familiarity, and comfort of the facility with either clipping or coiling. Some recommendations suggest that surgical clipping is preferable for aneurysms >10 mm or aneurysms with wide necks.

Whether clipping or coiling is preferred at a particular institution, early treatment is recommended. In a follow-up article looking at the ISAT data, early intervention with either clipping or coiling resulted in improved outcomes. Past recommendations dictated that treatment should either occur early (0–3 days) or, if a patient's condition warranted, be delayed (after 10 days). Intervention was not recommended between days 4 and 10 because of the increased risk for vasospasm. However, more recent studies have shown that intervention during days 5–10 yielded better outcomes than late interventions. The practice of delaying treatment is now questionable. Early intervention resulted in the best outcomes.

Medical management of SAH focuses on treating the complications of SAH. Rebleeding is the most treatable cause of poor outcomes. In unrepaired patients, the risk of rebleeding is 3%–4% within the first 24 hours, 2% on day 2, up to 20% within the first 2 weeks, and up to 50% by 6 months. Seizures are associated with increased risk of rebleeding in patients with untreated aneurysms. The only certain way to prevent rebleeding is aneurysmal clipping or coiling. Antifibrinolytics, such as aminocaproic acid (2–4 g loading dose, followed by 1 g/hour infusion) or tranexamic acid (1 g loading dose, followed by 1 g every 6–8 hours), have been used to prevent early rebleeding. However, because antifibrinolytics are associated with vasospasm, the current recommendation is to limit their use to the first 3 days. Both antifibrinolytics are to be employed cautiously in patients with histories of myocardial infarction, hypercoagulopathy, deep vein thrombosis, or pulmonary embolus. Lowering blood pressure with labetalol, nicardipine, or clevidipine has been shown to decrease risk of rebleeding.

Cerebral artery vasospasm can lead to worse mortality and disability in patients with SAH. It usually occurs between days 3 and 14 after SAH. Symptomatic vasospasm, defined as clinical deterioration secondary to vasospasm, is seen in 20%–40% of patients. Risk factors for the development of vasospasm include poor clinical status, thick blood on CT scan (>1 mm thick), hypertension, volume depletion, low cardiac output, smoking, fever, and vasospasm on initial angiography (higher risk of subsequent vasospasm).

The "gold standard" for diagnosis of cerebral vasospasm is cerebral angiography. Transcranial Doppler (TCD) ultrasound can be used at the bedside to diagnose vasospasm. Although changes in mean flow velocities of the middle cerebral artery of >200 cm/second are highly suggestive of cerebral vasospasm, other vascular territories are unreliable. TCD scans can be performed daily, and elevated velocities on TCD scans can precede symptoms by 2 days. If TCD suggests vasospasm, further investigation (e.g., CTA, MRA, cerebral angiography) should be performed to confirm the diagnosis.

Most patients with SAH are treated prophylactically to prevent vasospasm. At the present time, nimodipine is the only medication shown in clinical trials to improve outcomes. Nimodipine is usually given for 2–3 weeks, and the dose is based on blood pressure. A suggested protocol is 60 mg every 4 hours for systolic blood pressure (SBP) >140 mm Hg, 30 mg for SBP 120–140 mm Hg, and no drug for SBP <120 mm Hg. Normovolemia should be the goal in patients with SAH.

The treatment for patients who develop symptomatic vasospasm includes "triple H" therapy and direct arterial calcium channel blocker injection by cerebral angiography. "Triple H" therapy includes hypertension, hydration, and hemodilution. The goal is to increase the SBP 20–30 mm Hg above baseline but not >220 mm Hg. This goal can be accomplished with pressors, fluids, or both. Hemodilution is generally achieved by administering crystalloids to dilute the hematocrit, which also accomplishes hydration. If possible, repeat angiography should be performed to facilitate intraarterial injection of calcium channel blockers to relax the cerebral artery.

Hydrocephalus and elevated ICP can occur. Hydrocephalus is treated with an external ventricular device to divert CSF flow, which also treats increased ICP. Other management strategies for elevated ICP are hypertonic saline and mannitol to decrease brain swelling.

Seizures are a possible complication of SAH, and most patients are placed on prophylactic anticonvulsant therapy for the first 7 days. If the patient has a seizure or the aneurysm is not treated, anticonvulsant therapy is warranted for a longer period.

Hyponatremia usually occurs secondary to cerebral salt wasting syndrome and is not due to syndrome of inappropriate antidiuretic hormone (SIADH). Cerebral salt wasting is characterized by hyponatremia and dehydration with excessive urine output. Treatment entails correcting the hyponatremia with salt tablets or hypertonic saline and maintaining balanced fluid and urine outputs. It is important to rule out SIADH because treatment for SIADH (which is fluid restriction) should be avoided as it can worsen the patient's volume status and increase risk of vasospasm from dehydration.

### 4. How is increased intracranial pressure diagnosed and treated?

The cranial vault comprises brain (80%), blood (10%), and CSF (10%). Because the volume in the cranial vault

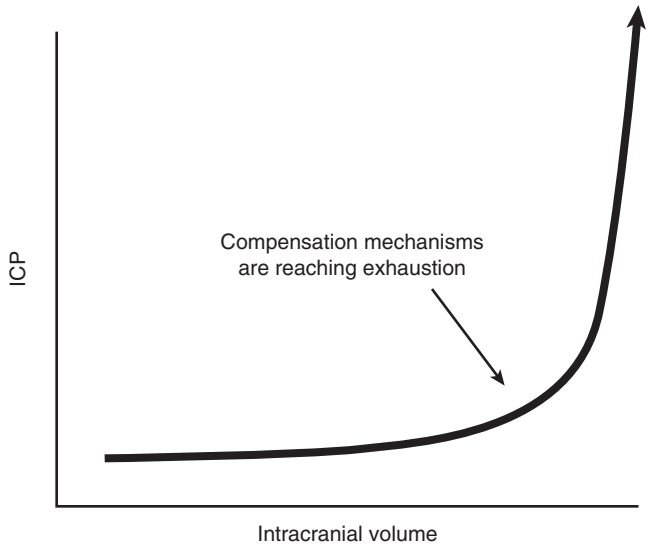


**FIGURE 91-1** ■ ICP changes with alteration in intracranial volume.

is fixed (noncompliant system), a small change in volume results in a large change in ICP. Some CSF and venous blood can shift extracranially to maintain ICP within normal limits (5–13 mm Hg). However, there is limited capacity for this compensatory mechanism (Figure 91-1). Elevated ICP is a medical and surgical emergency. *Irreversible brain injury or death can result if immediate action is not taken.*

Increased ICP occurs secondary to space-occupying lesions, increased CSF (i.e., hydrocephalus), increased cerebral blood volume, and cerebral edema (Box 91-2). In the setting of intact cerebral autoregulation, increases in cerebral blood flow do not usually result in increased cerebral blood volume. However, vascular abnormalities that disrupt cerebral autoregulation can lead to increased cerebral blood flow. Sinus thrombosis can lead to outflow obstruction of venous blood flow, causing elevated ICP. Cerebral edema leads to elevated ICP by four different mechanisms: vasogenic (vessel damage owing to mass, infection, or contusion), cytotoxic (ischemia, cell membrane failure), hydrostatic (increased transmural pressure secondary to hydrocephalus), and hypoosmolarity.

Increased ICP can lead to decreased cerebral perfusion pressure (CPP). CPP is calculated by subtracting the ICP from the mean arterial pressure (MAP). If central venous pressure (CVP) is greater than ICP, the CPP is calculated by MAP − CVP. Decreases in CPP can result in reductions in cerebral blood flow leading to ischemia (Figure 91-2). Neuronal injury can also result from direct brain tissue compression and herniation in the setting of increased ICP.

The generally acceptable threshold for ICP is <20–25 mm Hg. ICP >20–25 mm Hg mandates aggressive clinical management. Patients may intermittently have plateau waves of increased ICP >60–80 mm Hg, which are not associated with worse outcomes unless they last >30 minutes.

Signs of elevated ICP can be observed on neurologic examination. Mental status changes could range from

**BOX 91-2 Etiologies of Increased Intracranial Pressure**

**Space-Occupying Lesions**
- Tumor
- Hematoma
- Air
- Abscess
- Foreign body

**Cerebrospinal Fluid Accumulation**

***Obstructive***
- Cerebral aqueduct stenosis
- Tumor
- Congenital malformation (e.g., Chiari, Dandy-Walker)

***Nonobstructive (Communicative)***
- Impaired cerebrospinal fluid resorption
  - Hemorrhage (e.g., SAH, IVH)
  - Infection (e.g., meningitis, ventriculitis)
  - Scarring or fibrosis (from infection or inflammatory process)

***Increased Production***
- Choroid plexus papilloma

**Increased Cerebral Blood Volume**
- Loss of cerebral autoregulation
- Sinus thrombosis

**Cerebral Edema**
- Vasogenic
- Cytotoxic
- Hydrostatic
- Hypoosmolarity

*IVH*, Intraventricular hemorrhage. *SAH*, subarachnoid hemorrhage.

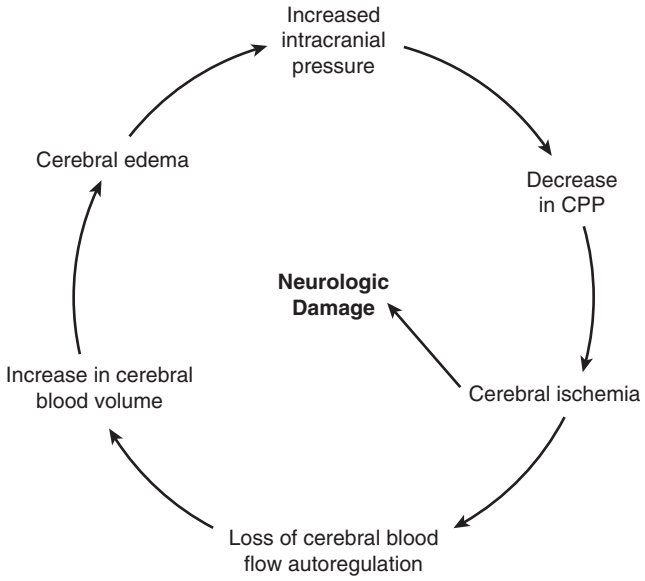


**FIGURE 91-2** ■ CPP and neurologic damage.

mild confusion to coma. Papilledema may indicate elevated ICP; however, it can be observed in patients with normal ICP. Uncal herniation produces an ipsilateral fixed and dilated pupil (cranial nerve [CN] III palsy). CN VI palsy, inability to turn the eye outward, may be present. Posturing, either decorticate (flexor) or decerebrate (extensor), is a nonspecific sign of elevated ICP. Decorticate posturing occurs when the injury is between the cortex and the red nucleus. Decerebrate posturing occurs when the injury is below the red nucleus. Posturing provides only general localizations and not absolute anatomic diagnoses. Abnormal respiratory patterns, such as Cheyne-Stokes respiration, central neurogenic hyperventilation, sustained inspiratory effort, clustered breathing, and ataxic breathing, can also be observed in patients with elevated ICP. The only definitive way to diagnose elevated ICP is to measure it directly.

The concept of CPP-directed treatment of increased ICP was introduced >30 years ago. There has been a small improvement in outcome statistics, but mortality still ranges from 20%–30%. When increased ICP is diagnosed, emergent treatment must be initiated. Surgical consultation should be sought immediately for possible evacuation of blood or excess fluid or ventricular drainage of CSF. The goals of therapy are to reduce ICP and attain a CPP of 60–100 mm Hg. CPP is optimized by increasing MAP and reducing ICP (Box 91-3). If ICP remains elevated, osmotherapy with either mannitol or hypertonic saline should be considered. Mannitol and hypertonic saline are the mainstays of treatment of neurologic emergencies related to cerebral edema and elevated ICP. There are no data showing superiority of either mannitol or hypertonic saline. However, mannitol should be administered with caution to patients with a low ejection fraction or renal failure.

More recently, small volumes of high-osmolarity solutions (23.4% saline) have been used to treat intracranial hypertension crises. The theory behind the use of high-osmolarity solutions is that they create a driving force to mobilize water from the interstitial and intracellular compartments of the brain into the intravascular compartment. Reduction in brain water can lead to a >50% reduction in ICP in the acute setting allowing additional time to arrange for other diagnostic or therapeutic interventions. Advantages of high-osmolarity saline include low cost; amenable to repeat administrations; low total volume; and freedom from allergenicity, which mannitol is not. Treatment with high-osmolarity saline does have some risks, although complications are uncommon. Recognized complications include hyperosmolarity, central pontine myelinolysis, subdural hematomas, congestive heart failure, acid-base derangements, and coagulopathies. This treatment still requires further investigation to determine the optimal dose as well as the safest and most effective mode of administration.

ICP monitoring is considered the standard of care in most clinical centers, although some studies have shown no change in mortality with ICP monitoring versus monitoring with imaging and clinical examinations only. Several techniques are available for ICP monitoring (Table 91-3). The goal of all these monitoring devices is to provide early warning of impending brain hypoxia or ischemia as well as improving cerebral hemodynamics and oxygenation. Some noninvasive methods allow the medical team to look for additional signs of elevated ICP.

Surgical intervention varies depending on the underlying cause of elevated ICP, the patient's clinical status, imaging studies, and overall prognosis. The two most common causes requiring surgical intervention are epidural hematoma and acute subdural hematoma. The most recent recommendations for treatment are based on the Brain Trauma Foundation guidelines published in 2007. Epidural hematomas >30 mL should be surgically evacuated regardless of the patient's Glasgow Coma Scale score. There is no ideal surgical intervention, but craniotomy allows for a more significant evacuation of the hematoma. An epidural hematoma <30 mL with <5 mm midline shift can be managed nonoperatively by serial CT scans and close neurologic monitoring. Acute subdural hematomas that are <10 mm thick or are causing a midline shift >5 mm on CT scan should undergo surgical intervention. Emergent surgery should also be performed if the subdural hematoma is <10 mm thick and there is <5 mm midline shift and one of the following conditions are present:

- Glasgow Coma Scale score decreased by >2 points since the time of the injury
- Signs of brainstem involvement (e.g., asymmetric or fixed and dilated pupils)
- ICP >20 mm Hg

Other treatment options that may be implemented are sedation, external ventricular CSF drainage, hypothermia,

**BOX 91-3 Treatment of Elevated Intracranial Pressure**

- Immediate surgical consultation
- Increase MAP
  - Vasopressors
  - Isotonic fluids
- Decrease intracranial pressure
  - Elevate head of bed 30–45 degrees
  - Avoid administration of free water
  - Maintain mildly elevated plasma sodium levels (150–155 mEq/L)
  - Avoid increases in cerebral metabolic rate
    - Avoid hyperthermia
    - Avoid shivering
  - Prevent seizures
  - Control pain
  - Continue normocarbia ($pCO_2$ 37–40 mm Hg)
    - May institute short-term hyperventilation ($pCO_2$ 30-32 mm Hg)
- If intracranial pressure remains elevated
  - Osmotherapy
    - Mannitol 20%
      - 0.5–1 g/kg bolus followed by 0.5 g/kg every 4–6 hours
      - Goal: 300–320 mOsm/L in serum
      - Caution in patients with low ejection fractions or renal failure
    - Hypertonic saline (3% NS)
      - 1 mg/kg/hour
      - Goal: Sodium 150–155 mEq/L

*NS*, Normal saline; *$pCO_2$*, carbon dioxide tension.

TABLE 91-3 **Intracranial Pressure Monitoring Techniques**

| Monitoring Technique | Advantages | Disadvantages |
|---|---|---|
| Ventricular catheter | "Gold standard"<br>Allows for CSF drainage | Invasive<br>Risk of infection<br>Risk of bleeding<br>Must be calibrated |
| Intraparenchymal catheter | Intraparenchymal or subdural placement<br>Easier to place than ventricular catheter<br>Lower infection rate | Drift of measurements over time<br>Measures localized pressure only where the sensor is placed |
| NIRS | Measures cerebral oximetry<br>Detects cerebral ischemia<br>Noninvasive | Lack of standardization among commercial NIRS cerebral oximeters<br>Risk of measuring extracranial blood oxygen levels |
| Optic nerve sheath diameter | Noninvasive<br>Optic sheath is a continuation of dura<br>Increase in optic sheath diameter correlates with increased ICP | Emerging technology<br>Change detected in millimeters |
| Transcranial Doppler | Noninvasive | Requires training<br>Assesses regional blood flow<br>Higher failure rate when difficult to obtain windows for Doppler |

*CSF,* Cerebrospinal fluid; *ICP,* intracranial pressure; *NIRS,* near-infrared spectroscopy.

and decompressive craniectomy. Propofol may be used for sedation; however, hypotension should be avoided because of its negative effect on CPP. Induced hypothermia to 32° C–34° C can reduce cerebral blood flow by decreasing metabolic demands. However, there are no data to support its use. Rewarming should be accomplished over at least 24 hours. Decompressive craniectomy for early neuroprotection is controversial but may be necessary as a lifesaving measure in severe refractory elevated ICP.

TABLE 91-4 **Causes of Traumatic Brain Injury**

| Cause | Frequency (%) |
|---|---|
| Falls | 35.2 |
| Motor vehicle accidents | 17.3 |
| Hit by a moving or stationary object | 16.5 |
| Assaults | 10 |
| Unknown/other | 21 |

## 5. What is traumatic brain injury?

Traumatic brain injury (TBI) has become a major social, economic, and public health problem in the United States and around the world. According to data from the U.S. Centers for Disease Control and Prevention, nearly 1.7 million people are diagnosed with TBI in the United States each year. TBI is caused by any trauma or penetrating injury to the head that creates a brain insult leading to disruption of the normal brain function. Disruption in brain function may be temporary or permanent. TBI is the third leading cause of traumatic death in the United States, approximating 52,000 deaths per year. Nearly 5.3 million people in the United States are living with disabilities resulting from TBI. The effects of TBI can last long after the initial injury, leading to profound impairments of cognitive, emotional, and physical abilities. These disabilities can further lead to disruption in a person's social, personal, professional, and family lives. The direct and indirect cost of TBI, including loss of productivity, is estimated at nearly $75 billion annually.

The incidence of TBI varies by age and sex. In every age cohort, males are more likely to sustain TBI, but for the age span of 0–15 years, females are more likely than males to die as a result of TBI. Young children (0–4 years old), adolescents (15–19 years old), and elderly adults (≥65 years old) are most likely to sustain TBI. Nearly 0.5 million emergency department visits per year are for TBI for children 0–14 years old. Adults >75 years old have the highest rate of hospitalization and death from TBI.

Many different mechanisms result in TBI (Table 91-4). The leading cause of TBI in the United States is falls (35.2%), accounting for half of all TBI in children 0–14 years old and 61% in adults ≥65 years old. In the United States, motor vehicle accidents are the second leading cause of TBI but account for the highest percentage of deaths related to TBI. Among active military personnel, TBI from explosive blasts are the leading cause of injury.

Types of forces causing injury play an important role in severity and mortality of TBI. Angular, rotational, shear, and translational forces as well as intensity, direction, and duration of forces are important in understanding the development and severity of TBI. The most common mechanism of TBI is a combination of impact and acceleration injury. Direct impact to the skull, termed "impact loading," most commonly results in focal injuries, whereas movement of the brain inside the skull, termed "inertial loading," most commonly results in diffuse injuries. Shock waves from impact injuries or penetrating injuries can also cause tissue damage.

The terms "coup" and "contrecoup" injury refer to the brain injury location in relation to the site of impact. Coup injuries are directly below the site of impact and are usually present when a moving object strikes a stationary head. Contrecoup injuries are on the opposite side of the impact and are usually present when a moving head hits a stationary object.

The history of events surrounding the traumatic injury is important for elucidating the possibility of TBI. It is also important to elicit other factors, such as alcohol or drug use, that might interfere or confound the neurologic examination. Seizures at the scene or en route, other medical conditions, baseline dementia or altered mental status, medications given in the field, and hypothermia all are possible factors that could confound neurologic examination and assessment of TBI severity.

A full history and physical examination are important to determine the severity (mild, moderate, or severe) of TBI. Signs and symptoms of TBI depend on the type, severity, and area of brain affected. The Glasgow Coma Scale is the most commonly used score (Table 91-5) to grade TBI severity (Table 91-6). Signs and symptoms of TBI can be physical, emotional, or cognitive. Symptoms associated with mild TBI include headache, nausea, vomiting, dizziness, tinnitus, blurred vision, poor motor coordination, impaired balance, fatigue, and sleep disturbance. Emotional or cognitive symptoms associated with mild TBI include behavioral or mood changes, confusion, difficulties with memory, poor concentration, impaired attention, and trouble thinking.

Symptoms of moderate or severe TBI may be more prolonged, recurrent, and severe. These patients may also present with aphasia, dysarthria, focal neurologic symptoms, and weakness or loss of sensation in the extremities. Physical signs are the signs of trauma and may include scalp lacerations, skull fractures, CSF leakage from ears or nose, raccoon eyes (periorbital ecchymosis), or Battle sign (mastoid ecchymosis). Often, physical signs will be absent. A full neurologic examination is imperative. GCS scores <8 are considered coma and are associated with severe TBI. Associated increased ICP requires emergent treatment (see Question 4).

TABLE 91-5 **Glasgow Coma Scale**

| | |
|---|---|
| **Verbal** | |
| Alert, oriented, and conversant | 5 |
| Confused, disoriented but conversant | 4 |
| Intelligible words, not conversant | 3 |
| Unintelligible sounds | 2 |
| No verbalization | 1 |
| **Eye opening** | |
| Spontaneous | 4 |
| Verbal stimuli | 3 |
| Painful stimuli | 2 |
| None | 1 |
| **Motor** | |
| Follows commands | 6 |
| Localizes | 5 |
| Withdraws from pain | 4 |
| Flexor posturing | 3 |
| Extensor posturing | 2 |
| No response to painful stimuli | 1 |

TABLE 91-6 **Classification of Traumatic Brain Injury**

| Severity | Glasgow Coma Scale Score | Loss of Consciousness | Posttraumatic Amnesia |
|---|---|---|---|
| Mild | 13–15 | 0–30 minutes | 0–1 day |
| Moderate | 9–12 | >30 minutes to <24 hours | >1 day and <7 days |
| Severe | 3–8 | >24 hours | >7 days |

A noncontrast CT scan of the head is indicated in most cases of symptomatic mild TBI and all moderate-to-severe cases. According to the National Institute for Health and Clinical Excellence (NICE) guidelines, any person with a GCS score <13 or who fails to reach a GCS score of 15 within 2 hours needs an urgent CT scan of the head. Negative head CT scans in severe TBI are associated with favorable prognoses, whereas obliteration of the basal cisterns is associated with poor outcomes. Contusions and subdural hemorrhage are the most common findings in severe TBI. SAH is also common and can lead to ischemic injury secondary to vasospasm in severe cases. Serial head CT scans at least every 6 hours should be obtained in patients with TBI to monitor for progression of pathology and appearance of delayed traumatic intracerebral hematomas until the lesions are stable. The Marshall Classification of Head Injury (Table 91-7) is used to classify the extent of TBI based on head CT scan findings.

Not all TBI can be visualized on CT scan of the head. Patients with diffuse axonal injury, owing to brain axon shearing, may exhibit symptoms and disability greater than that expected by head CT scan results. MRI may be used to elucidate changes in the brain suggestive of diffuse axonal injury as well as cerebral edema and infarction otherwise missed on CT scan of the head.

The primary survey should focus on the ABCs (airway, breathing, circulation) of patient management. Comatose patients require immediate intubation to normalize oxygenation and ventilation (arterial carbon dioxide tension [$PaCO_2$] 35–40 mm Hg). Signs or symptoms of elevated ICP are indications for ICP monitoring. Transfer to a neurocenter should be considered for hemodynamically stable patients. Patients with moderate-to-severe TBI attain better outcomes in neurotrauma or neurocritical centers.

Recommendations for resuscitation and supportive care are based on findings from the IMPACT study. These recommendations include avoidance of hypotension, hypoxia, dextrose-containing fluids, and hypotonic fluids. Good glucose control (without hypoglycemia),

TABLE 91-7 **Marshall Classification of Head Injury**

| Classification | Criteria |
|---|---|
| Diffuse injury I | No pathology on head CT scan |
| Diffuse injury II | Cisterns present; midline shift <5 mm, no lesion >2.5 cm |
| Diffuse injury III | Cisterns compressed or absent, no lesion >2.5 cm |
| Diffuse injury IV | Midline shift >5 mm, no lesions >2.5 cm |
| Evacuated mass | Any lesion that has been surgically evacuated |
| Nonevacuated mass | Lesion >2.5 cm that has not been surgically evacuated |

*CT,* Computed tomography.
From Czosnyka M: Increased intracranial pressure: what to do about it and when? Crit Care Med 41:688, 2013.

normal to slightly elevated sodium levels, correction of elevated international normalized ratios with fresh frozen plasma, and correction of platelet counts to >100,000/mm$^3$ are also recommended.

Many complications of TBI may require management in the acute and postacute phases of the disease. Elevations in ICP are correlated with worse outcomes and should be aggressively treated (Box 91-3). Intracranial hemorrhage (enlarging masses, subdural or epidural hematomas) and other lesions may require surgical intervention if they result in a midline shift. Seizures may require short-term treatment with anticonvulsants in the acute phase, and epilepsy that develops after TBI may require anticonvulsants indefinitely. In severe TBI, seizures occur in 15% of patients and can manifest several years after injury. Cognitive and emotional effects can be devastating and debilitating. Patients with TBI may never fully recover.

## 6. What are the risks of acute ischemic stroke, and how is stroke diagnosed and treated?

Worldwide, strokes are a leading cause of mortality, of which 85% are ischemic in origin. The main cause of ischemic strokes is cardioembolic or large vessel occlusion. Patients who present to the ICU with acute ischemic strokes have cerebral edema and swelling, referred to as cytotoxic edema. In approximately 10% of ischemic strokes, this edema can lead to elevated ICP, brain herniation, and death. Cytotoxic edema is more common in women and usually develops within 24 hours.

In 2008, stroke dropped from the third leading cause of death in the United States to the fourth leading cause. The reasons for this improvement are likely multifactorial, but aggressive initial evaluation, treatment, and management play an important role in patient survival. Neurosurgical and radiologic intervention and improvements in critical care management have benefited mortality and functional outcomes for patients with acute ischemic strokes.

The main priority in stabilizing these patients is to identify life-threatening diagnoses, such as brain herniation, status epilepticus, and obstructive hydrocephalus from edema, hemorrhagic conversion, and ongoing brain ischemia. Initial evaluation includes assessment of airway patency, adequate breathing, hemodynamic status, and seizure activity. The physical examination should focus initially on ruling out signs of impending herniation. Change in vital signs (Cushing triad—hypertension, bradycardia, and respiratory irregularity), nausea and vomiting, abnormal breathing (hyperventilation or hypoventilation, Cheyne-Stokes respiration, apnea), and arrhythmias can be indicative of increased ICP leading to brain herniation. Other signs of impending herniation include increasing lethargy, asymmetric pupils, contralateral or bilateral motor posturing, and lower extremity rigidity.

Once immediate life-threatening conditions are addressed, a complete neurologic examination should be performed. Anterior circulation strokes usually manifest with depressed mental status, gaze deviation, aphasia, visual field defects, and occasionally hemiparesis. Posterior circulation strokes also manifest with depressed mental status but are more likely to affect cranial nerves, pupil size and reaction, and brainstem reflexes.

The National Institutes of Health Stroke Scale (NIHSS) score is an evaluation tool that has a strong correlation with patient outcomes when performed on admission to the hospital. Repeated scores can be used to follow the patient's clinical status and to assess treatment effectiveness. The NIHSS comprises 11 evaluation items that are individually scored. Depending on the item, scores may range from 0–4, with a possible total score of 0–42. Scores <6 are associated with good recovery, whereas scores >16 are associated with patient death.

A noncontrast CT scan of the head should be performed immediately after initial neurologic examination. Although there is low sensitivity to detect brain ischemia in the first 24 hours, the main goal of the initial noncontrast CT scan is to rule out hemorrhage or other findings that would contraindicate the use of a thrombolytic. At a later date, CTA or MRA can be performed to assess the etiology and presence of collateral circulation. This imaging is particularly helpful if ongoing ischemia is suspected. Initial laboratory testing, including complete blood count, electrolytes, and coagulation profile, should be performed to prepare for possible interventional treatment.

Patients suspected to have seizure activity should have electroencephalography (EEG) monitoring. ICP monitoring (see Table 91-3) should be considered as well.

The primary treatment goal for acute ischemic stroke is revascularization; it is extremely important to obtain a timeline from the onset of symptoms during the initial assessment of the stroke patient. The American Heart Association (AHA) and American Stroke Association developed guidelines for the use of intravenous thrombolysis (e.g., tissue plasminogen activator). Indications for intravenous thrombolysis are onset of symptoms within 3 hours, measurable neurologic deficits, and age ≥18 years. Contraindications are primarily related to risk of bleeding (Box 91-4). Relative contraindications include recent major surgery in the past 14 days, gastrointestinal bleeding, myocardial infarction within 3 months,

**BOX 91-4 Contraindications to Intravenous Thrombolytic Therapy for Acute Ischemic Stroke**

**Diagnostic**
- Hemorrhage or multilobar infarction involving >33% of cerebral hemisphere on noncontrast CT scan of the brain

**History**
- History of stroke or head trauma within 3 months
- Previous intracranial bleed, intracranial mass, aneurysm, or arteriovenous malformation
- Recent intracranial or intraspinal surgery
- Arterial puncture at noncompressible site within 7 days

**Clinical Symptoms**
- Suggestive of SAH
- Persistent elevated blood pressure
  - Systolic >185 mm Hg
  - Diastolic >110 mm Hg
- Acute bleeding diathesis

**Laboratory Findings**
- Platelet count <100,000/mm$^3$
- Current anticoagulant use with INR >1.7 or PT >15 seconds
- Heparin use within 48 hours and elevated aPTT
- Current use of direct thrombin inhibitor or direct factor Xa inhibitor with evidence of anticoagulant effect on coagulation studies
- Hypoglycemia (glucose <50 mg/dL)

*aPTT*, Activated partial thromboplastin time; *INR*, international normalized ratio; *PT*, prothrombin time; *SAH*, subarachnoid hemorrhage.

and pregnancy. It is important to involve a neurologist to determine risks and benefits of treatment. If an intravenous thrombolytic is administered, the patient should be carefully monitored for signs of bleeding, including hemorrhagic conversion of an ischemic stroke. A repeat head CT scan is indicated for mental status changes, severe headache, hypertension that acutely worsens, nausea, or vomiting.

More recent literature suggests that patients who do not present within the 3-hour time window or have other contraindications to intravenous thrombolytic therapy can be treated with intraarterial thrombolysis in the interventional radiology suite. The timeline for intraarterial thrombolysis is within 6 hours for anterior circulation thrombosis or 24 hours for posterior circulation thrombosis. In medical centers where mechanical thrombectomy is possible, it should be performed within 8 hours.

Patients who receive intravenous thrombolytic or other interventional reperfusion therapy require close hemodynamic monitoring afterward. Reduction of blood pressure within the first 24 hours exacerbates clinical outcomes by decreasing cerebral perfusion in the acute setting. Blood pressures that limit intravenous thrombolytic therapy or interventional procedures are tolerated after treatment (i.e., systolic blood pressure 180–220 mm Hg or diastolic blood pressure 105–120 mm Hg). Labetalol or nicardipine can be used to treat escalating hypertension (i.e., blood pressures >180/105 mm Hg). In patients who do not receive intravenous thrombolytic therapy, permissive hypertension is allowed. However, blood pressure should be lowered if it is >220/120 mm Hg.

Continued evaluation is important to identify signs and symptoms of stroke progression that may require further interventions. Patients developing brainstem dysfunction with mental status changes require tracheal intubation and mechanical ventilation. Reassessment of neurologic status for signs of increasing ICP or cerebral edema is required. There is limited evidence that aggressive medical management of cerebral edema improves outcomes. However, medical management is required if it is a bridge to surgical intervention (i.e., decompressive hemicraniectomy). Hyperventilation should be used short-term only. Steroids have not been shown to be effective and are not recommended for cerebral edema secondary to ischemic stroke.

Prophylactic antiseizure treatment is not recommended for patients with acute ischemic stroke; however, the presence of seizures exacerbates cerebral edema. Patients suspected to have seizure activity should be treated and monitored with EEG.

Fever is clearly linked to worsening morbidity and mortality after ischemic stroke and should be treated. Although fever has been shown to exacerbate brain injury, there is no evidence to show that induced hypothermia improves outcomes. Other causes of fever should be investigated.

Hyperglycemia may worsen outcome after ischemic stroke. Dextrose-containing solutions should be avoided, and hyperglycemia should be treated with insulin. Insulin infusion may be necessary for improved glucose control. The guidelines from the AHA and American Society of Anesthesiologists recommend aggressive treatment for hyperglycemia to achieve serum glucose levels of 140–180 mg/dL.

Surgical intervention may be required for patients with large cerebellar or hemispheric strokes. Cerebellar strokes can lead to hydrocephalus and brainstem involvement. Hemispheric strokes may require surgical intervention to allow the swollen brain to expand outside the cranial vault, improving CPP. Reduced mortality rates were seen when surgical intervention occurred early (<24–48 hours) and in younger patients (<50–60 years old).

## 7. How common are seizures after head injury, and how are they treated?

Approximately 3% of adult patients in the ICU present with seizures during some portion of their ICU stay. Seizures represent hypersynchronous paroxysmal cortical discharges with motor, sensory, or cognitive dysfunction. There are many neurologic disturbances (e.g., posturing, myoclonic jerking) that manifest similarly to a seizure. However, these movements represent motor responses that are initiated from lower centers of the neuraxis. There is no element of cortical excitation.

There are multiple etiologies for seizures in the ICU setting (Box 91-5). Identifying the cause of the seizure is important to guide appropriate therapy and to prevent future episodes.

**BOX 91-5 Etiologies of Seizures**

- Drug toxicity
  - Antibiotics
  - Antidepressants
  - Local anesthetics
  - Cocaine
  - Amphetamine
  - Immunosuppressive agents
  - Antipsychotics
- Drug withdrawal
  - Barbiturates
  - Benzodiazepines
  - Opioids
  - Alcohol
  - Anticonvulsant noncompliance
- Infection
  - Febrile seizures
  - Sepsis
  - Meningitis
  - Encephalitis
  - Brain abscess
- Central nervous system
  - Head trauma
  - Brain tumor
  - Stroke
- Metabolic
  - Hyponatremia
  - Hypocalcemia
  - Hypermagnesemia
  - Hypophosphatemia
  - Hypoglycemia
- Anoxia
- Ischemia
- Organ failure
  - Renal
  - Hepatic

Status epilepticus (SE) is classified based on clinical criteria. In the ICU, the most common type is generalized convulsive SE. Generalized convulsive SE seizures are characterized by a loss of consciousness, generalized convulsions, and tonic and clonic phases. Nonconvulsive SE (i.e., loss of consciousness without generalized convulsions) is usually the consequence of partially treated generalized convulsive SE. Sometimes, very subtle low-amplitude clonic activity can be observed in some part of the body (most often face or hands). Nonconvulsive seizures may continue even after convulsive activity has stopped. It is often difficult to diagnose nonconvulsive SE. Any patient treated for generalized convulsive SE that does not awaken after 15–20 minutes should be assumed to be in nonconvulsive SE. These patients should receive therapy with EEG monitoring. Other types of seizures that occur in the ICU include simple partial or complex partial SE. Complex partial seizures manifest with an aura and can be followed by generalized tonic-clonic seizures.

The European Society of Intensive Care Medicine has published recommendations on the use of EEG monitoring in critically ill patients. Patients with generalized convulsive seizures do not need EEG monitoring because these seizures are diagnosed clinically. EEG monitoring is recommended for patients who do not wake up within 60 minutes after the administration of antiseizure medication because nonconvulsive seizures may be present. Patients with refractory seizures, which are usually nonconvulsive, should receive urgent EEG evaluation. Patients who underwent therapeutic hypothermia after cardiac arrest and remain comatose after rewarming should undergo EEG within 24 hours to rule out nonconvulsive seizures.

Treatment of seizures must be initiated quickly because recurrent seizures or SE results in sympathetic overdrive mediated by increased circulating catecholamines. This condition results in hyperthermia, acidosis, rhabdomyolysis, trauma, and cardiac arrhythmias. Loss of airway reflexes increase the risk of aspiration. Prolonged seizures can result in cerebral damage. Seizure treatment in the ICU involves elimination of current seizure activity and prevention of future episodes. The first-line therapy for current seizure activity is a benzodiazepine, a γ-aminobutyric acid A receptor agonist that rapidly inhibits signal transmission in the brain. Midazolam, lorazepam, and diazepam are efficacious. For intractable seizures, propofol or barbiturates may be used for greater control. When the seizure is controlled, prevention of future seizures consists of anticonvulsant therapy and treatment of the underlying cause if known. Monotherapy, if possible, is preferable to decrease drug interactions. Medications commonly administered for prevention of future seizures include phenytoin or fosphenytoin, carbamazepine, levetiracetam, and valproic acid. Phenytoin must be infused slowly because it is highly caustic to veins and can result in hypotension and cardiac arrhythmias. Fosphenytoin has greater water solubility allowing for faster infusion, but it too can cause hypotension and cardiac arrhythmias. Valproic acid does not cause sedation or hypotension. If seizures recur, initial treatment consists of a benzodiazepine followed by increasing serum concentrations of the maintenance anticonvulsant or adding a second agent. For drug-induced seizures, a benzodiazepine and barbiturate (e.g., phenobarbital, thiopental) provide better seizure control because phenytoin is not usually effective.

The most common side effect of anticonvulsants is sedation. Drug concentrations need to be monitored to avoid potential toxicity. Phenytoin requires free drug level testing because critically ill patients have altered serum albumin levels that increase the potential of phenytoin toxicity.

Prophylactic therapy for seizures should be considered in patients with hemorrhagic stroke or intracranial tumors. The guidelines for acute ischemic stroke do not support prophylactic anticonvulsant therapy because the risk of seizures is significantly lower. The evidence is lacking regarding prophylactic anticonvulsants in patients with moderate-to-severe head injury. However, there are strong data for the use of prophylactic anticonvulsants in patients after surgical evacuation of subdural hematomas.

## 8. What is encephalopathy, and how is it treated?

Encephalopathy is a broad term that encompasses many different organic and inorganic causes that lead to either

temporary or permanent changes in mental status and brain function. The National Institutes of Health defines encephalopathy as "any diffuse disease of the brain that alters brain function or structure." Coma is defined as a GCS score of <8 and is at the end of the continuum of deterioration of mental status in patients with encephalopathy. Although the list of possible causes of encephalopathy is exhaustive and outside the scope of this chapter, there are several important causes to consider that have an impact on evaluation and treatment of critically ill patients, especially in the neurocritical care setting.

Patients with TBI or other intracranial lesions often present to the emergency department with encephalopathy as their primary complaint. Altered mental status is the hallmark symptom of encephalopathy and is often the manifesting symptom for many subacute causes of TBI, such as elevated ICP, chronic subdural hematomas, and meningitis. Other symptoms include agitation, personality changes, decreased cognitive function, difficulty concentrating, lethargy, somnolence, loss of consciousness, seizures, and coma. Symptoms of encephalopathy can be subtle and easily missed leading to delayed diagnosis of not only TBI but also other medical and surgical illnesses; this is especially true in pediatric and elderly patients, in whom agitation, irritability, or disturbances in sleep-wake cycles may be the only symptoms.

Encephalopathy can manifest at any time during critical illness. In TBI, new-onset encephalopathy can be a sign of progression, change, or new disease. For instance, in the case of SAH, development of symptoms of encephalopathy on day 5 or later is likely a sign of symptomatic vasospasm that requires immediate attention and treatment. TBI-related encephalopathy could develop years after the inciting event. Late development of chronic traumatic encephalopathy is associated with contact sports such as American football and boxing. The cumulative damage to the brain becomes additive over time, resulting in permanent disability. Chronic hypoxia has also been shown to result in delayed-onset and late-onset encephalopathy.

In neurocritically ill patients, encephalopathy is not always related to the underlying neurologic disease; this can present a problem when evaluating the extent of neurologic disease, especially if encephalopathy manifests as coma or unresponsiveness secondary to TBI. The initial neurologic examination often is unrevealing or confounded by sedation, anesthesia, analgesia, alcohol, illicit drug use, or other metabolic derangements associated with critical illness. Conclusions about the extent of neurologic disease cannot be made until all other possible causes are treated or ruled out.

Critically ill patients can present with or develop a host of complicating factors that are known to cause encephalopathy. Box 91-6 lists important comorbid conditions that are known to cause encephalopathy. In the TBI setting, hypothermia, intoxication, hypovolemia, and hypoxia are likely to be present. If the injuries are severe enough to require surgery, anesthetics and muscle relaxation may complicate the presentation as well. Correction of comorbid conditions is of paramount importance before assessing the effects of brain trauma.

Diagnosis of encephalopathy requires a thorough history and physical examination. Knowledge of events surrounding the neurologic injury can provide important information regarding other possible conditions that may contribute to encephalopathy. For example, an elderly man found on his bathroom floor with a subdural hematoma may also have rhabdomyolysis, dehydration, hypovolemia, or renal failure. These comorbid conditions in isolation can cause encephalopathy without TBI. A full neurologic examination is also important to establish a baseline. Important diagnostic tests include complete blood count, complete metabolic panel, liver function tests, coagulation panel, arterial blood gases, lactic acid level, serum alcohol level, toxicology screen, creatinine kinase, ammonia level, and CT scan of the head.

**BOX 91-6 Causes of Encephalopathy**

Hypothermia
Hypoxia
Hypovolemia
Intoxication (alcohol, illicit drugs, and others)
Sepsis
Liver failure
Renal failure

Sepsis and septic shock are among the most common causes of encephalopathy in medical ICUs. Although the exact etiology is unknown, many factors have been implicated. Metastatic infectious microemboli and microhemorrhages have been noted on autopsy of patients who had septic encephalopathy. Various inflammatory mediators in sepsis (e.g., tumor necrosis factor, interleukin-6 or interleukin-8, platelet activating factor) have been suspected in the pathogenesis of encephalopathy. Hypotension, hypoxia, organ dysfunction leading to increased levels of toxic metabolites, and acidosis all have been considered in the pathogenesis of sepsis-induced encephalopathy.

Treatment starts with the initial survey and ensuring the patient is stable. Assessment of ABCs is done first. Tracheal intubation should be considered in obtunded patients, especially patients in a coma, or if the patient's condition is progressively getting worse. A patient in septic shock may require volume resuscitation and vasopressors. Once stabilization is accomplished, treatment for the specific cause of encephalopathy can be initiated.

Treatment is focused on treating the underlying cause of encephalopathy. Elevated ICP should be aggressively corrected. In the case of septic encephalopathy, management is based on the "Surviving Sepsis Campaign" guidelines. Symptomatic management with volume resuscitation, vasopressors, and antibiotics while treating the underlying infection or source of sepsis is the hallmark of sepsis therapy. Septic encephalopathy usually reverses as sepsis resolves. Encephalopathy associated with renal failure, liver failure, seizures, hypoxia, drug intoxication, or drug overdose is treated by correcting the underlying condition.

Iatrogenic causes of encephalopathy are important in the ICU. Sedation and analgesia used to manage intubated patients on mechanical ventilation are an important cause of encephalopathy. Not only can discontinuation of prolonged sedation lead to disorientation and confusion, but also withdrawal from the medications leading to encephalopathy is often overlooked, especially when

opioids, benzodiazepines, or both are abruptly stopped. Withdrawal is a common cause of delayed encephalopathy in patients treated with benzodiazepines for suspected alcohol withdrawal syndrome. Tacrolimus, an important drug in transplant patients, is associated with encephalopathy.

## 9. What is brain death, and how is it diagnosed?

The concept of brain death became applicable after the introduction of positive pressure mechanical ventilators in the 1950s. Before the advent of ventilators, death was determined by loss of respiration or circulation. However, with ventilators, physicians were able to keep patients "alive" despite irreversible destruction of the brain that would have previously led to termination of cardiorespiratory function. The first widely accepted criteria for diagnosing brain death, the Harvard Criteria, were published in 1968 in the *Journal of the American Medical Association*.

Only 1%–2% of all deaths per year in the United States are brain deaths. Brain death requires an irreversibly nonfunctional brain; however, the determination of brain death varies according to state law and hospital policies. In 1981, the Uniform Determination of Death Act was published by a presidential commission providing guidelines on the determination of brain death in the United States. The Act states that patients are dead if they have irreversible cessation of circulatory or respiratory functions or if they have irreversible cessation of all functions of the entire brain, including the brainstem. Although state laws and hospital policies may vary slightly, they all must follow the guidelines determined by the Uniform Determination of Death Act.

In 1995, the American Academy of Neurology (AAN) published practice parameters for establishing brain death in adult patients. The guidelines stress the need for determination of whole brain death and irreversible loss of function. According to an evidence-based guideline update by the AAN in 2010, there were no published reports of recovery of neurologic function after the clinical diagnosis of brain death had been established according to the 1995 AAN practice parameters.

The diagnosis of brain death needs to be made by a physician. Some hospitals require brain death testing to be done by a neurologist or neurosurgeon. Some states require that two physicians make the determination. Brain death usually follows some form of neurologic injury, of which trauma is the most frequent cause. Other etiologies include hypertensive hemorrhage, aneurysmal hemorrhage, brain tumors, and anoxic brain injury.

There is no evidence regarding how many examinations are required or what time period of observation is required before a declaration of brain death. There are four elements that are fundamental to all published brain death criteria based on the Uniform Determination of Death Act: (1) irreversibility, (2) absence of neurologic function, (3) apnea, and (4) additional confirmatory tests.

### *Irreversibility*

Irreversibility requires determination of the mechanism of injury to the brain and the anatomic findings to prove such injury. CT scan or MRI is useful to demonstrate damage to the brain. All reversible factors that could account for altered brain function, including hypothermia (temperature $<32.2$ °C), drug intoxication or poisoning, sedative drugs, neuromuscular blocking agents, severe electrolyte abnormalities, severe acid-base abnormalities, shock, and endocrine disorders, need to be corrected. In addition, the neurologic examination must not show improvement over time. There is no minimal amount of time a patient needs to be observed before declaring brain death.

### *Absence of Neurologic Function*

Total absence of functioning of the entire brain is a fundamental feature of brain death. All brainstem functions are absent. The pupils are fixed and unreactive to light. Ocular movements are absent to oculocephalic and oculovestibular reflex testing. Corneal, pharyngeal (gag), and tracheal reflexes are absent. The patient does not grimace or move in response to painful stimuli (unresponsive coma). The presence of spontaneous motor responses in the limbs secondary to spinal reflexes do not negate the diagnosis of brain death. However, decorticate or decerebrate posturing does negate the diagnosis of whole brain death.

### *Apnea*

Before performing the apnea test, the patient should be normotensive, normothermic, euvolemic, eucapnic, and not hypoxic. $PaCO_2$ must increase sufficiently (generally to at least 60 mm Hg) to stimulate spontaneous respirations. Patients with lung disease may not tolerate this period of apnea because of oxygen desaturation before achieving a high enough $PaCO_2$ to stimulate respirations. In patients with chronic obstructive pulmonary disease, a higher target $PaCO_2$ may be necessary to stimulate respirations. Generally, a good rule is to target a $PaCO_2$ 20 mm Hg higher than the patient's baseline. Hypoxia should be avoided during apnea testing because it may result in exacerbation of neurologic injury in patients who are not brain dead.

### *Additional Confirmatory Tests*

Confirmatory tests are not required for the diagnosis of brain death, which is a clinical diagnosis. However, in some European countries, confirmatory tests are mandatory. Their use is recommended when the clinical examination, including the apnea test, cannot be performed completely or reliably; if the cause of brain death has not been established; or if there is a questionable confounder mimicking brain death. These tests evaluate either cerebral function or intracranial blood flow. They each have limitations and should be used only in conjunction with other established criteria for brain death.

The most sensitive confirmatory test for brain death is cerebral angiography. A lack of intracerebral filling at the level of the carotid bifurcation or the circle of Willis supports the diagnosis of brain death. This test is rarely used because it is difficult to perform, requires administration of contrast medium, and is expensive.

EEG is also very helpful and is a more accessible test. Cerebral activity seen on EEG negates the diagnosis of brain death because it indicates some brain tissue is functional. The absence of EEG activity is defined as electrocerebral silence and is consistent with brain death. In 20% of cases, EEG is susceptible to interpretation error or is uninterpretable. "Noise" in the ICU from the multitude of machines creates artifacts that lead to false-negative results. False-positive results occur if the patient is sedated with drugs or is hypothermic.

TCD has been used to evaluate cerebral blood flow. Patients with brain death have absent flow or reversal of flow in diastole with sharp systolic upstroke or small spike waveforms either above or below the baseline at the beginning of systole.

Technetium-99m hexamethylpropyleneamine oxime brain scan can also be used as a confirmatory test. In brain death, there is no uptake of the isotope in the brain. There is a strong correlation between the results of this test and cerebral angiography.

The diagnosis in most patients with brain injury is persistent vegetative state rather than brain dead. The diagnosis of persistent vegetative state is made after the patient is in a vegetative state for >1 month after the inciting event. These patients have total loss of forebrain function with partially preserved brainstem function after an anoxic insult or TBI. These patients are not considered dead medically or legally.

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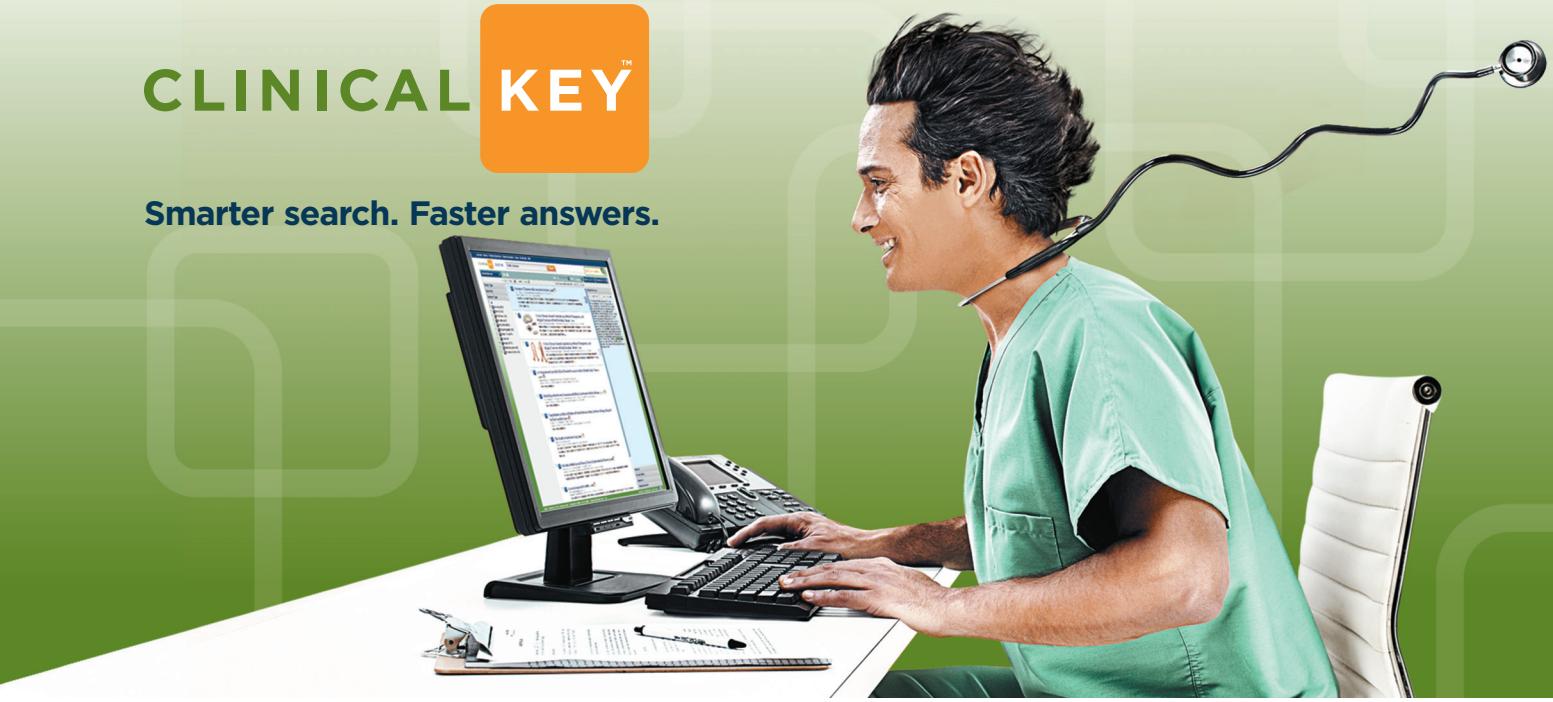

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